Original Investigation

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Effect of intraperitoneal cetuximab administration on colonic anastomosis and early postoperative adhesion formation in a rat model

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ABSTRACT

Objective: We aimed to evaluate the effect of intraperitoneal cetuximab administration on the healing of anastomosis and development of early adhesion formation in a rat model.

Materials and Methods: Twenty-four female rats were used. A colon segment was resected and end-to-end anastomosis was performed. The rats were randomized into three groups after the performance of colonic anastomosis and received 10 mL of intraperitoneal solution including study drugs after closure of abdominal cavity: normal saline was administered to the normal saline group (n=8), cetuximab (400 mg/m^2) was administered to the postoperative 1 group (n=8) 1 day after surgery, and cetuximab (400 mg/m^2) was administered to the peroperative group (n=8) during surgery.

Results: The mean adhesion grade was 2.63±0.92, and 0.50±0.76 and 0.63±0.74 for control and test groups, respectively. Cetuximab reduced adhesion formation in test groups ($p<0.05$). When all groups were compared, it was found that vascular endothelial growth factor levels decreased significantly only in the abdomen ($p<0.05$). Hydroxyproline levels and anastomosis bursting pressure were examined, and a statistical difference was found between groups (hydroxyproline $p<0.05$, bursting pressure $p<0.05$). However, when postoperative 1 day group was compared with the control group, it was found that there was no difference between groups according to these parameters ($p>0.05$), but when peroperative group was compared with the control group a significant decrease was observed in both parameters. Histopathological healing score was also evaluated. No statistical difference between groups was found.

Conclusion: Twenty-four hours later from the operation, intraperitoneal cetuximab therapy may be a safe and feasible treatment for metastatic colorectal patients.

Keywords: Intraperitoneal chemotherapy, cetuximab, anastomosis healing, adhesion formation

INTRODUCTION

Peritoneal spreading from colorectal cancer (CRC) is refractory to chemotherapy. In recent years, intraperitoneal (IP) chemotherapy (IPCT) developing as a new oncological treatment has been used for locoregional control and long-term survival (1). Immediate IPCT after surgical procedure for colon cancer exterminates cancer cells that may have been spreaded during resection. It prevents micrometastasis (2-4). This is an important factor determining the outcome of patients since the peritoneal surface may be the only site of metastatic disease (5, 6).

While IPCT improves the outcome of CRC patients it can disturb the healing of anastomosis. This impact increases the risk of anastomotic leakage. It may cause peritoneal spreading and thus can result in low-survival rates. Nevertheless, early postoperative adhesion formation is another issue in these patients, which can reduce the effect of IPCT. They may inhibit the distribution of the antineoplastic agents.

There are many questions requiring clarification on factors affecting anastomosis healing and development of early adhesion formation after IPCT, and there is a need to search for new drugs and application modalities to reduce these important complications. In the pertinent literature, there are a small number of studies investigating the effects of intraperitoneally administed new chemotherapeutic agents on anastomotic healing and on development of early adhesion formation (6, 7).

Cetuximab targets the epidermal growth factor receptor (EGFR) to inhibit its signaling and exhibits antitumour effects by binding to EGFR (8, 9). Its efficacy has been shown in the treatment of EGFR-positive metastatic CRC (mCRC) patients (10). It provides clinical benefit either when administered alone or in combination with other drugs in these patients (10, 11). Cetuximab has a merit to be used as a drug for IPCT. We think that it will be useful to evaluate cetuximab in an experimental study for its possible complications related to IPCT.

The main aim of this study was to asses the effect of IP cetuximab administration on the healing of anastomosis and development of early adhesion formation in a rat model.

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MATERIAL AND METHODS

Twenty-four mature female rats weighing 220 to 270 g. were used. All animals were placed in the laboratory 2 weeks before the study and they were kept under 12 h light/12 h dark conditions at standard temperature (22°C). They were fed laboratory food and tap water ad libitum. This study was performed in the Laboratory of Institute of Experimental Medicine (DETAE), Istanbul University, Istanbul, Turkey. Ethics committee approval was received for this study from the Ethics Committee of Istanbul University Experimental Medicine Research Institute. This study was performed according to the Helsinki Declaration.

Study Design

The rats were randomized into three groups after the performance of colonic anastomosis and received 10 mL of intraperitoneal solution including study drugs after closure of abdominal cavity: normal saline was administered to the normal saline group preoperatively (n=8), postoperative 1 day group (n=8), and peroperative group (n=8). The effect of administration of cetuximab (Erbitux®) (400 mg/m^2) intraperitoneally twenty-four hours after surgery (postoperative 1 group) and peroperatively (peroperative group) on the healing of anastomosis and development of early postoperative adhesion formation was assessed. Rats were sacrified on the seventh day after procedure, and then anastomoses and intraabdominal adhesions were examined. Blood, peritoneal fluid, and colonic tissue samples were collected.

Surgical Procedure

Ketamine and xylazine hydrochloride anesthesia (Ketalar; Eczacibasi and Rhompun, Abdi İbrahim, Istanbul, Turkey) was applied to all animals intramuscularly. Laparotomies were performed. The transverse colons were identified, then 1 cm of middle transverse colon was resected standardly, and end-to-end anastomoses were performed. Catheters were fixed through the abdominal wall, and the abdomens were closed continuously. Then, the test materials were given intraperitoneally via the catheter. Normal saline group (n=8) received normal saline, postoperative 1 group (n=8) received cetuximab (400 mg/m^2) 1 day after surgery, and peroperative group (n=8) received cetuximab (400 mg/m^2) during surgery.

Postoperative Period

The rats were awaken from anesthesia in a cage. Animals were monitored by the same surgeon for the days after surgery to control wound healing. Seven days after surgery, ketamine anesthesia was performed to rats, blood samples were obtained, and they were sacrified with high dose of anesthetic. The laparotomies were done. The peritoneal fluid cytologies were obtained. Several parameters were recorded including; integrity of the anastomosis, the existence of perianastomotic abscesses or peritonitis, and adhesion formation. Two independent supervisors evaluated the results depending on the scale of van der Ham et al. (12) as follows: 0, no adhesions; 1, minimal adhesions; 2, moderate adhesions; and 3, severe and extensive adhesions, including abscess formation.

Anastomosis Bursting Pressure

Following sacrification, a colon segment that included the anastomosis at the center and 2.5 cm of colon on each side was resected along with the adhesions. The colon segment was purified from feces and was ligated. A catheter connected to a sphygmomanometer was inserted into the distal bowel and the proximal site of the bowel was ligated. An isotonic (NaCl 0.09%) solution was infused at a rate of 1 mL/min. The bursting pressure (in mm-Hg) was measured when either saline leakage or gross rupture was observed.

Histopathology

Pathologic specimens of the colon were preserved in phosphate-buffered formalin (10%) and embedded in paraffin. Sections were stained with hematoxylin-eosin. Then, slides were evaluated with binocular optical microscope. All sections were examined by a practicing pathologist who is unaware of the tissue source. Mucosal and muscular continuity, reepithelialization, inflammatory reaction recruitment (polymorphonuclear leukocytes [PMN], macrophages, fibroblasts, and lymphocytes), and neovascularization were graded from 0 to 3 as follows: 1, absent; 2, moderate; and 3, dense. The total score was calculated for histological healing.

Hydroxyproline Tissue Levels

The anastomotic colon segment was frozen with liquid nitrogen and stored at −80°C for hydroxyproline measurements. Estimation of hydroxyproline tissue contents was based on alkaline hydrolysis of the tissue homogenate, and evaluation of free hydroxyproline in hydrolyzates was completed as described by Reddy and Enwemeka (13).

Immuno-histochemical Evaluation

All anastomotic segments were resected for pathologic evaluation at the 7th day and fixed in a 10% neutral formalin solution for 48 hours and then embedded in paraffin. Each section was immunohistochemically stained with VEGF. Phosphate-buffered solution (Sigma Chemical, St Louis, MO, USA) was used for washing all samples. Hydrogen peroxide block solution was used as the blocking solution (Lab Vision, California, USA). Then, VEGF antibody (Quartett, Berlin, Germany) was used for incubating the samples after washing three times with phosphate-buffered solution and a 60-minute incubation with secondary antibody. AEC chromogen (Lab Vision, Fremont, CA, USA) was used for staining the slides. Then, they were rinsed with water and counterstained with hematoxylin.

Statistical Analysis

Qualitative variables were presented as frequencies and percentages. Quantitative variables were summarized by using means with 95% confidence intervals and medians with ranges from minimum to maximum. Kruskal-Wallis test was chosen for comparing the differences among groups, with respect to non-normally distributed parameters, while Mann-Whitney U test was used for pairwise differences. Statistical Package for the Social Sciences 16 software (SPSS Inc; Chicago, IL, USA) was used for conducting the analyses. All reported P values were two-tailed with $p<0.05$ considered as statistically significant.

RESULTS

The study was completed with a total of 24 rats. No complications occurred in any rats. After sacrificing the rats, the anastomoses were detected to be intact without any evidence of dehiscence, leak, or IP fluid collection. Intraperitoneal fluid

sampling was performed for cytology. The presence and status of adhesions were recorded.

Table 1 presents the adhesion scores of the normal saline, postoperative day 1, and preoperative groups. Overall, a significant difference was detected among study groups with regard to adhesion score (p=0.001). Cetuximab used in the postoperative day 1 and peroperative groups significantly reduced the adhesion score as compared to the normal saline group (p=0.001). The effect of cetuximab used in the postoperative day 1 and peroperative groups was not significantly different with regard to adhesion score (p>0.05).

Table 2 shows VEGF levels in blood, IP fluid, and tissues of study groups. Overall, a significant difference was observed among the study groups with regard to intraperitoneal VEGF levels (p=0.004); however, there was no difference in the blood and tissue VEGF leves of the study groups (p>0.05). Cetuximab used in the postoperative day 1 and peroperative groups significantly reduced the intraperitoneal VEGF level as compared to the normal saline group (p=0.001). The effect of cetuximab used in the postoperative day 1 and peroperative groups was not significantly different in terms of intraperitoneal VEGF level (p>0.05).

Table 3 presents the hydroxyproline tissue level and anastomosis bursting pressure and healing score of the study groups. Overall, a significant difference was detected among the study groups with regard to these study parameters (p<0.05). Cetuximab used in the peroperative group significantly reduced the hydroxyproline tissue level and anastomosis bursting pressure as compared to the normal saline and postoperative day 1 groups (p=0.001). The effects of cetuximab used in the normal saline and postoperative day 1 groups were not significantly different with regard to hydroxyproline tissue level and anastomosis bursting pressure (p>0.05). Cetuximab used in the peroperative group significantly reduced the anastomosis healing score as compared to the normal saline group (p=0.001). The effect of cetuximab used in the postoperative day 1 and peroperative groups was not significantly different with regard to the anastomosis healing score (p>0.05).

DISCUSSION

Intraperitoneal cetuximab administered during operation and on postoperative day 1 reduced IP adhesions. Intraperitoneal cetuximab also reduced VEGF levels in the IP fluid but not in blood and tissue samples. Intraperitoneal cetuximab administered preoperatively reduced hydroxyproline tissue level as well as anastomosis bursting pressure; however, IP cetuximab administered on postoperative day 1 did not reduce hydroxyproline tissue level or anastomosis bursting pressure.

Cetuximab used peroperatively reduced the anastomosis healing score. The effect of cetuximab administered in two ways did not produce meaningfully different effects on the anastomosis healing score.

The results of this study indicated that although IP administration of cetuximab reduces adhesion formation it results in impairment of anastomotic healing when administered in the standard dose (400 mg/m^2) IP during the operation. However, time of administiration has significance, cetuximab can be administered IP without any additional risk to anastomotic leakage twenty-four hours after the operation.

Cancer that has spread to the peritoneal cavity is known as peritoneal carcinomatosis. It occurs in 10-15% of colorectal cancer patients (2). This situation was corporated with short survival (5, 14). A new treatment strategy combining cytoreductive surgery and IPCT has recently shown promising results. Clinical studies reported that these patients have prolonged survival rates (15-17).

Table 1. Adhesion scores of study groups

	Mean ± SD	Range	95% CI	Significance
Normal saline	2.63±0.92[a]	1-4	1.86-3.39	p=0.001
Postoperative day 1	0.50±0.76	0-2	0.13-1.13	
Peroperative	0.63±0.74	0-2	0.00-1.25	

Data were analyzed with Kruskal-Wallis ANOVA with Mann-Whitney U test for pairwise comparisons.
[a]p<0.05 vs. postoperative day 1 and peroperative groups. SD: standard deviation; CI: confidence interval.

Table 2. VEGF levels in blood samples, intraperitoneal fluid, and tissues of study groups

VEGF levels	Groups	Mean±SD (ng/dL)	Range	95% CI	Significance
Blood	Normal saline	56.1±19.9	39.4-72.7	33.2-89.3	
	Postoperative day 1	44.1±8.1	37.3-50.8	36.0-57.8	p=0.3
	Peroperative	37.5±8.0	30.8-44.1	28.8-53.6	
Intraperitoneal fluid	Normal saline	653.9±177.3[a]	505.7-802.1	479.4-955.6	
	Postoperative day 1	268.2±194.2	105.9-430.6	141.8-643.2	p=0.004
	Peroperative	380.3±253.1	168.7-591.8	150.2-748.2	
Tissue	Normal saline	560.7±128.3	453.4-667.9	402.8-754.8	
	Postoperative day 1	590.7±216.1	410.0-771.3	267.0-880.4	p=0.14
	Peroperative	429.9±135.1	317.0-542.9	305.8-687.4	

Data were analyzed with Kruskal-Wallis ANOVA with Mann-Whitney U test for pairwise comparisons.
[a]p<0.05 vs. postoperative day 1 and peroperative groups. VEGF: vascular endothelial growth factor; SD: standard deviation; CI: confidence interval.

Table 3. Hydroxyproline tissue level and anastomosis bursting pressure and healing score of study groups

	Groups	Mean±SD	Range	95% CI	Significance
Hydroxyproline (µg/mg)	Normal saline	94.1±27.3	71.3-117.0	47.1-139.4	
	Postoperative day 1	86.1±19.5	69.8-102.4	60.7-121.1	p=0.01
	Peroperative	55.68±23.8[a]	35.8-75.6	26.3-98.9	
Anastomosis bursting pressure (mm-Hg)	Normal saline	156.9±22.7	137.9-175.8	125.0-195.0	
	Postoperative day 1	157.5±27.0	134.9-180.1	115.0-195.0	p=0.001
	Peroperative	113.1±21.5[b]	95.1-131.1	85.0-150.0	
Anastomosis healing score	Normal saline	10.4±2.3	7-14	8.5-12.3	
	Postoperative day 1	9.5±2.4	7-15	8.6-12.6	p=0.04
	Peroperative	7.5±2.0c	4-12	5.3-9.2	

Data were analyzed with Kruskal-Wallis ANOVA with Mann-Whitney U test for pairwise comparisons.
[a,b]p<0.05 vs. normal saline and postoperative day 1 groups. [c]p<0.05 vs. normal saline group. SD: standard deviation; CI: confidence interval

One of the main advantage of IPC is better penetration of chemotherapeutic agents to the tumor nodules where the blood supply is poor (18). Intraperitoneal chemotherapy prevents micrometastases, local recurrence and distant metastases (2, 19). According to this data, IP administration of cytostatic drugs (5-fluorouracil, mitomycin C and oxaliplatin) were used in the postoperative period as an adjuvant therapy. However, there are other new chemotherapeutic agents that are still being investigated.

Cetuximab (Erbitux, Merck, Darmastadt, Germany) pointed out that patients with wild-type Kirsten rat sarcoma viral oncogene homolog (KRAS) colon tumors respond to anti-VEGF agents (20). Other studies verified the safety and efficacy of cetuximab treatment (21, 22).

Unfortunately, after colorectal surgery early postoperative adhesions are observed. The distribution of chemotherapeutic agents can be affected from such situations.

The IP adhesion-reducing effect of IP bevacizumab therapy has been demonstrated in our previous study (7). In this study, we observed that IP cetuximab application reduces early postoperative adhesions in both application types (peroperative and twenty-four hours after the operation). Arıtaş et al. (23) pointed out that there was a correlation between adhesion formation and VEGF expression. Similiarly, we observed that VEGF levels decreased in both application types.

Several surgical complications were reported in the literature. Anastomosis leakage was the most common complication in colorectal surgery. Reported rates of colonic anastomosis leakage vary between 8% and 20% after IPCT (24-26). Averbach et al. (27) pointed out that the incidence of anastomotic leakage after colorectal surgery was 6%. After additional treatment with heated peritoneal chemotherapy, this percentage increased to 20 percent.

CONCLUSION

This study shows that 24 hours after the operation, IP cetuximab therapy may be a secure additional treatment for metastatic colorectal patients. Considering this as a preliminary study, it may be suggested as a promising candidate for IPCT application. Its long-term effects and related problems should be examined prospectively.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of İstanbul University Experimental Medicine Research Institute.

Peer-review: Externally peer-reviewed.

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Original Investigation

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Recurrent pilonidal disease surgery: Is it second primary or reoperative surgery?

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ABSTRACT

Objective: Pilonidal sinus disease (PSD) effects mainly young men's social and work life with frequent recurrence rate. Reoperation for unimproved or recurrent disease is somehow troublesome. Surgeons may think that changing treatment strategy after recurrence may prevent further relapses of PSD. We analyzed patients with recurrent pilonidal sinus to determine their predisposing features for recurrence and the outcomes of the preferred surgical methods.

Material and Methods: From 2007 to 2012, out of 95 recurrent pilonidal sinus disease (rPSD) patients, 62 operated cases were included and examined retrospectively. Their retrospective data were examined for demographics, 1st and 2nd operation types, patient satisfaction and pain scores. For cases with insufficient preoperative or postoperative data, phone call and interviews were done to obtain data. Some were kindly invited to the outpatient examination. Student's t test, Mann-Whitney U test, and Kaplan Meier test for disease free survival time were used where appropriate. P values less than 0.05 were accepted to be statistically significant.

Results: Total of 62 rPSD patients were examined. Male:female ratio was 2.9:1. The mean age after 1st and 2nd operations were 24.7 and 28.1 years, respectively. One and five-year recurrence rates were 33.9% and 66.1%, respectively. The mean interval between the 1st and 2nd operations was 45.6 months. Excision and midline closure was the most frequent type of operation followed by flap reconstructions and excision-lay open procedures. The 1st operation types of rPSD cases were different from that of 2nd operations. Pain perception and satisfaction scores were better in flap reconstruction groups.

Conclusion: Reoperative surgery of rPSD is satisfactory with certain precautions. Relapses after flap reconstruction procedures with a well-being period should be referred as second primary disease. Changing surgical strategy is not always indicated as some patients with recurrence have relapsing or second primary disease that have distinct clinical course. Re-flap surgery after any kind of relapse is well appreciated.

Keywords: Recurrent, pilonidal, surgery, reoperation

INTRODUCTION

Pilonidal sinus disease (PSD) leads to serious social, economic and health care problems. Its prevalence is 1-4 per 25000 population, with a 40% five-year recurrence rate (1-3). Approximately 70% of PSD patients are between 20-30 years of age (4). Risk factors include obesity, smoking, poor hygiene, sedentary life style, African race, family history, and high amount of hair on the body. The recurrence rates for PSD after lay open and primary closure techniques are 17% and 30%, respectively (1). Primary closure techniques are divided into two main categories. The first category deploys the suture line lateral to the natal cleft while flattening it (such as Karydakis, Bascom, Rhomboid excision and Limberg flap reconstruction) whereas the second category leaves the suture line in the midline within the natal cleft. The latter technique results in significantly higher recurrence rates as compared to the former (7-40% and 0-3%, respectively) (5-7). Limberg technique seems to have the lowest wound related complication and recurrence rate (8-11). However, excision and primary midline suturing has been the most frequently used method with the highest postoperative complication and recurrence rates (12).

Since the longest time interval for recurrence has been reported as 22 years in the literature, five year follow up is recommended for determination of the true recurrence rate (2). Recurrence after one and five years are reported as 12-15% and 60-80%, respectively (1, 2).

Recurrent PSD (rPSD) is somehow more annoying than primary disease both for the patient and the surgeon. Surgeons have less willingness to deal with rPSD in contrast to primary disease. This may influence the surgical approach to the rPSD in practice. The idea of changing the type of surgery applied at the first intervention comes in mind for recurrent cases in order to avoid tertiary or further recurrences since the procedure chosen for the first operation is deemed as ineffective.

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MATERIAL AND METHODS

Patients admitted to surgery for rPSD between 2007 and 2012 were recruited to this retrospective study. A total of 95 rPSD cases were extracted from the registry. Fifteen patients could not be reached and five patients refused to participate. Sufficient data could be obtained in 75 cases. Age, sex, occupation, body mass index (BMI), operation satisfaction, smoking status, comorbidity, preoperative and postoperative status, type of operation for primary and secondary interventions and demographic data were recorded. If the data in patient files or computer based charts were not enough, patients were contacted by phone for a brief interview. Estimated intraoperative lesion dimension, early and late postoperative complications were extracted from operative notes and patient observation notes. We excluded three patients with three or more operations. Moreover, 10 patients who had been operated in different hospitals were excluded. Finally, the study group consisted of 62 rPSD cases with sufficient data.

Duration of symptoms before the operation (months), time to return to work (days), and the highest pain perception independent of the postoperative period were recorded. We developed a questionnaire to understand the overall satisfaction level of the patient in terms of social life and physiological status. Patients were asked to choose the best item that reflected their status after the 1st and 2nd operations, the answers are listed in Table 1.

Statistical Analysis

All statistical analysis was performed using Statistical Package for the Social Sciences software version 22 (SPSS Inc.; Chicago, IL, USA). For group comparisons, Student's *t* test was used for parametric data, while Mann-Whitney U test was used for nonparametric data. Chi-square test was used for comparing two categorical variables. Risk factors for complications and recurrence were evaluated by multivariate logistic regression analysis. Disease free survival time was estimated by using Kaplan-Meier method. P values less than 0.05 were considered to indicate statistical significance.

This study was carried on with respect to the principles of World Medical Association Declaration of Helsinki.

RESULTS

A total of 62 rPSD cases were evaluated via the hospital registry system. We realized that some crucial data such as BMI, occupation, smoking status, and lifestyle were not listed. We made phone calls to all cases to fill up the desired parameters for this study.

The mean age at the time of first and second operations were 24.7 (14-34) and 28.1 (19-39) years, respectively. Female/male ratio was 1:2.9 with 46 (74%) male and 16 (26%) female patients. Smoking prevalence was 39 (85%) in male and 7 (44%) in females. The status of the PSD lesion before the 1st operation was asked. If the relapses were clustered into years after the first operation; 21 (33.9%) recurred within the first year, 14 (22.6%) in the second year, 15 (24.2%) in the third year, 5 (8%) in the fourth year, and 7 (11.3%) in the fifth year. The interval between the onset of complaints and surgery before the 1st and 2nd operations were 4 (2-14) months and 8 (4-18) months, respectively. Mean interval between the operations was 26.5 (4-66) months. Data are listed in Table 2. There was a statistically significant difference between the intervals among the onset of symptoms and surgery before the 1st and 2nd operations (p=0.007). Mean hospitalization time was 3 (1-9) and 4 (1-9) days, respectively. Type of surgeries selected and mean pain scores are listed in Figure 1. The mean pain scores after the 1st and 2nd operations were not different but the mean pain scores for flap reconstruction surgeries after 1st or 2nd interventions were found to be lower in comparison to other types of surgeries (p=0.004). Operation dependent recurrence rate after the 1st intervention was significantly high for excision and primary midline closure surgery, followed by flap reconstructions and excision-lay open procedures The mean volume of the excised lesions at the first and second operations were 24 (12-108) cm^3 and 30 (18-144) cm^3, respectively. Unfortunately, pathologic examination reports of the specimens did not include surgical margin status, i.e. whether the sinus tract(s) were in continuation at the edges of the specimen or not.

Summary of the answers to the questionnaire is listed in Figure 1. If the increased frequency of first and second item answers are accepted as increased satisfaction, there is a statistically significant difference between the group of patients choosing first and second item answers in comparison to the

Table 1. Pain perception questionnaire

1. I was cured completely after the operation.
2. I still feel some problems at the disease site but I am better than the condition before the operation. I can continue my social life and work without limitations.
3. The operation was futile. Nothing has changed. I am the same as what I have been before the operation.
4. I am worse as compared to the time before the operation. My social and work life got worse. I am doubtful for one more operation.
5. I am in big trouble now. I wish I had refused the operation. My social and work life have strong limitations now.

Table 2. Patient characteristics

	After 1st operation	After 2nd operation
Age	24.7 (14-34)	28.1 (19-39)
Sex (Male:female)	46:16	
Smokers (Male:female)	39:7	
Body mass index	29.1 (22-34)	31.1 (24-38)
Duration of symptoms before the operation (months)	4 (2-12)	8 (4-18)
Excised lesion diameter (cm^3)	24 (12-108)	30 (18-144)
Length of hospital stay (days)	3 (1-9)	4 (1-9)
Time to return to work (days)	28 (14-35)	31 (13-44)

group choosing third, fourth, fifth item answers after the 1st and 2nd operations (p=0.024). This indicates that the surgeon can expect satisfactory results after the 2nd operation. For the same two groups described above, there was a statistically significant difference between the patients who underwent the same operation, regardless of the type of surgery, as 1st and 2nd time interventions and the patients who underwent different types of operations as 1st and 2nd line interventions (p=0.011).

Postoperative pain perception was asked to compare pain scores between 1st and 2nd operations by using the numeric pain scale from zero to 10, where zero refers to the weakest pain the patient ever felt lifelong or no pain at all while a score of 10 refers to the strongest pain he or she felt throughout their lives. Answers are listed in Table 3. The change of perceived pain between two operations were noted for each patient and for each kind of operation. Excision plus primary midline suturing and excision plus flap reconstruction were the most abundant types as 1st and 2nd operations, respectively. Even the distribution of the type of the operations differs significantly, average difference between the pain scores for each kind of operation types were statistically insignificant (Table 4). BMI at the first and second operations were 29.1 kg/cm^2 (22-34) and 31.1 kg/cm^2 (24-38), respectively. Comparison of the different types of operation at the 1st intervention revealed that patients who had undergone flap reconstruction at the 1st surgery would not undergo flap reconstruction surgery again as a 2nd intervention. This means that surgeons in our clinic hesitate to perform flap reconstruction again for a second time. On the other hand, patients who had undergone surgery by not using a flap at the 1st time, underwent this type of operations as a 2nd intervention (p=0.047, p=0.027 respectively) (Table 5). The interval between the 1st and 2nd operations and return to work were 28 (14-35) and 31 (13-44) days, respectively. There was no statistically significant difference in returning to work after 1st and 2nd operation.

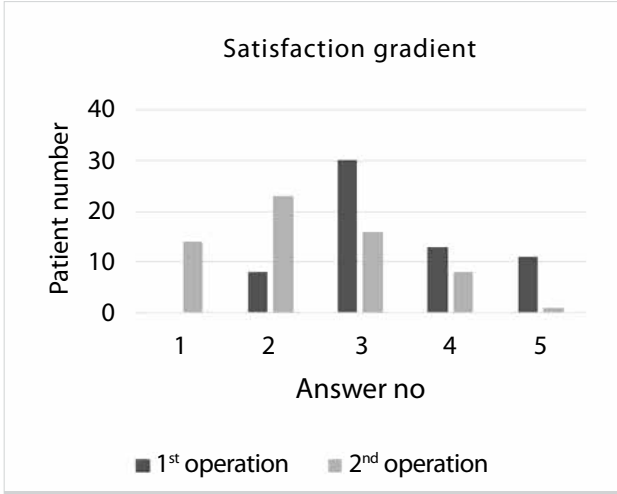

Figure 1. Satisfaction components

Table 3. Number of operations at 1st and 2nd intervention and mean pain scores

	Number of the operation and the mean pain score after 1st operation		Number of the operation and the mean pain score after 2nd operation		Net difference (%)
Type of operation	n	PS	n	PS	
Simple excision and lay open	0	0	3	6.1	NA
Excision and marsupialization	1	6.7	7	6.5	1.52% ↓
Excision and primary midline closure	43	7.3	14	7.9	3.94% ↑
Excision and flap reconstruction	18	4.5	38	5.1	6.25% ↑

n: Number; PS: Pain score; NA: not applicable

Table 4. The mean pain scores after 1st and 2nd operations

Pain score	After 1st operation		After 2nd operation	
	n	%	n	%
0	0	0	0	0
1	2	3.2	3	4.8
2	1	1.6	1	1.6
3	4	6.4	3	4.8
4	12	19.5	10	16.1
5	13	20.9	17	27.4
6	0	0	5	8
7	18	29	8	14
8	8	12.9	14	22.5
9	4	6.4	2	3.2
10	0	0	0	0
Mean	5.74		5.72	

DISCUSSION

Primary or rPSD mainly affect the young adult population. There is no consensus on the true incidence of the disease. Reported incidence rates are reported as 1/1000, 10-26/100 000 and 26-700/100 000 population in the literature (2, 3, 9, 13). The disease is more frequent in the male population with a male: female ratio of 4.1 to 8.1 (13). Based on these rates, it is estimated that countries in which working life is mainly supported by young males suffer more from PSD. Interestingly all the patients who denied participating in the study were females. This was somehow explained by Onder et al. (13), like any other anorectal disease, females refrain from getting help until the disease is unbearable or it results in marked limitation. This is somehow true for the male population as well. Patients with PSD have less willingness to apply to a surgeon for cure. This may be due to the location of the lesion which makes patients shy or unaware of their illness at the early stages of the disease. This leads to presentation of patients with PSD to the surgeon at an advanced state with problematic abscess, cellulitis, numerous draining sinuses etc. During the

Table 5. Swap numbers and operation change characteristics from 1st interventions to 2nd interventions

	Type of the operation at 2nd intervention			
Type of the operation at 1st intervention	**Simple excision and lay open (n=3)**	**Excision and marsupialization (n=7)**	**Excision and primary midline closure (n=14)**	**Excision and flap reconstruction (n=38)**
Simple excision and lay open (n=0)	0	0	0	0
Excision and marsupialization (n=1)	0	0	0	1
Excision and primary midline closure (n=43)	0	1	5	37
Excision and flap reconstruction (n=18)	3	6	9	0

n: Number

postoperative period, expecting the patient to clean the diseased site and to shave is somehow not proper since shaving the intergluteal region is difficult, and since patient relatives or friends may hesitate to help. This stands correct for the entire postoperative period. The surgeon should help the patient for shaving the diseased site since hairlessness and cleanness of the diseased site is always recommended postoperatively. Preventing hair growth by cosmetic materials or periodic shaving during the postoperative period may not be helpful in several cases. This brings up the theory of congenital natal cleft dimple instead of the acquired disease theory, which is supported with the presence of PSD in females having very few hairs on her body and in patients with irrelevant occupation with continuous relapses.

There are controversies in the literature about the best surgical technique in terms of postoperative complication and recurrence rate. A meta-analysis comparing open wound healing with primary closure showed that the recurrence risk was 58% lower in the open surgical technique (4% and 11.7%, respectively), probably due to reduced tension at the surgical site (14). If we divide primary closure techniques, recurrence rate is significantly higher in midline closure as compared to off midline closure techniques (1.4% and 10.3%, respectively) (14). Nevertheless, each PSD surgical or non-surgical management has opponents and supporters in the literature. Limited surgeries like sinus excision or unroofing and curettage have also been advised with low recurrence rate and early return to work (15, 16).

The time to "returning to work" is not as easy to estimate as we think as surgeons. Surgical recovery level is not the sole determinant to return to work for all patients. In other words, characteristics of their duty, their working environment, receptiveness of the boss to the patients' physical limitations etc. are also strong determinants for returning to work, and they may obscure or overpower the impact of the type of surgery. Surgical techniques that leave the diseased site open obviously lead to delayed returning to work. Patients with a suitable job or patients working in their own business are more likely to turn back to work earlier than the others.

Although the most commonly selected type of surgery in our study was excision and primary midline closure, the recurrence rate was significantly higher. Interestingly, once a recurrence was detected surgeons have shifted from this surgery to flap reconstruction methods for the 2nd intervention and vice versa. There seems to be a tendency to become more conservative for the 2nd intervention when the 1st intervention was aggressive such as flap reconstruction surgery. On the other hand, if the 1st intervention was conservative then the procedures were more aggressive in recurrent cases. Opting for limited surgical approaches after flap reconstructions were frequent in our study. The reason for this approach is probably the belief that repeated flap maneuvers are less promising. However, rhomboid or Karydakis flaps are favorable and convenient choices for rPSD as well (17, 18).

Pain scores after the 1st and 2nd operations did not differ significantly. Moreover, unexpectedly low pain scores may be detected in flap reconstructions since some patients experienced flap numbness in the postoperative period. This can be a matter of preference of flap reconstruction surgery for primary or rPSD.

The diameter and the number of the sinus tracts, volume of the excision material are also found to be important parameters for recurrence even if an R_0 resection was obtained (19, 20).

We did not compare the excision material volumes, the number and diameter of the sinus tracts with non-recurrent cases since recordings of these parameters were unreliable in our database.

Answers to our questionnaire clearly displayed the disease status after 2nd operation. The first item stands for complete cure after surgery, while the second stands for a disease which is cured but still creating ongoing discomfort, probably due to anatomic changes and sequel after two operations such as fibrosis. There may be a limited number of patients in this two answer groups who will probably present with PSD again in the future. Items three, four and five reflect an ineffective treatment. Patients with these answers are candidates for a third intervention in the future, and should be considered different from the patients with answers one and two. Patients with different operation types for 1st and 2nd interventions had more satisfaction than patients with the same operation in both in-

terventions. We speculate that any given type of surgery with unsatisfactory result should divert us to choose another type of surgery for the following operations. Since the interval between the onset of complaints and surgery before the 1st and 2nd operations were significantly different, this reflects that patients have much more reservation for a 2nd operation than the 1st one. Patients with rPSD take much longer than those with primary disease for the decision to apply for another operation.

The patients without a "well-being" period between the 1st and 2nd operations should be differentiated from others. We believe that they should not be called rPSD. Their surgery should be called as "re-operative surgery" since the primary disease was not cured at all. They should be referred as wound healing failure cases. Recurrent cases after excision and primary midline closure operation should be called as rPSD. Finally, rPSD after flap reconstruction surgeries and with a postoperative well-being period should be called as "second primary" disease. Namely we speculated to divide rPSD into three categories as 1: Relapsing PSD, 2: Recurrent PSD, and 3: Second primary PSD.

Although spending great effort, we could only reach two thirds of all rPSD cases. The data of non-contacted patients may change the results of our study. The fact that all cases who denied to participate were all female may augment this topic. The pain score registry was created a long time after the operation, which may have caused differences in pain perception than the actual peri-operative period.

CONCLUSION

Either primary or recurrent, PSD frequently effects young males and creates significant delay in returning to work in the population. The recurrence rate is very high, and predisposing factors should be taken into consideration as well as surgical approach preferences. Surgical excision and lay open technique for secondary healing seems to produce the best result in terms of recurrence rate. Repeated episodes of PSD are heterogeneous and somehow should be classified as relapsing, recurrent or second primary PSD. Favorable results can be achieved with flap reconstruction techniques for recurrent and second primary PSD. Relapsing PSD should be considered as management or follow-up failure since the patient never healed at all, and if reoperation is to be considered then the preferred surgery type should be changed.

Ethics Committee Approval: Authors declared that the research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects", (amended in October 2013).

Informed Consent: Written informed consent was not obtained since patients were interviewed with phone call without face to face conversation.

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Original Investigation

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Etiology of childhood burns and parental awareness in Turkey

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ABSTRACT

Objective: Burns continue to be a devastating trauma worldwide. Most of the childhood burns are due to preventable injuries. Burns occurring as a result of negligence of the parents'/carers' may cause mortality or life-long morbidities. Identification of the etiologies will direct the precautions that should be undertaken.

Material and Methods: One hundred consequent burn patients admitted to our clinics were included to the study. A questionnaire was filled in with the information gathered from the parents/carers.

Results: The mean age of the patients was 3.74±3.07 years, and 52% was male. Most of the injuries occurred in the noon (median 12:45). Seventy-eight percent of the burns occurred at children's own home. Parents/carers were close enough to prevent the child from injury in 66% of the cases. While there was no first intervention in 21% of burns, 14% applied ice and 1% yoghurt. Taxi was the means to reaching the hospital in 45%. Hot liquids were the leading etiology ($p<0.003$). Sixty-two percent of the patients were dining at the living room and on the floor.

Conclusion: The occurrence of the majority of injuries near parents/carers can be related to inadvertence or lack of awareness. To decrease burns incidence among children in our country, dining at the floor and stove heating should be avoided as much as possible. Not cooling the burn with running tap water at the time of injury leads to deepening of the burn, which consequently makes management more complex. Based on our study, there is an apparent need for determination of preventive measurements and to raise public awareness.

Keywords: Burn, child, awareness, etiology

INTRODUCTION

Burn is a trauma with high mortality rates and serious morbidity in children as much as in adults. In burn injuries, as in other diseases, age has a significant effect on both the etiology and treatment.

The first and most important issue in burn injuries is to prevent the burn. Protecting children from burns can be considered as the most important duty of parents and carers when the children are at an age when they have not completed their mental and physical development. Incidents of burns in children are associated with (a) the child's not having completed her/his development, (b) lack of care and concentration of the parents, and (c) curiosity of the child to burn agents. In Turkey, burns are often related to accidents during the traditional tea brewing technique and to production of dairy products in rural areas (1, 2).

In addition, 10% of child abuse is associated with burns (3-5). Therefore, it is necessary to approach burns in children carefully. For example, diapers protect the buttocks, hips and upper thighs of infants, so burns in those areas are rarely seen (6). When children present with burns in those areas, abuse in the form of placing the child in hot water as punishment must be kept in mind. In addition, the epidemiology and etiology of pediatric burns may vary according to regional, cultural and economic conditions. For example, in eastern Turkey, burns from tandoori ovens may be seen, whereas these types of burns are rarely seen in the western regions of the country.

Factors affecting mortality in childhood burns are age, burn surface area and the depth of the burn injury (7). The extent of the surface area of the burn has a greater effect in children than in adults, as anatomically the skin of a child is thinner than that of an adult. Therefore, exposure to the same severity of burn injury will cause a deeper burn in a child. In addition, the rule of '9' that is used in adults is not usually appropriate except for the adolescent age group. The Lund-Browder Scale is more suitable for children (8).

Pediatric burns require a multi-disciplinary approach. This team should include a trained burns specialist, a plastic and reconstructive surgeon, a physical therapy and rehabilitation specialist, and a pediatric infectious diseases specialist. In a study conducted in Taiwan, it was stated that burns reach a peak in two periods, one of which is the pediatric group aged <5 years (9). In another study, it was reported

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that pediatric burns occur especially in early childhood (10). A study in the USA placed burns as the 3rd most common cause of trauma-related childhood deaths (11).

Data obtained by a study on childhood burns would be useful in terms of determining the precautions to be taken to protect the children from burn injury as well as in establishing what parents or carers should do after a burn trauma until the hospital is reached. The actions taken immediately after a burn injury have a direct effect on treatment outcome. Appropriate early stage treatment will make management easier and can seriously reduce the high costs of treatment and rehabilitation. That is why this study was planned with the aim of shedding light on what should be done and the preventative steps to be taken by the target group, and determining the etiology of pediatric burns for which the treatment is difficult and the costs are extremely high.

MATERIAL AND METHODS

The study included 100 consecutive children aged 0-14 years who presented to the Ankara Numune Education and Research Hospital Burns Treatment Center. Children were excluded from the study if they spent most part of the day at a day-care center. Patients were enrolled if the parent or legal guardian willingly completed the prepared study forms in addition to the hospital records. The Burns Treatment Center has 9 beds for adult patients (6 intensive care beds and single or double rooms with intensive care features where they can be monitored) and 3 beds for pediatric burns. There is also a burns outpatient clinics serving to both adult and pediatric patients.

In this study, a datasheet containing the epidemiologic and demographic features of pediatric patients who presented to our clinic was filled-in. Using a prepared questionnaire, a record was also made of the medical and social events experienced in the process from the time of the incident until arriving to the hospital. The questions included in the questionnaire that was filled-in by the parents/care takers included insurance status, occupational status, time of the incident, place of the incident, place of the residence, first medical intervention applied, first medical facility attended and the preferred medication at the facility, patient transport, place of parents at the time of incidence, family population, heating type of the house, if the house was owned or rented, number of rooms in the house, socio-economical and socio-cultural level, and family's dining location.

RESULTS

The patients consisted of 52 (52%) males and 48 (48%) females. The mean age was 3.74 years (median 2.50; standart deviation 3,07 and range 1-14 years). The healthcare insurance status of the parents was found to be 54 (54%) Social Security Institution (governmental), 19 (19%) green card (governmental coverage), 6 (6%) Unaffiliated Companies Security Institution, 4 (4%) retirement fund, which are all part of the state national insurance scheme, and 17 (17%) had no form of health insurance. Ninety-five mothers were housewives (95%), and only 5 (5%) had an education level of university degree or above. Of the fathers, 12 (12%) were educated at the university degree level or above.

The place of residence was Ankara and surrounding towns in 80 (80%) cases and 20 (20%) came from other cities. When the time of the incidents was examined, the median time was 12:45 and the mean time was determined as 14:10 (Table 1). In 78 (78%) cases, the burn injury occurred in their own home and in 22 (22%) cases the burn occurred outside the home (Table 2).

Sixty-four (64%) parents made a first intervention with water, 14 (14%) with ice and 21 (21%) made no intervention (Table 3). After the incident, 27 (27%) presented directly at our clinic, 47 (47%) went to the university or a state hospital, and 26 (26%) presented at a first-stage or private healthcare center. In 80% of the patients who presented to medical centers a medical application was performed, and no medical application was applied in 20 (20%) cases. The most common medication used was silver sulfadiazine in 66 (66%) patients, followed by nitrofurazone cream in 12 (12%) patients. In 5 patients transferred to our hospital, no dresssing had been applied at the first centre, 2 patients came from private hospitals, 2 patients from a first-stage health care facility, and 1 patient from a state hospital.

Transport to the hospital was provided by the family car in 24 (24%) cases, by private taxi in 45 (45%) cases, and by ambulance in 7 (7%) cases. It was also determined that 10 (10%) patients had transportation by an inter-city bus (Table 3).

When the incident occurred, 66 (66%) of the parents were near their child and 34 (34%) were at a distance. The number of the children in the family were a single child in 26 (26%) cases, 2 children in 44 (44%) cases, and 3 children in 20 (20%) cases. While no burn injuries had been seen previously in any children of the family in 87 (87%) cases, there was a history of burns to the children in 13 (13%) families.

With respect to the family's residence, 41 (41%) were homeowners and 57 (57%) were rental houses, and 56 (56%) families lived in a townhouse and 44 (44%) were in an apartment block. The houses of 91 (91%) patients had 3 or fewer rooms, and 65 (65%) used a wood/coal-burning stove for heating. Taking the national socio-economic and sociocultural level into

Table 1. The time of injury

	Exact time of injury
Mean	14:10
Median	12:45
Standard Deviation	03:58
Earliest	08:00
Latest	23:45

Table 2. The location where the burn injury occurred

Place where burn injury occurred	n	%
Own house	78	78.0
Another house	12	12.0
Outdoor	9	9.0
Workplace	1	1.0

Table 3. The first interventions applied to the patient, the healthcare institution first consulted, means of transport and treatment applied

First interventions		n	%
	None	21	21.0
	Water	64	64.0
	Ice	14	14.0
	Yoghourt	1	1.0
Healthcare institution first consulted			
	Ankara Numune Hospital, Burns Center	27	27.0
	State hospital	44	44.0
	Private clinic	14	14.0
	State local healthcentre	12	12.0
	University hospital	3	3.0
Transport			
	Taxi	45	45.0
	Own car	24	24.0
	Inter-city bus	10	10.0
	Ambulance	7	7.0
	Minibus	7	7.0
	City bus	7	7.0
Dressing applied at the first medical centre			
	None	21	21.0
	Silver sulfadiazine	66	66.0
	Nitrofurazon	12	12.0
	Povidone-iodine	1	1.0

consideration, 56% of the families were seen to be living in substandard conditions. In 91% of these families, a crowded lifestyle was demonstrated with having only 1 or 2 rooms of living space. When the incident took place, the majority of parents were occupied with various forms of housework, 8 (8%) were dealing with another child, 9 (9%) were watching television, while 20 (20%) reported that they were with the child (Table 4). Table shows that 66% of the children were within controlling distance of the parent at the time of injury and that in fact 35% of the burn injuries occurred while the parent was engaged in an activity with the child.

It was reported that 67% of the families had their meals in the living room and 33% in the kitchen, and that 72 (72%) ate sitting on the floor while 28 (28%) preferred a dining table. When the mealtime habits of the families were examined, it was determined that 92.5% ate in the living room sitting on the floor. As can be seen from Table 5, only 5% of the patient population ate meals in a dining room and used a dining table.

The causes of the burns were determined as hot liquid (82%), flames (10%) and contact burns (6%). According to age groups, 63 (63%) patients were in the 0-3 years age group and

Table 4. Location and activity of the parent/carer at the time of Injury-Cross-tabulation

	Location of the parent/carer		
Activity of the parent/carer at the time of the injury	**Close**	**Far**	**Total**
With the child	20	0	20
Watching television	9	0	9
With other children	3	5	8
Busy with housework	14	15	29
Cooking	5	10	15
At the neighbour's	0	4	4
Eating a meal	13	0	13
In the bathroom	1	0	1
Serving tea	1	0	1
Total	66	34	100

37 (37%) were aged over 3 years. In the 0-3 year age group, the most common burn agent was hot liquid in 54 (54%) cases. In the group aged over 3 years, the agents were hot liquid in 29 (29%) patients, flames in 8 (8%) and no contact burns (Table 6).

Consistent with the literature, hot liquid burns was the most common agent, being the cause in 84% of the whole patient group. In the patient group aged over 3 years, the leading burn agent was hot liquids in 78.3%, followed by flammable materials in 21.7%.

DISCUSSION

Parallel with the literature, the frequency of male patients was higher within the pediatric study group (12).

The fact that only 4% of the parents were eligible for retirement from a qualified healthcare insurance supported previous reports in the literature stating that burn injuries occur more in families with a low socio-economic and education level (13, 14). Although various insurance institutions in Turkey have now been combined under the umbrella of the Social Security Institution, it was important to make this separate grouping to show how many parents had worked in a position that qualified for insurance coverage.

The time of the incident often followed lunchtime, when the mother (95% of the mothers in this study were housewives) was clearing away the meal, when she was preparing for the evening meal planned for after the father's returning from work, or when other children were returning from school and she was busy with preparations and thus was distracted and paying less attention to the child.

In a 2003 study by the same authors, the rate of presentation to the clinic from outside the region was reported as 36.2% (15). The reduction of this rate to 20% is thought to be due to new burn units that became active in the intervening period, both in our region and in Turkey in general. This has been a positive

Table 5. The place and manner of mealtimes

			Manner of eating meals		
			Floor	Table	Total
Place where meals are eaten	Living room	Number	62	5	67
		% within place where meals are eaten	92.5%	7.5%	100.0%
	Kitchen	Number	10	23	33
		% within place where meals are eaten	30.3%	69.7%	100.0%
Total		Number	72	28	100
		% within place where meals are eaten	72,0%	28.0%	100.0%

p<0.001

Table 6. Burn agents according to age groups

		Age groups		
		0-3 years	>3 years	Total
Burn agents	Liquid	55 (87.3%)	29 (78.3%)	84
	Contact	6 (9.5%)	0	6
	Flammable material	2 (3.2%)	8 (21.7%)	10
Total		63	37	100

p<0.003

development that reduced unnecessary patient transport and increased chances of treatment in patient's area of residence.

It is noticeable that 64% of patients were treated in the early stage with cooling water, which is the correct application. However, 14% of the patients had ice application for cooling as the first invention. Cooling with ice causes a worse outcome by adding the trauma of the cold on top of heat trauma (16). In addition, 21% of the patients were found to have had no treatment applied. A total of 36% of the patients did not have the correct procedure as a first intervention. When a burn incident has unavoidably occurred despite preventative measures, it must be strongly emphasized that after taking the etiological factors into account, the first stage should be to cool the burn area under running tap water.

Transport of the patients to a clinic by ambulance or other vehicles is acceptable depending on the severity of the burn injury. However, the overall situation of not being able to treat a patient in their own residential area and requiring a bus journey between cities is a subject that requires attention. According to the Inpatient Healthcare Burns Units Foundation and Action Directive, a 'Burns Room' was established in all inpatient treatment centres as a mandatory requirement to provide treatment in the area of residence for all minor burns patients with indications for hospitalization (17).

Thus, it is necessary to prevent these patients with minor burns travelling to other regions by bus. In this context, attention should be directed at the necessity of education on the subject of burns treatment at graduate and postgraduate level as well as directed to those who quit school earlier. By travelling outside their own region, this group of patients have experienced economical, physical and psychological trauma, created an increased workload at the reference centre, and removed themselves from the labour force for that period.

The fact that 13% of the patients were the second burn case within the same family indicates that the family is careless to precautions against fire. Child abuse should also be taken into consideration in these families with repeated burn injuries. There is a need for nationwide studies to inform and create awareness on both of these topics.

It has been previously reported that crowded living conditions and heating with stoves play a role in the etiology of burns (18). Similarly, in this study, the crowded nature of the family living condition is a factor facilitating exposure of the child to burns as well as related distractions. The stove, which is used for heating is located in the centre of the living area, has been suggested as one of the leading factors in burns in children who have not yet completed their physical and mental development.

In this situation, in the sense of protecting children from burns, it can be thought that either parents are not aware of preventative measures or the families are careless due to repeated burn injuries within the same family. There is an urgent need for educational programs to correct this. Awareness can be raised in families on anticipated negligence and what needs to be done, thus overcoming the problems and preventing these burns.

Evaluation of mealtime habits of the families (Table 5) shows that improper ways of eating can make it easier for a child to be in contact with hot pans or teapots. In the same way, there is an increased likelihood of uncontrolled spillage of hot liquids or food by running into another person. These events can be interpreted as a reflection of the socio-cultural level of the family, as depicted by table . Taking this factor into consideration in the etiology of burns injuries, informing families about eating in the living room and more importantly at a table emerges as a requirement.

In the patient group aged over 3 years, it is more significant that rather than the reduction in contact and hot liquid burns,

an increase is seen in burns from flammable materials. At this age children are mobile and are curious about their surrounding environments, and if they can touch and reach everything that attract their attention, this may result in exposure to burn injuries. In this sense, the preventive programs to be applied should emphasize that the families must be warned of the potential dangers that are encountered along with the physiological and mental development of children. Parents and carers must be warned and made aware of requirements to prevent children of this age group, with increased movement ability and an awareness of their surroundings, from reaching combustible agents.

CONCLUSION

The etiology of burn injuries may differ according to the sociocultural and socio-economic status of each country. The results of this and similar previous studies conducted in Turkey have shown that crowded living conditions, the heating systems used, and the traditional custom of eating meals sitting on the floor are significant etiologic factors in pediatric burn injuries. Therefore, the planning of collaborative programs by public and private civil organizations and clinicians who provide the treatment for burns to change these habits and customs would be of great importance in reducing the incidence of burns, which are known to be one of the most serious traumas.

Ethics Committee Approval: The study only includes the etiology of burns and do not include any sort of treatment. Also, all the parameters were gathered via past history of the injury. For this reason, an ethical committee approval was not obtained for this study.

Peer-review: Externally peer-reviewed.

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Local bupivacaine for postoperative pain management in thyroidectomized patients: A prospective and controlled clinical study

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ABSTRACT

Objective: We aimed to evaluate the effect of bupivacaine and to compare the routes of administration of bupivacaine in the management of postoperative incision site pain after thyroidectomy.

Material and Methods: Consecutive patients who were planned for thyroidectomy surgery were randomized into three groups of 30 patients each: Group 1 (control group): standard thyroidectomy surgery without additional intervention; Group 2 (paratracheal infiltration with bupivacaine): following thyroidectomy, 0.25% bupivacaine was applied on the surgical area; Group 3 (subcutaneous infiltration with bupivacaine): following thyroidectomy, 0.25% bupivacaine was injected into the cutaneous, subcutaneous region and fascia of the surgical area. Postoperative pain was evaluated by a visual analog scale (VAS) at 1st, 4th, and 12th hours after thyroidectomy. Total daily requirement for additional analgesia was recorded.

Results: The mean age of 90 patients was 44.37±13.42 years, and the female:male ratio was 62:28. There was no difference between study groups in terms of age, thyroid volume, TSH and T4 levels. VAS score of patients in paratracheal infiltration with bupivacaine group was significantly lower than control group patients at 1st, 4th and 12th hours following thyroidectomy (p=0.030, p=0.033, p=0.039, respectively). The need for analgesics was significantly lower in both paratracheal infiltration and subcutaneous infiltration groups than the control group (86.7%, 83.0%, and 73.3%, respectively, p=0.049).

Conclusions: Intraoperative local bupivacaine application is effective in decreasing postoperative pain in patients with thyroidectomy.

Keywords: Bupivacaine, postoperative pain, thyroidectomy

INTRODUCTION

Pain in the incision site is a common complaint among patients who undergo thyroidectomy, a widely applied procedure in endocrine surgery (1-3). The postoperative pain following thyroidectomy is due to extensive tissue dissection and tension during the operation (4). Many patients with thyroidectomy suffer from incision site pain especially in the first days after surgery, which delays early discharge and causes a significant burden on both patients and healthcare teams (5-8).

Pain following thyroidectomy is commonly managed with nonsteroidal anti-inflammatory drugs (NSAIDs) or opioid analgesics (9, 10). However, NSAIDs have been reported to be associated with potential adverse events including cardiovascular events, surgical bleeding and renal impairment (11). Opioid analgesics also have side effects such as nausea and vomiting (12).

Local anesthetics have been used in surgery for a long time to reduce postoperative pain and the need for analgesics (13). The use of local anesthetics particularly in abdominal and hernia surgery has been known to effectively decrease postoperative pain (14, 15). For this purpose, long-acting local anesthetics are preferred more frequently.

Bupivacaine is a long-acting local anesthetic that effectively reduces postoperative pain (16). In practice, bupivacaine is used for infiltration anesthesia, nerve blocks, epidural, and caudal anesthesia (17). It has a more selective effect on sensory nerve fibers as compared to motor nerve fibers, therefore is preferred for epidural anesthesia in obstetrics (18). However, there are limited studies on the use of local anesthetics in neck surgery. Bupivacaine has been used for preoperative wound infiltration (19), and intraoperative bilateral superficial cervical plexus block in thyroidectomy to prevent postoperative pain (20, 21). However, there is ongoing debate on the effectiveness and the route of application of bupivacaine to control pain following thyroidectomy (17, 19, 20, 22, 23).

Based on the current knowledge, in this study, we aimed to evaluate the effect of bupivacaine and to compare the routes of administration of bupivacaine in the management of postoperative incision site pain after thyroidectomy.

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MATERIAL AND METHODS

Patients and Study Design

This was a prospective, three-arm, controlled study performed in Atatürk Training and Research Hospital Department of General Surgery. The study was approved by the Institutional Ethics Committee of the Hospital for Clinical Studies (date, 19/02/2014; no, 21). The study was conducted in accordance with Helsinki Declaration, and written informed consent was obtained from all patients before participation.

Patients who were planned for a total thyroidectomy between February 2013 and October 2013 were randomized into three groups of 30 patients each. Patients who did not want to participate in the study, had undergone previous thyroid surgery, or had undergone thyroid resection in combination with neck dissection were excluded.

Study groups were as follows: Group 1 (control group): standard thyroidectomy surgery following standard anesthesia protocol without additional intervention; Group 2 (paratracheal infiltration): following standard thyroidectomy surgery, Surgicel® (Johnson and Johnson Medical, Arlington, TX, USA) impregnated with 10 mg (4 mL) 0.25% bupivacaine (Marcain 0.5%, 20 mL/flakon, Eczacıbaşı, İstanbul, Turkey) diluted with equal rate of saline was applied on the frontal aspect of the trachea in a way that it expands 1 cm laterally on each side on the surgical area; Group 3 (subcutaneous infiltration): following standard thyroidectomy surgery, local infiltration of the wound was performed by the surgeon at the end of surgery just before wound closure. A 23-gauge needle was inserted along the incision line and 10 mg of 0.25% bupivacaine was applied into the anterior group cervical muscles and subcutaneous tissue in both flaps (top and bottom).

Operation Technique

A 4–7 cm skin incision (depending on the size of the thyroid) was made. Sub-platysmal flaps were elevated, the strap muscles were separated in the midline and reflected laterally. In none of the patients the strap muscle was transected. The inferior, middle, and superior thyroid vessels were then divided. The same steps were repeated for removal of the contralateral lobe. Finally, the wound was irrigated and closed using interrupted 3-0 polyglactin sutures (Vycril, Ethicon) to approximate the strap muscles and the platysmal layer. The skin was closed subcutaneously. Suction drains were routinely used in all patients. Suction drains were removed at the first postoperative day, and no hematomas or seromas were observed in any patients.

Assessment of Postoperative Pain

Postoperative pain of the patients was evaluated by a visual analog scale (VAS) at 1, 4, and 12 hours after thyroidectomy by an investigator blinded to study groups. VAS is scored on a scale of 0 to 10 (0=no pain, 10=worst pain imaginable). For patients with a VAS score over 5, additional analgesia was provided with intramuscular 75 mg/amp diclofenac sodium. The total daily requirement for additional analgesia was recorded.

Calculation of Thyroid Gland Volume

Ellipsoid formula with correction factor, which is the most commonly used two-dimensional ultrasonographic mathematical method to estimate thyroid gland volume was used for calculation (24-26). This formula refers to width ´ depth ´ length ´ 0.524 for each lobe. For this calculation, both thyroid lobes were scanned with ultrasonography (Sonoline Ultrasonography Equipment, Siemens, Munich, Germany) individually in the transverse and longitudinal planes. Estimated error rate of this formula is approximately 15%.

Statistical Analysis

Study data were summarized using descriptive statistics (e.g., mean, median, standard deviation, range, frequency, percentage). Kolmogorov-Smirnov test was used to test whether continuous variables were distributed normally or not. Data of the three study groups were compared with analysis of variance (ANOVA) test, and secondary comparisons between two groups were performed with post-hoc Tukey test. For the comparison of data at different time points, repeated measured ANOVA test was applied. For comparison of categorical variables, chi-square and Fisher's exact tests were used. Statistical analysis was performed using Statistical Package for the Social Sciences version 16.0 (SPSS Inc; Chicago, IL, USA). Statistical significance was set to $p<0.05$.

RESULTS

Clinical and Demographic Characteristics of Study Patients

The mean age of 90 patients included in the study was 44.37±13.42 years (range 18-67 years), and the female:male ratio was 62:28 (females, 68.9%; males, 31.1%). The indication for thyroidectomy was a significantly large nodule (n=26, 28.9%), toxic goiter (n=20, 22.2%), malignancy (n=14, 15.6%), suspicion of malignancy (n=8, 8.9%), atypia of undetermined significance (n=8, 8.9%), insufficient thyroid fine needle aspiration biopsy (n=6, 6.7%), follicular lesion of undetermined significance (n=4, 4.4%), and difficulty in swallowing (n=4, 4.4%).

The mean thyroid volume calculated by the ellipsoid volume formula was 37.16±23.59 cm^3. There was no difference between study groups in terms of age, thyroid volume, TSH and T4 levels ($p>0.05$). T3 level was significantly lower in the control group than subcutaneous bupivacaine infiltration group ($p=0.006$) (Table 1). Considering TSH, T4 and T3 levels together, study groups were not different in terms of hyperthyroidism that may interfere with the duration of surgery, amount of intraoperative bleeding, and postoperative pain by increasing vascularization in the surgical area. In each group one patient developed transient hypocalcemia, no additional complication was observed.

VAS Score

VAS score of all study patients decreased significantly after the thyroidectomy operation at all time points ($p<0.001$ for all groups) (Table 2). VAS score of patients in the paratracheal infiltration with bupivacaine was significantly lower than control group patients at 1, 4, and 12 hours following the thyroidectomy operation ($p=0.030$, $p=0.033$, $p=0.039$, respectively) (Table 2).

Analgesic Requirement

Of all study patients (n=90), 72 (66.7%) required analgesics in addition to bupivacaine application. The need for analgesics was significantly lower in both the paratracheal infiltration and subcutaneous infiltration groups as compared to the control group (86.7%, 83.0%, and 73.3%, respectively, $p=0.049$) (Table 3).

DISCUSSION

The elimination or reduction of postoperative pain following thyroidectomy enhances patients' quality of life and allows patients to quickly return to normal daily activities. For the management of postoperative pain following throidectomy, NSAIDs and/or opioid analgesics are used commonly in practice. To decrease the postoperative pain and reduce the need for analgesics following thyroidectomy surgery, preoperative oral controlled-release analgesia with opioids and alternative regional techniques such as incisional local anesthesia, intraoperative bilateral superficial and/or deep cervical plexus block, local wound infiltration with local analgesia have also been suggested recently (20, 21, 23, 27-29). Performing thyroidectomy under local or regional anesthesia rather than general anesthesia has also been suggested to control postoperative pain (30).

In the present study, we evaluated whether bupivacaine is effective in postoperative pain control in thyroidectomy surgery, and compared the two administration ways of bupivacaine: paratracheal infiltration and subcutaneous infiltration. Bupivacaine is a local anesthetic with minimum effect on motor nerve conduction (16). Since postoperative pain following thyroid surgery is related to increased excitability of the dorsal horn neurons, blocking superficial branches of the cervical plexus was proposed in order to prevent postoperative pain. Local injection of bupivacaine may provide blockage of superficial branches of the cervical plexus. Bilateral superficial cervical plexus block with bupivacaine has been shown to significantly reduce pain intensity in the postoperative period after thyroid surgery, but did not provide optimal pain relief alone (31). We found that paratracheal infiltration with bupivacaine is effective in decreasing postoperative pain as assessed by VAS score. On the other hand, the need for analgesia with diclofenac sodium, an NSAID, was lowest in subcutaneous infiltration with bupivacaine group. In previous studies on the effect of bupivacaine on the control of postoperative pain, various dose intervals and routes were implemented with conflicting results. Sardar et al. (23) applied bilateral superficial cervical plexus block with 0.25% bupivacaine intraoperatively to decrease pain after thyroid surgery, but did not find decrease in postoperative analgesic requirement. In a prospective controlled study, Ayman et al. (19) compared preoperative incision site infiltration of bupivacaine 0.5% and ropivacaine 0.75% to decrease postoperative pain in total thyroidectomy, and concluded that wound infiltration with local analgesia

Table 1. Clinical and demographic characteristics of study patients

	Total (n=90)	Control (n=30)	Paratracheal infiltration of bupivacaine (n=30)	Subcutaneous infiltration of bupivacaine (n=30)	p
Age	44.37±13.42	47.1±12.79	45.37±13.88	44.38±13.43	0.159
Thyroid volume (cm^3)	37.16±23.59	30.07±17.61	40.71±24.61	37.17±23.6	0.130
TSH (U/mL)	1.03±1.00	1.2±1.1	0.74±0.66	1.04±1.01	0.137
T3 (pg/mL)	3.50±1.87	2.74±0.64	3.59±2.05	3.51±1.88	0.009[a]
T4 (ng/dL)	2.15±5.31	1.44±0.88	1.45±0.65	2.16±5.32	0.197

TSH: Thyroid stimulating hormone; T3: triiodothyronine; T4: thyroxine
[a]p=0.163 for Control vs. paratracheal infiltration; p=0.006 for Control vs. subcutaneous infiltration; p=0.400 for Paratracheal infiltration vs. subcutaneous infiltration groups.

Table 2. VAS scores (mean±standard deviation) of study groups at 1, 4, and 12 hours after the thyroidectomy operation

VAS scoring time	Control (n=30)	Paratracheal infiltration of bupivacaine (n=30)	Subcutaneous infiltration of bupivacaine (n=30)	p
1st hour	6.64±1.76	5.37±2.42	5.4±1.36	0.026[a]
4th hour	4.14±2.12	2.93±1.60	3.33±1.71	0.038[b]
12th hour	1.94±0.95	1.6±0.9	1.78±0.63	0.048[c]
p	0.001	0.001	0.001	

VAS Score: Visual Analog Scale Score
[a]p=0.030 for Control vs. paratracheal infiltration; p=0.882 for Control vs. subcutaneous infiltration; p=0.092 for Paratracheal infiltration vs. subcutaneous infiltration groups.
[b]p=0.033 for Control vs. paratracheal infiltration; p=0.210 for Control vs. subcutaneous infiltration; p=0.672 for Paratracheal infiltration vs. subcutaneous infiltration groups.
[c]p=0.039 for Control vs. paratracheal infiltration; p=0.272 for Control vs. subcutaneous infiltration; p=0.622 for paratracheal infiltration vs. subcutaneous infiltration.

Table 3. Patients who required analgesia in study groups

	Control (n=30)	Paratracheal infiltration of bupivacaine (n=30)	Subcutaneous infiltration of bupivacaine (n=30)	p
Requirement for analgesics	26 (86.7%)	25 (83.0%)	20 (73.3%)	0.049[a]
No requirement for analgesics	4 (13.3%)	5 (17.0%)	10 (26.7%)	

[a]p=0.037 for Control vs. paratracheal infiltration; p=0.020 for Control vs. subcutaneous infiltration; p=0.0791 for paratracheal infiltration vs. subcutaneous infiltration groups.

had limited efficacy in decreasing postoperative pain in the short period up to 4 hours after surgery, and ropivacaine was more effective than bupivacaine in this manner. In contrast, Herbland et al. (32) found that bilateral superficial cervical plexus block with ropivacaine did not prevent postoperative pain after total thyroidectomy. However, Karthikeyan et al. (20) reported that intraoperative bilateral superficial cervical plexus block with bupivacaine was effective in reducing postoperative pain and analgesic requirements in thyroidectomy. In a study comparing preoperative oral controlled release morphine, postoperative sublingual buprenorphine and intraoperative wound infiltration with 0.25% bupivacaine, sublingual buprenorphine was found to provide better analgesia after thyroidectomy than the other interventions (22). Gozal et al. (27) reported that bupivacaine 0.5% wound infiltration at the end of surgery reduced postoperative pain and opioid demand. In a recent study by Ryu et al. (33), spraying 0.25% levobupivacaine on the dissection area after robotic thyroidectomy reduced postoperative pain and patient-controlled analgesia consumption without adverse events. We determined that VAS score of patients with paratracheal infiltration of bupivacaine was significantly lower at 1, 4 and 12 hours following thyroidectomy, which indicates that paratracheal infiltration with bupivacaine is effective in decreasing postoperative pain in both the short and long term. The need for analgesics decreased in both paratracheal infiltration and subcutaneous infiltration groups. We think that our overall findings suggest the efficacy of bupivacaine by paratracheal infiltration in the management of postoperative pain following thyroidectomy; however, further studies are required to determine the most appropriate route of administration. Since total thyroidectomy was applied on all patients, we do not think that the difference between preoperative T3 values of the groups is a factor that may affect postoperative pain. We believe this to be pure coincidence (34).

Our findings along with previous reports indicate that bupivacaine application may be promising for control of postoperative pain following thyroidectomy. Recently, the advent of a liposomal formulation of bupivacaine has provided more favorable pharmacokinetics that reduces the risk of amide-related toxicity and provides long-lasting postoperative analgesia (13, 18, 35, 36). Potential risks and benefits of liposomal bupivacaine, a very recently approved formulation of bupivacaine, need to be elucidated for postoperative pain control (36, 37). It is obvious that bupivacaine is used in high doses for motor and sensory blockade in both spinal anesthesia and peripheral nerve block. However, there were no signs of motor blockage in any of our operations (38).

In spite of our findings in favor of the analgesic efficacy of bupivacaine, the main limitation of our study is the small sample size precludes us from reaching a definite conclusion. Further studies with a larger sample size and those comparing different application routes are required to conclude on the efficacy of and the most efficient application route of bupivacaine for postoperative pain control.

In addition, the absence of data on operation durations, the volume of pathologic specimens, and comparison with the ultrasonographic volume measurements may be considered as other limitations of our study.

CONCLUSION

Intraoperative local bupivacaine application is effective in decreasing postoperative pain in patients undergoing thyroidectomy. Effective pain management following thyroidectomy should be implemented in order to increase the quality of postoperative care, to reduce both opioid consumption and subsequent dose-related complications.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Yıldırım Beyazıt University School of Medicine.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

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Factors affecting surgical site infection rate after elective gastric cancer surgery

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ABSTRACT

Objective: Surgical site infection (SSI) is a common complication after surgery and is an indicator of quality of care. Risk factors for SSI are studied thoroughly for most types of gastrointestinal surgeries and especially colorectal surgeries, but accumulated data is still lacking for gastric surgeries. We studied the parameters affecting SSI rate after gastric cancer surgery.

Material and Methods: Consecutive patients, who underwent elective gastric cancer surgery between June and December 2013, were included. Descriptive parameters, laboratory values and past medical histories were recorded prospectively. All patients were followed for 1 month. Recorded parameters were compared between the SSI (+) and SSI (-) groups.

Results: Fifty-two patients (mean age: 58.87±9.25 [31-80]; 67% male) were included. SSI incidence was 19%. ASA score ≥3 ($p<0.001$), postoperative weight gain ($p<0.001$), smoking ($p=0.014$) and body mass index (BMI) ≥30 ($p=0.025$) were related with a higher SSI incidence. Also patients in the SSI (+) group had a higher preoperative serum C-reactive protein level ($p=0.014$).

Conclusion: We assume that decreasing BMI to <30, stopping smoking at least 3 weeks before the operation, and preventing postoperative weight gain by avoiding excessive intravenous hydration will all help decrease SSI rate after gastric surgery.

Keywords: Gastric cancer, surgical site infection, risk factors

INTRODUCTION

The incidence of gastric cancer has been decreasing throughout the last decades after effective eradication of Helicobacter pylori infection, improved sanitation, refrigeration and a shift towards the consumption of fresh fruit and vegetables rather than red meat and high fat diet (1, 2). Nevertheless, gastric cancer still remains to be the third most common cause of cancer related deaths (3), and gastric cancer surgery is a commonly performed surgery in especially busy tertiary care centers.

Surgical site infections (SSI) are responsible for 38% of nosocomial infections (4, 5), and is one of the most prominent morbidity after gastric surgery. Surgical site infections causes prolonged hospitalization and increased surgery related costs (6, 7). ASA score, wound classification and duration of the operation are the 3 SSI-related factors established by the National Nosocomial Infection Surveillance (NNIS) (8-10). Risk factors for SSI are studied thoroughly for most types of gastrointestinal surgeries and especially colorectal surgeries, but accumulated data is still lacking for gastric surgeries (11, 12).

Our hospital is a tertiary care center with more than 200 gastric cancer surgeries a year. In our clinic, we experience a higher SSI rate than the stated rate (3-16%) for gastric surgeries in the literature (13-15). In this study, our goal is to determine the factors affecting SSI rate after gastric surgery.

MATERIAL AND METHODS

Patients and Study Design

The subjects of our prospective observational cohort study were consecutive patients who underwent elective gastric surgery (distal subtotal or total gastrectomy with D2 lymphadenectomy) for gastric cancer. The inclusion criteria were: (1) patients diagnosed with resectable gastric cancer and undergoing laparotomy; (2) being older than 18 years of age; (3) giving informed consent to participate in the study. The exclusion criteria were: (1) signs of a clinically prominent infection detected on the day of admission; (2) an ASA score of ≥4; (3) laparoscopic surgery (seldomly performed in our clinic for gastric cancer surgery).

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Data Collection

Patient age, gender, ASA score, BMI, history of co-morbidities as diabetes mellitus (DM) and chronic obstructive pulmonary disease (COPD), type of surgery, anastomosis technique (hand-sutured vs. stapled), operation duration, blood transfusion, ICU admission, tumor stage, body weight on the day of hospital admission, daily changes in body weight postoperatively, length of hospital stay, readmission to the hospital, hospital costs, preoperative and postoperative laboratory studies were recorded prospectively. In the NNIS report, the operation duration was grouped according to the third percentile which was 180 minutes for gastric cancer surgeries (16, 17). We also used third percentile as a cut-off point which was 135 minutes in our study. Patients were followed one month for SSI. They were asked to visit the outpatient clinic on postoperative day 15 and day 30. Although it is not routinely done in our clinic for all surgical site infections, swab culture was obtained from all patients during the diagnosis of SSI for this study.

Definitions

All patients were operated by a single surgeon with more than 25 years of experience. Surgical residents assisted during the surgery and no students scrubbed in. In our institution, we remove hair using a clipper 30 minutes before surgery in the operating room. We use povidone-iodine as the antiseptic solution. For prophylaxis, we use first generation cephalosporins. If the patient is allergic to penicilline then we use fluoroquinolones. In this study, no patient was allergic to penicilline thus fluoroquinolones were never used.

Blood tests were taken on the day of hospital admission. Body weight was also measured on the day of admission and each postoperative day. Mean values for postoperative body weight measurements were calculated and compared to the body weight measurement on the hospital admission day. If the mean postoperative body weight was more than the admission day body weight, the patient was accepted as 'gained weight' postoperatively. Patients who never smoked or stopped smoking prior to 3 weeks before surgery were considered as nonsmokers.

The criterias used to define and classify SSI's were established according to the guidelines of the Committee of Disease Control (CDC) (Table 1) (4, 18, 19). Our study is designed and conducted according to the Helsinki declaration.

Statistical Analysis

Student's t test was used to compare continous variables, while *chi-square* test was used to compare categorical values. Statistical Package for Social Sciences (SPSS) software version 18.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. A p value less than 0.05 was considered as statistically significant.

RESULTS

In this study, 52 patients were included from June to December 2013. The mean age was 58.87±9.25 [31-80] years. The proportion of males was 67% (n=35) in our cohort. 21% (n=11) of

Table 1. Center for disease control classification of surgical site infection

Superficial Incisional SSI
Infection within 30 days after the operation and only involves skin and subcutaneous tissue of the incision and at least one of the following:
• Purulent drainage with or without laboratory confirmation, from the superficial incision.
• Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision.
• At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat and superficial incision is deliberately opened by surgeon, unless incision is culture-negative.
Diagnosis of superficial incisional SSI made by a surgeon or attending physician.
Deep Incisional SSI
Infection occurs within 30 days after the operation if no implant is left in place or within one year if implant is in place and the infection appears to be related to the operation and infection involves deep soft tissue (e.g. fascia, muscle) of the incision and at least one of the following:
• Purulent drainage from the deep incision but not from the organ/space component of the surgical site.
• A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever (>38°C), localized pain or tenderness, unless incision is culture-negative.
• An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
Diagnosis of deep incisional SSI made by a surgeon or attending physician.
Organ/Space SSI
Infection occurs within 30 days after the operation if no implant is left in place or within one year if implant is in place and the infection appears to be related to the operation and infection involves any part of the anatomy (e.g., organs and spaces) other than the incision which was opened or manipulated during an operation and at least one of the following:
• Purulent drainage from a drain that is placed through a stab wound into the organ/space.
• Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space.
• An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
Diagnosis of organ/space SSI made by a surgeon or attending physician.
SSI: Surgical site infection

the patients had a family history of gastric cancer. 14% (n=7) of the patients had an ASA score of ≥3. 23% (n=12) of the patients had a BMI of ≥30. 37% (n=19) of the patients were smoking. 8% (n=4) of the patients had a diagnosis of COPD and 14% (n=7) of the patients had a diagnosis of DM (Table 2).

In our study, 55% (n=28) of the patients had a tumor stage ≥3. 54% (n=28) of the patients had a distal subtotal gastrectomy and 46% (n=24) had a total gastrectomy. The mean operation duration was 130.47±50.48 [45-300] minutes. 27% (n=14) of the patients received blood transfusion during their hospital stay. 23% (n=12) of patients were transferred to the ICU after surgery. 23% (n=12) of the patients gained weight after surgery. Mean discharge day was 5.29±3.05 [3-24]. The readmission rate was 6% (n=3). The mean hospital cost was 5305.77±2268.94 [1933-13603] USD (Table 2).

The incidence of SSI was 19% (n=10). All patients diagnosed with SSI had a superficial incisional infection. 50% (n=5) of the SSI's occurred during the hospital stay while the other 50% (n=5) were diagnosed on the 15th day outpatient clinic visit (Table 3). From the swab culture of 1 patient, group G streptococcus "*Streptococcus disgalactia* and *Streptococcus anginosus*" were obtained. *Enterobacter aerogenes* was obtained from the swab culture of another patient. *Staphylococcus epidermidis* and *Streptococcus mitis* were obtained from the swab cultures of 8 patients in the SSI (+) group (Table 4).

When the SSI (+) and SSI (-) groups were compared an ASA score of ≥3, a BMI of ≥30, and smoking history were more commonly encountered in the SSI (+) group (50% vs. 5%, p<0.001; 50% vs. 17%, p=0.025 and 70% vs. 29%, p=0.014, respectively). Postoperative weight gain was also more common in the SSI (+) group (70% vs. 12%, p<0.001) (Table 5). Patients in the SSI (+) group had a higher preoperative serum C-reactive protein value in comparison to the other group (60.44 (±54.31) mg/L vs. 19.38 (±17.69) mg/L; p=0.01) (Table 6).

Age, gender, tumor stage, co-morbidities (COPD and DM), type of surgery, anastomosis technique, operation duration, blood transfusion, ICU admission, length of hospital stay, readmission rate and hospital costs were similar between the two groups (Table 5).

DISCUSSION

The incidence of gastric cancer is inclined to decrease in the past decades. Nevertheless, gastric cancer surgery is still frequently performed in tertiary care hospitals. According to various studies in the literature, SSI is one of the most common comorbidities after gastric surgery with an incidence of 3-28% (5, 13-15). Factors affecting SSI after colorectal surgery is thoroughly studied in the literature (11, 12), but data still needs to be accumulated for gastric surgery.

The incidence of SSI was 19% in our study. Although our rate was similar to the rates reported from other developing countries (5), it was above the rates reported from developed countries (13, 14). When we compared the SSI (+) and SSI (-) groups an ASA score of ≥3, a BMI of ≥30, postoperative weight

Table 2. Descriptive factors

Age (years) (mean±SD [Range])	58.87±9.25 [31-80]
Gender, n (%)	
Male	35 (67)
Female	17 (33)
Family history of gastric cancer, n (%)	11 (21)
ASA score ≥3, n (%)	7 (14)
BMI ≥30 (kg/m^2) n (%)	12 (23)
Smoking history, n (%)	19 (37)
Diagnosis of COPD, n (%)	4 (8)
Diagnosis of DM, n (%)	7 (14)
Tumor stage ≥3, n (%)	28 (55)
Surgery type, n (%)	
Distal subtotal gastrectomy	28 (54)
Total gastrectomy	24 (46)
Operation duration (minutes) (mean±SD[Range])	130.47±50.48 [45-300]
Receiving blood transfusion, n (%)	14 (27)
ICU admission, n (%)	12 (23)
Patients gained weight after surgery, n (%)	12 (23)
Hospital stay (day) (mean±SD[Range])	5.29±3.05 [3-24]
Readmission rate, n (%)	3 (6)
Hospital cost (USD) (mean±SD [Range])	5305.77±2268.94 [1933-13603]

COPD: chronic obstructive pulmonary disease; DM: diabetes mellitus; USD: United States dollars. BMI: body mass index; ICU: intensive care unit

Table 3. SSI incidence and types	**n (%)**
Incidence of SSI	10 (19)
SSI classification	
Superficial	10 (100)
Deep	0 (0)
Organ/space	0 (0)
Date of SSI diagnosis	
During hospital stay	5 (50)
Postoperative day 15	5 (50)
Postoperative day 30	0 (0)

SSI: surgical site infection

Table 4. Swab culture results	**n (%)**
Group G *Streptococcus*	
S. disgalactia	1 (5)
S. anginosus	1 (5)
Enterobacter aerogenes	1 (5)
Staphylococcus epidermidis	8 (42)
Streptococcus mitis	8 (42)

Table 5. Comparison of descriptive factors	SSI (-)	SSI (+)	p
Age (years) (mean [±SD])	58.38 (±10.87)	60.9 (±7.62)	0.4
Gender, n (%)			
Male	30 (71)	5 (50)	0.194
Female	12 (29)	5 (50)	
ASA score, n (%)			
<3	40 (95)	5 (50)	<0.001 OR 20 [3-131.7]
≥3	2 (5)	5 (50)	
BMI (kg/m^2) n (%)			
<30	35 (83)	5 (50)	0.025 OR 5 [1.1-2.2]
≥30	7 (17)	5 (50)	
Smoking history, n (%)			
Negative	30 (71)	3 (30)	0.014 OR 5.8 [1.3-26.4]
Positive	12 (29)	7 (70)	
COPD, n (%)			
COPD (-)	39 (93)	9 (90)	0.761
COPD (+)	3 (7)	1 (10)	
DM, n (%)			
DM (-)	36 (86)	9 (90)	0.721
DM (+)	6 (14)	1 (10)	
Anastomosis technique, n (%)			
Hand-sutured	34 (85)	7 (78)	0.712
Stapled	6 (15)	2 (22)	
Operation duration (minutes) n (%)			
<135	28 (78)	6 (67)	0.732
≥135	8 (22)	3 (33)	
Erythrocyte suspension transfusion, n (%)			
Transfusion (-)	31 (74)	7 (70)	0.807
Transfusion (+)	11 (26)	3 (30)	
Intensive care unit admission, n (%)			
Admission (-)	37 (88)	3 (30)	0.761
Admission (+)	5 (12)	7 (70)	
Postoperative weight gain, n (%)			
Weight gain (-)	37 (88)	3 (30)	<0.001 OR 17.3 [3.3-89.3]
Weight gain (+)	5 (12)	7 (70)	
Type of surgery, n (%)			
Distal subtotal gastrectomy	22 (52)	6 (60)	0.664
Total gastrectomy	20 (48)	4 (40)	
Tumor stage, n (%)			
<3	16 (39)	7 (70)	0.182
≥3	25 (61)	3 (30)	
Discharge day (mean [±SD])	5.27 (±3.24)	5.4 (±2.22)	0.88
Readmission n (%)	2 (4.8)	1 (10)	0.65
Hospital cost (USD) (mean [±SD])	2596 (±1131)	2235 (±814)	0.26

SSI: surgical site infection; COPD: chronic obstructive pulmonary disease; DM: diabetes mellitus; USD: United States dollars. BMI: body mass index

Table 6. Comparison of preoperative laboratory tests

	SSI (-) Mean (±SD)	SSI (+) Mean (±SD)	p
Carcinoembryogenic antigen (ng/mL)	10.07 (±7.62)	2.67 (±2.17)	0.28
Hemoglobin (g/dL)	11.12 (±2.28)	11.13 (±2.01)	0.99
Hematocrit (%)	33.58 (±6.09)	33.03 (±5.5)	0.79
White blood cells (uL)	7816 (±2131)	7920 (±2225)	0.89
Platelet (uL)	284404 (±101993)	324100 (±112620)	0.33
Glucose (mg/dL)	93.88 (±22.78)	97.50 (±19.14)	0.61
Total protein (g/dL)	6.75 (±0.46)	5.83 (±0.47)	0.2
Albumin (g/dL)	3.91 (±0.71)	3.78 (±0.3)	0.4
Blood urea nitrogen (mg/dL)	16.21 (±5.91)	16.18 (±5.60)	0.99
Creatinine (mg/dL)	0.99 (±0.1)	0.85 (±0.39)	0.33
C-reactive protein (mg/L)	19.38 (±17.69)	60.44 (±54.31)	0.01

SSI: surgical site infection

gain during hospital stay, smoking history, and preoperative high CRP values were significantly more common in the SSI (+) group.

Patients who gained weight during the postoperative period were more commonly diagnosed with SSI in our study. The most common reason of weight gain during the early postoperative period is excessive IV fluid administration. Excessive IV fluid causes an increase in body weight and effects the mobility of the patient negatively. It also impairs tissue oxygenation by accumulating in the interstitial space and raises susceptibility to SSI (20, 21). We think that balancing IV fluid treatment meticulously and measuring patient weight on a daily basis will help decrease SSI incidence.

Impaired tissue oxygenation is also encountered among smoking individuals. It is well established that nicotine use delays primary wound healing and increases the risk of SSI by reducing the amount of oxygen carried to the wound by red blood cells (22, 23). Also in our study smoking history was significantly more common in the SSI (+) group. Stopping smoking at least 3 weeks before surgery will reduce susceptibility of the patient to SSI after gastric surgery.

When the ASA score was first generated, the goal was not to predict the SSI risk but anesthetic procedure related morbidity and mortality (22). Nevertheless, during the following years ASA score has become a predictor of underlying disease severity and susceptibility of the patient to SSI. In the literature, studies have been published reporting a correlation between ASA score and SSI (8, 24-26). In our study, ASA scores of 3 and 4 were found more commonly in the SSI (+) group. We think that ASA score is a reliable factor that aids the surgeon in defining the susceptibility of the patient to SSI.

In our study, subjects with a BMI over 30 were more prone to SSI. The correlation between BMI and SSI was reported in the literature repeatedly (14, 27, 28). The composition of adipose tissue is relatively avascular, and a wound with a higher amount of adipose tissue will have a lower tissue oxygenation. Similar to the mechanism which excessive IV fluid causes susceptibility to SSI, the less oxygenated adipose tissue is more prone to SSI. Also technical difficulties in obese patients and necessity of a wider incision all contribute to the SSI risk of the obese patient (29, 30). The interval between diagnosis and surgery is generally not long in gastric cancer patients, and the patient might not be able to lose a considerable amount of body weight. In our clinic, there is usually a 2-3 week interval between the time of diagnosis and surgery. Taking into consideration the fact that obese patients lose weight more rapidly, we think it is reasonable to advise the patient on the date of diagnosis to lose as much weight as possible before surgery under the supervision of a dietician.

In the SSI (+) group, patients had significantly higher preoperative serum CRP levels. As an acute-phase reactant CRP level can increase due to an underlying infection. It can also be elevated in numerous noninfectious inflammatory processes (31). Serum CRP value is a marker of chronic systemic inflammation and is positively associated with the amount of adipose tissue in a healthy individual. Obese individuals tend to have twice as high CRP levels as normal body weight individuals (32-34). We think that the reason of higher CRP levels in the SSI (+) group was because more patients with a BMI ≥30 were within this group. We don't think that routine preoperative CRP level measurement will help decrease the SSI rate.

Most of the studies in the literature reporting operation duration as a factor affecting SSI rate were conducted in multiple centers with different expertise levels of surgeons and various operation durations (13). In our study, the operation duration was slightly higher in the SSI (+) group but the difference was not statistically significant. A single surgeon with more than 25 years of experience operated on all the patients, and similar operation durations were obtained for most cases. We think that operation duration is a factor reflecting the expertise level of the surgical team. Because of the single center design of our study, operation duration was not found as a factor affecting the SSI rate.

Although this study can be criticized with it's small cohort size, according to our knowledge, postoperative weight gain was previously not reported as an SSI related factor after gastric surgery, and our study will make a contribution to the literature.

CONCLUSION

We assume that decreasing BMI to <30, stopping smoking at least 3 weeks before the operation, and preventing postoperative weight gain by avoiding excessive IV hydration will all help decrease SSI rate after gastric surgery.

Ethics Committee Approval: Authors declared that the research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects", (amended in October 2013).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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Laparoscopic partial cholecystectomy: A safe and effective alternative surgical technique in "difficult cholecystectomies"

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ABSTRACT

Objective: Laparoscopic cholecystectomy has become the ''gold standard'' for benign gallbladder diseases due to its advantages. In the presence of inflammation or fibrosis, the risk of bleeding and bile duct injury is increased during dissection. Laparoscopic partial cholecystectomy (LPC) is a feasible and safe method to prevent bile duct injuries and decrease the conversion (to open cholecystectomy) rates in difficult cholecystectomies where anatomical structures could not be demonstrated clearly.

Material and Methods: The feasibility, efficiency, and safety of LPC were investigated. The data of 80 patients with cholelithiasis who underwent LPC (n=40) and conversion cholecystectomy (CC) (n=40) were retrospectively examined. Demographic characteristics, ASA scores, operating time, drain usage, requirement for intensive care, postoperative length of hospital stay, surgical site infection, antibiotic requirement and complication rates were compared.

Results: The median ASA value was 1 in the CC group and 2 in the LPC group. Mean operation time was 123 minutes in the CC group, and 87.50 minutes in the LPC group. Surgical drains were used in 16 CC patients and 4 LPC patients. There was no significant difference between groups in postoperative length of intensive care unit stay (p=0.241). When surgical site infections were compared, the difference was at the limit of statistical significance (p=0.055). Early complication rates were not different (p=0.608) but none of the patients in the LPC group suffered from late complications.

Conclusion: LPC is an efficient and safe way to decrease the conversion rate. LPC seems to be an alternative procedure to CC with advantages of shorter operating time, lower rates of surgical site infection, shorter postoperative hospitalization and fewer complications in high-risk patients.

Keywords: Cholelithiasis, laparoscopic partial cholecystectomy, difficult cholecystectomy, conversion cholecystectomy, safe cholecystectomy, bile duct injury

INTRODUCTION

Laparoscopic cholecystectomy (LC) has become the gold standard for the surgical treatment of benign gallbladder diseases owing to its shorter hospitalization, more rapid recovery, and much fewer wound complications when compared to open cholecystectomy (1-4). However, a direct vision is essential for safe dissection of Calot's triangle - outlined by the cystic duct, right liver lobe, and the common hepatic duct-, which indicates the importance of a clear anatomical demonstration of the cystic duct and cystic artery to perform a safe cholecystectomy (5). While early on its routine application, LC was considered to be contraindicated in situations such as severe adhesions in Calot's triangle, acute cholecystitis, and cirrhosis, it is currently being applied successfully even in challenging cases due to introduction of novel techniques and increased experience (6).

Severe inflammation and fibrosis of the gallbladder may increase the risk of bleeding and biliary tract injury during Calot's triangle dissection (7). Open subtotal cholecystectomy has been used safely in patients at high-risk of bile duct injury due to disruption of natural anatomy due to severe fibrosis and inflammation (8). With improvements in laparoscopic techniques, laparoscopic partial cholecystectomy (LPC) has become an effective and safe method of decreasing the rates of conversion to open surgery (9, 10).

The quality of life improvement after LC is markedly better than open cholecystectomy (11). Laparoscopic completion of the procedure is recommended especially for the elderly since it is associated with lower incidence of pulmonary infection, reduced rates of postoperative complications and better quality of life (12, 13).

Our aim was to investigate the feasibility, effectiveness and safety of LPC in difficult cases of cholecystectomy.

MATERIAL AND METHODS

Clinical and operative data of 40 patients who underwent LPC and 40 patients in whom the operation initiated with laparoscopic technique has been converted to open surgery (conversion cholecystecto-

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my-CC) for symptomatic cholelithiasis without an associating malignancy were retrospectively investigated. The study included patients who were operated between January 2008 and January 2011. For standardization, all patients were operated by the same surgeon. In order to evaluate differences between procedures, 40 LPC and 40 CC cases were selected by a computerized randomization program out of the database including all patients who underwent laparoscopic partial cholecystectomy and conversion cholecystectomy.

The laparoscopic intervention was performed in the same manner in both groups using two 10-mm and two 5-mm trocars. All patients met the criteria of difficult cholecystectomy that was defined as the presence of phlegmonous gallbladder due to adherence of the colon and greater omentum or severe thickening of the gallbladder wall due to inflammation.

Laparoscopic partial cholecystectomy was defined as procedures where the posterior wall of the gallbladder was left in the hepatic bed. The triangle of Calot was exposed, and the cystic duct was ligated in all patients. Dissection was initiated at the fundus and advanced with a traditional retrograde dissection. Cauterization with an argon beam device was performed to the posterior gallbladder wall mucosa to prevent subhepatic fluid collection, and this part was left in place. All gallstones were extracted with a laparoscopic endobag. The intraperitoneal cavity was irrigated with sterile isotonic solution and the intraabdominal fluid collection was aspirated at the end of the procedure.

Conversion to open surgery was performed via a right subcostal incision in all CC patients. Demographic variables, ASA (American Society of Anesthesiology) scores, operation times, rate of drainage tube usage, length of intensive care unit and hospital stay, rates of surgical site infection, antibiotic requirement rate and complication incidence were compared between the two groups. Any complication occurring within the first month of surgery was defined as an "early complication".

Statistical Analysis

Statistical analysis were performed by Statistical Package for the Social Sciences version 20.0, (SPSS Inc; Chicago, IL, USA) software. The Shapiro-Wilk test was used to verify the normality of distribution. The Mann-Whitney U test and Student's T-test were used for intergroup comparisons. Chi-square test and Fisher's Exact test were used for comparison of categorical data. Results were evaluated within 95% confidence interval and $p<0.05$ was considered to be statistically significant.

RESULTS

The mean age was not significantly different between the two groups (p=0.541) (Table 1).

There was a significant difference between the two groups in terms of gender distribution (p=0.013). Female gender was more frequent in the CC group while male gender was more common in the LPC group (Table 2).

ASA scores were significantly different between the two groups (p=0.008). The median ASA score was 1 in the CC group and 2 in the LPC group. LPC patients were at higher operative risk (Table 3).

The mean operation duration was significantly different between two groups (p=0.001). The mean time of operation was 123 minutes in the CC group and 87.50 minutes in the LPC group (Table 4).

The rate of surgical drain usage was significantly different between two groups (p=0.005). Surgical drains were used in 16 CC patients and 4 LPC patients, and one subhepatic passive drain was inserted in all (Table 5).

There was no significant difference between the groups in terms of length of postoperative intensive care unit stay (p=0.241). Three patients in the CC group required a postoperative intensive care stay for one day. None of the patients in the LPC group required postoperative intensive care stay.

When surgical site infections were compared between groups, the difference was at the limit of statistical significance (p=0.055). None of the LPC patients and five CC patients developed surgical site infection. Rates of postoperative antibiotic use were not significantly different between the two groups (p=0.201) (Table 6).

Table 1. Age distribution between groups (p=0.541)

Group		n	Mean	SD
CC	Age	40	56.20	14.819
LPC		40	58.35	16.473

CC: conversion cholecystectomy; LPC: laparoscopic partial cholecystectomy; SD: standard deviation

Table 2. Gender distribution between groups (p=0.013)

Group		Gender		Total
		Male	Female	
CC	n	12	28	40
	%	30.0	70.0	100.0
LPC	n	24	16	40
	%	60.0	40.0	100.0
Total	n	36	44	80
	%	45.0	55.0	100.0

CC: conversion cholecystectomy; LPC: laparoscopic partial cholecystectomy

Table 3. Comparison of ASA scores between groups (p=0.008)

Group		ASA
CC	Median	1.00
	Minimum	1
	Maximum	3
LPC	Median	2.00
	Minimum	1
	Maximum	4

CC: conversion cholecystectomy; LPC: laparoscopic partial cholecystectomy; ASA: American Society of Anesthesiology

The mean postoperative length of hospital stay was significantly different between the two groups (p=0.001). The mean time of hospitalization was three days in the CC group and one day in the LPC group (Table 7).

Early complication rates were not significantly different between the two groups (p=0.608). Early complications were observed in three patients in the CC group and one patient in the LPC group. Two patients in the CC group underwent local wound exploration due to wound infection and pain. The remaining patient in the CC group was complicated by a postoperative paralytic bowel obstruction that resolved with conservative treatment. An early complication of postoperative anemia was observed in one LPC patient. Any identifiable cause of anemia was not present and the patient's condition improved with conservative treatment.

Late complication rates were significantly different between the two groups (p=0.001). None of the patients in the LPC group suffered from late complications whereas 13 patients in the CC group developed complications, all of which were incisional hernias (Table 8).

DISCUSSION

The laparoscopic technique has replaced open surgery and become the gold standard in cholecystectomy since its first introduction for gallbladder operations in the mid-1980s by Erich Mühe in Germany and Philippe Mouret in France (14). More than 770.000 laparoscopic cholecystectomies are being performed annually in the United States (15). Advantages of LC include rapid improvement in physical activity and quick return to normal life, short hospital stay, increased operative safety with magnified view, low morbidity rates, low cost, less tissue trauma, better cosmesis and less postoperative pain (16).

Rates of conversion to the open technique and iatrogenic injury are significantly higher in difficult cholecystectomies. Risk factors for difficult cholecystectomy include male gender, advanced age, acute presentation, thick-walled gallbladder with chronic inflammation, dilated and short cystic duct, gallbladder fistulas, previous history of upper abdominal surgery, obesity, cirrhosis, anatomic variation, cholangiocarcinoma and surgical inexperience (17). Application of subtotal cholecystectomy and retrograde dissection technique and usage of perioperative cholangiogram have decreased the rates of conversion to open technique (17, 18).

Open subtotal cholecystectomy has been used safely in patients who are at high risk of injury to the structures within the triangle of Calot due to severe fibrosis and inflammation (8).

Table 4. Comparison of operation times between groups (p=0.001)

Group		Operation times (min)
CC	Median	125
	Minimum	100
	Maximum	140
LPC	Median	87.50
	Minimum	80
	Maximum	105

CC: conversion cholecystectomy; LPC: laparoscopic partial cholecystectomy

Table 5. Comparison of drainage tube use between groups (p=0.005)

Group		Drainage tube		Total
		-	+	
CC	n	24	16	40
	%	60.0	40.0	100.0
LPC	n	36	4	40
	%	90.0	10.0	100.0
Total	n	60	20	80
	%	75.0	25.0	100.0

CC: conversion cholecystectomy; LPC: laparoscopic partial cholecystectomy

Table 6. Comparison of surgical site infection between groups (p=0.055)

Group		Surgical site infection		Total
		-	+	
CC	n	35	5	40
	%	87.5	12.5	100.0
LPC	n	40	0	40
	%	100.0	0.0	100.0
Total	n	75	5	80
	%	93.8	6.3	100.0

CC: conversion cholecystectomy; LPC: laparoscopic partial cholecystectomy

Table 7. Postoperative length of hospital stay (p=0.001)

Group		Postoperative length of hospital stay (days)
CC	Median	3
	Minimum	2
	Maximum	20
LPC	Median	1
	Minimum	1
	Maximum	4

CC: conversion cholecystectomy; LPC: laparoscopic partial cholecystectomy

Table 8. Comparison of late complications between groups (p=0.001)

Group		Late complications		Total
		-	+	
CC	n	27	13	40
	%	67.5	32.5	100.0
LPC	n	40	0	40
	%	100.0	0.0	100.0

CC: conversion cholecystectomy; LPC: laparoscopic partial cholecystectomy

By the advances in laparoscopic technique, it was noted that LPC decreased the rates of biliary tract injuries and of severe hepatic bed hemorrhages, and provided a marked decrease in the rates of conversion to open surgery in patients with benign cholecystitis (1, 6, 9, 10).

Advanced age was evaluated as a risk factor for difficult cholecystectomy (19, 20). Studies suggested that LC was safe, did not increase complication rates, shortened the time of hospitalization, and was associated with a marked improvement in the quality of life for the elderly. Surgeons were recommended to complete an operation in the laparoscopic setting as much as possible in patients with advanced age (12, 21-25). In our study, the mean age did not significantly differ between the two groups. The mean age was 56.20 in the CC group and 58.35 in the LPC group. Both CC and LPC patients were in the difficult cholecystectomy group in terms of their ages.

Male gender was also evaluated as a risk factor for difficult cholecystectomy (26). Male sex was reported among the risk factors for conversion to open surgery in some previous studies (27-30). In our study, male gender was significantly more frequent in the LPC group. Combining facts that male gender is a risk factor for difficult cholecystectomy and that conversion to open surgery is more prevalent in the male population, LPC technique is likely to decrease the rate of conversion to open surgery and seems to be a safe option for men. Al-Mulhim et al. (31) reported that male gender did not cause an adverse impact on LC outcomes. In our study, LPC technique was successfully performed in the treatment of difficult cholecystectomy in both male and female patients.

In high-risk patients, LC seems to be a better option than open cholecystectomy concerning overall mortality (31, 32). Frazee et al. (33) suggested that LC was associated with improvement in pulmonary function when compared to the open technique. Mimica et al. (34) reported that the open technique was associated with a higher risk of anesthesia-related complications in the postoperative period as compared to LC. Koivusalo et al. (35) reported that pneumoperitoneum was not associated with an additional risk in ASA III and ASA IV elderly patients during LC. Luo et al. (36) concluded that LC is beneficial for restoration of stress hormones, nitrogen balance, and energy metabolism but that it may also cause acidemia and pulmonary hypoperfusion due to pneumoperitoneum. In our study, ASA scores were significantly different between the groups, the LPC group consisted of higher risk patients. Anesthesia-related complications were not observed in the LPC group whereas such complications occurred in 3 patients in the CC group who required an intensive care unit stay.

Patients that meet the definition of difficult cholecystectomy were older and in the high-risk group (5-8). Therefore, it is important to shorten the duration of operation to reduce anesthesia-related complications. In previous studies, mean operation times were ranging from 53.60 to 95 minutes (1, 5-7). In our study, the mean operation time was 87.50 minutes. Laparoscopic partial cholecystectomy was compared with LC in studies performed by Ersöz et al. (6) and Ji et al. (7). However, we suggest that LPC should not be considered as an alternative to LC, and that it should be rather regarded as an alternative to the open technique. We believe that LPC would not be required in cases where total LC is possible in the standard fashion except for occasional cases with a risk of bleeding in which the gallbladder is embedded into the hepatic bed. In our study, LPC was considered as an alternative to the CC technique. Thus, conversion to open procedure was not required in the LPC group. Moreover, the mean operation duration was significantly different between the two groups. The average time of surgery was shorter in the LPC group, and this provided additional benefit for at-risk patients due to difficult cholecystectomy.

Previous studies demonstrated that use of surgical drains after cholecystectomy had no benefit for the patient (37-39). Tzovaras et al. (37) found no difference in mortality, morbidity and hospital stay between patients in whom drains were and were not used. However, they concluded that postoperative pain was significantly lower in patients in whom drains were not used. In a prospective randomized trial (39), Lewis et al. (39) concluded that usage of drainage tubes was not necessary in elective cholecystectomy. Moreover, in a prospective randomized trial including 479 patients Monson et al. (38) suggested that usage of drainage tubes should be abandoned since the incidence of wound infections, pulmonary infections, subhepatic fluid collection and length of hospitalization were higher in the drainage group. In a review of six patients, Gurusamy et al. (40) concluded that wound infection rates and hospital length of stay were higher in patients with drainage tubes. In our study, drainage tubes were used in 16 CC patients and 4 LPC patients. Usage of drainage tubes was significantly different between the two groups. LPC technique decreased the need for surgical drain usage and prevented patients from harmful effects of their unnecessary use.

Wound infection was also found to be lower in the LPC group ($p=0.55$). According to 2003 National Nosocomial Infections Surveillance System report that included 54,504 cases of cholecystectomy, LC was associated with a lower risk of surgical site infection when compared with open cholecystectomy (15). In our study, postoperative antibiotic usage was not significantly different between the two groups ($p=0.201$). In a review of 11 clinical trials, Sanabria et al. (41) found no significant difference regarding surgical site infection and antibiotic use. In our study, surgical site infection was not encountered in the LPC group while it occurred in 5 CC patients. The difference between groups was at the limit of statistical significance ($p=0.055$). This finding was considered likely to be due to the decrease in surgical site infection because of reduced requirement for converting to the open technique during LC.

Several reports suggested that postoperative hospital stay was significantly shorter in LC series when compared with CC series (2, 4, 22, 42-44). Ivatury et al. (45) concluded that postoperative stay after LC was associated with ASA score. In our study, although ASA values were higher in the LPC group, their postoperative stay was significantly lower than the CC group. This condition makes LPC technique more advantageous by providing a shorter postoperative stay in high-risk patients.

Complications are more common after open cholecystectomy than laparoscopic procedures, particularly at the site of incision (4, 22, 46, 47). Brune et al. (20) observed that the rate of incision site complications was higher after CC when compared to LC, and they showed that this was related to the size of the

incision. In addition, Lim et al. (42) reported the rate of incision site complications to be significantly higher in the CC group. In our study, late complications were not observed in the LPC group. Incision site complications were significantly higher in the CC group, which may be considered as another issue that makes LPC more advantageous.

Although postoperative bile leak was detected in the studies by Henneman et al. (48) and Kaplan et al. (49), we did not observe any bile leak in our study. We were able to ligate the cystic duct in each and every patient; however, ligation is not indispensable. Persistent bile leak may occur, but biliary drainage will decrease and cease with time with postoperative endoscopic sphincterotomy that reduces the intraluminal biliary tract pressure (48).

Study Limitations

The major limitation of this study was its retrospective nature. Randomized controlled trials in larger series are needed to achieve accurate results.

CONCLUSION

With advances in laparoscopic technique, LPC has become an effective and safe method for decreasing the rates of conversion to open surgery in patients with benign gallbladder disease and difficulties during their operations. In this preliminary study, we suggest that LPC is a good and safe alternative to CC due to its shorter operation duration, a lower rate of surgical site infection, shorter length of postoperative hospital stay, and lower incidence of postoperative complications.

Ethics Committee Approval: Ethics Committee approval was not required as the study was retrospective.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

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Predictive value of fine needle aspiration biopsy of axillary lymph nodes in preoperative breast cancer staging

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ABSTRACT

Objective: Diagnosis of axillary nodal involvement is significant in the management of breast cancer as well as in predicting prognosis. In this prospective study, we evaluated the efficiency of US-guided fine needle aspiration biopsy (FNAB) in preoperative axillary staging of early breast cancer.

Material and Methods: Between January 2011 and July 2013, 46 women were prospectively enrolled in the study. Ultrasound guided-FNABs for axillary assessment were performed preoperatively. Cytology results were compared with histopathology reports to determine its sensitivity, specificity, negative and positive predictive value and accuracy.

Results: Nineteen cases that had malignant cytology on FNAB also had axillary involvement in axillary lymph node dissection (ALND) without any false-positive results. The sensitivity and specificity of US-guided FNAB were 63.3% and 100%, respectively. US-guided FNAB was accurate in predicting the status of the axilla in 76.1% of patients.

Conclusion: Although this technique is favorable due to its minimally invasive nature, it is not as effective as sentinel lymph node biopsy (SLNB) in terms of detecting axillary metastasis preoperatively. The low sensitivity and low accuracy rates decrease the usefulness of the technique. Therefore, it seems that US-guided FNAB alone could not replace SLNB. Nevertheless, combining some other molecular studies may be useful in increasing the technique's sensitivity. These issues should be determined by comprehensive clinical trials.

Keywords: Breast cancer, axillary ultrasound, axillary staging, axillary lymph node sampling, axillary fine-needle aspiration biopsy

INTRODUCTION

It is evident that breast surgery for breast cancer has changed largely and will be changing in the future as well in a dynamic fashion. Identifying the presence of axillary node metastasis in patients with invasive breast cancer is critical for determining prognosis and for deciding on appropriate treatment. The benefits of preoperative identification of axillary metastasis include allowing the surgeon to proceed directly to axillary lymph node dissection (ALND), to avoid an unnecessary sentinel lymph node biopsy (SLNB) as well as the requirement for a second surgical procedure involving the axillary nodes.

Thanks to both increase in awareness and advances in diagnostic techniques for breast cancer, patients are being detected at earlier stages. Axillary lymph node dissection is associated with more adverse consequences than benefit in women undergoing breast-conserving therapy who don't have palpable, suspicious lymph nodes, who have tumors 3.0 cm or smaller, and who have 3 or fewer positive nodes on sentinel node biopsy (1). Breast conserving surgery was found to be as safe as modified radical mastectomy in terms of disease free and total survival rate in early breast cancer (2).

Knowing the axillary involvement status preoperatively is of great significance. In recent years, breast-conserving surgery has been preferred over modified radical mastectomy while SLNB became the standard axillary staging procedure. However, SLNB also has complications. SLNB is a time-consuming, costly and invasive technique (3). Ultrasound (US)-guided axillary lymph node (LN) biopsy can be an appreciable alternative that would avoid the necessity of SLNB.

In this study, we aimed to evaluate the accuracy and sensitivity rates of US-guided fine needle aspiration biopsy (FNAB) in determining axillary lymph node involvement through comparing FNAB cytology and post-operative histopathologic data, and if this technique could replace SLNB.

MATERIAL AND METHODS

This study included 46 patients with breast cancer who were treated in our clinic between January 2011 and July 2013. Those patients who had stage I and II early breast cancer were enrolled prospectively and informed consents were obtained. The cases who fulfilled the criteria for malignancy in mammography

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and/or ultrasound or had palpable breast lump confirmed by tru-cut biopsy as invasive breast cancer constituted the study group.

Patient Selection Criteria
This study included clinically node-negative early breast cancer patients. Patients with a previous history of axillary-breast surgery and/or axillary-breast radiotherapy and those diagnosed with excisional biopsy were excluded. Patients who received neo-adjuvant chemotherapy were also excluded.

All patients' demographic properties, tumor characteristics (size, grade, estrogen, progesterone receptor status, HER-2 neu status), cytopathology results of FNAB and SLNB, and post-operative pathologic findings were prospectively recorded. The FNAB, SLNB, and ALND data were compared and evaluated along with patient and tumor characteristics.

Radiologic Technique and Criteria
Patients who were histopathologically diagnosed with breast cancer preoperatively were referred to the interventional radiology department for axillary lymph node FNAB. The FNABs were performed by one particular radiologist experienced in breast ultrasound before the surgical intervention, after evaluating the axillary lymph node status in gray-scale using 13.5 mHz linear probe and Hitachi Avius High Vision device.

The axillary LNs were inspected with regard to size, shape (round, ovoid), contour, central and cortical echogenicity in gray-scale ultrasound. The abnormal sonographic findings concerning lymph nodes were accepted as enlargement, rounding or circular configuration, irregularity and lobulation of contour, hypoechoic internal echo, greater than 3 mm of cortical thickness and absence of fatty hilum.

The most suspicious looking LNs were selected for FNAB. If there was more than one malignant looking LN then the largest one was chosen for aspiration. US-guided FNAB was performed a few times from the cortex by a 20-22 G syringe. The thickest or focally thickened part of the suspicious LNs was sampled. When all the axillary nodes looked normal, the biopsy was obtained from the subcapsular cortex of the largest node.

Pathologic Technique and Criteria
The aspirated material was smeared and fixed with 95% alcohol, and was stained using the Papanicolaou method. Cell-block and cytospin were also prepared. An experienced pathologist examined and classified the specimens into four groups: Malignant, benign, suspicious for malignancy and inadequate for assessment.

Surgical Technique
The patients with malignant FNAB underwent complete ALND at the time of definitive surgery. The patients with benign, suspicious or insufficient FNABs underwent SLNB using blue-dye and/or radiocolloid injection.

Twenty-three of the patients had a mastectomy, and the other 23 patients had breast-conserving surgery according to patient's needs and both the patient's and the surgeon's choice. Sentinel lymph node biopsy was performed in twenty-three cases peroperatively.

Statistical Analysis
The cytology findings of the FNABs were compared with the pathologic reports of SLNB and ALNDs. The FNAB diagnoses were compared with the histological diagnosis of either SLNB and/or ALND, and the sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV) and accuracy rates were calculated.

In the evaluation of US-FNAB accuracy, the presence of metastasis and atypical cytologic results were regarded as positive. Inadequate sampling on FNAB was considered as a negative result since patients with inadequate sampling also underwent SLNB as in negative cytology.

When evaluating the findings obtained in this study, statistical analyses were performed using Statistical Package for the Social Sciences program, version 17.0 (SPSS Inc; Chicago, IL, USA). The data was evaluated as a diagnostic screening test (sensitivity, specificity). Cohen Kappa analysis and chi-square test were used for comparison of quantitative data and intergroup comparisons, along with descriptive statistical methods (median, minimum, maximum value). The results were evaluated at 95% confidence interval and the significance was set at $p<0.05$.

RESULTS

Findings
Fine needle aspiration biopsy was applied to 46 cases to determine the requirement for an axillary surgical procedure and axillary staging. All of the patients, except one, were women with a median age of 54 years (29-71 years). The comparative data of these cases is shown in Table 1. The FNABs revealed 19 malignant and 23 benign results.

Three cases had inadequate samples, and one had findings suspicious for malignancy. Both SLNB and ALND showed malignant findings in the patient with cytology findings suspicious for malignancy.

None of the patients with inadequate axillary sampling had metastatic lymph nodes on axillary dissection (Table 2).

Statistical Analysis
Cytologic and histopathologic axillary findings are summarized in Table 2. As seen in this table there was no false positive result but six false negative results. Inadequate and suspicious FNAB results were considered as negative cytology for practical reasons; hence, 19 positive and 27 negative results were included in the assessment (Table 3).

The diagnostic power of FNAB as a screening tool for identifying metastatic lymph nodes was evaluated statistically. In terms of predicting axillary lymph node status, the sensitivity of axillary FNAB was 63.3%, with a positive predictive value of 100%, specificity of 100%, negative predictive value of 59.3%, and an accuracy rate of 76.1%. The consistency of axillary FNAB with final axillary histopathologic data was evaluated with Cohen Kappa analysis. In the comparison of the two procedures, a statistically significant and positive relationship was detected (Kappa: 4,155; $p<0.001$).

All nine patients who underwent SLNB as the only axillary procedure had negative results in final histopathology. The final

Table 1. Comparison of patient's demographic and histopathologic properties with final axillary histopathology results (n=46)

	Axilla (+)		Axilla (-)		
Properties	**n**	**%**	**n**	**%**	**p**
Age					0.367
≤50	9	32,1	9	50.0	
>50	19	67,9	9	50.0	
Axillary side					0.503
Right	15	53,6	7	38.9	
Left	13	46,4	11	61.1	
Menopausal status					0.367
Premenopausal	9	32,1	9	50.0	
Postmenopausal	19	67,9	9	50.0	
Family history					0.552
Negative	27	96,4	16	88.9	
Positive	1	3,6	2	11.1	
cT stage					0.948
I	14	50,0	8	44.4	
II	14	50,0	10	55.6	
cN stage					0.453
N0	22	78,6	16	88.9	
N+	6	21,4	2	11.1	
Clinical stage					0.300
I	13	46,4	7	38.9	
IIA	10	35,7	10	55.6	
IIB	5	17,9	1	5.5	
Histologic type					0.054
Invasive ductal carcinoma	28	100,0	15	83.3	
Other	0	0,0	3	16.7	
Surgery					0.131
BCT	11	39,2	12	66.6	
Mastectomy	17	60,8	6	33.4	
Axillary procedure					**<0.001***
SLNB	0	0,0	9	50.0	
ALND	17	60,7	6	33.3	
SLNB+ALND	11	39,3	3	16.7	
Estrogen receptor					1.000
Negative	6	21,4	4	22.2	
Positive	22	78,6	14	77.8	
Progesterone receptor					0.728
Negative	6	21,4	5	27.8	
Positive	22	78,6	13	72.2	
Hormone receptor					1.000
Negative	5	17,9	3	16.6	
Positive	23	82,1	15	83.4	
Cerb-B2					0.072
Negative	14	50,0	14	77.8	
Positive	14	50,0	4	22.2	
FNAB					
FNAB (+)	19	67,9	0	0.0	**<0.001***
FNAB (-)	6	21,4	17	94.4	
FNAB (Inadequate)	3	10.7	1	5.6	

Chi-square Test, *p<0.05. c: clinical; BCT: breast-conserving therapy; SLNB: sentinel lymph node biopsy; ALND: axillary lymph node dissection; FNAB: fine needle aspiration biopsy

histopathology reports were positive in 92.9% and negative in 7.1% of 14 cases who underwent both SLNB and ALND. Within the 23 patients with only ALND, 73.9% had positive and 26.1% negative results in their final histopathology reports. According to these findings, the histopathologic axillary lymph node involvement showed statistically significant difference between different types of axillary surgery (p≤0.001).

All 19 patients who had positive FNABs were found to be positive in the final axillary histopathology. Twenty-seven cases had negative FNABs, 11 of which (29.6%) were found to have positive results in the final histopathology (p≤0.001).

While 28 of 43 cases (65.1%) with invasive ductal carcinoma as the histological type had positive lymph nodes in the final histopathology, none of the other histologic tumor types had a positive lymph node. The obtained data revealed that histopathologic axillary lymph node involvement rate had a statistically significant difference between different tumor types (p=0.054).

DISCUSSION

US-Guided FNAB as a Minimally Invasive Technique in Axillary Staging

Ultrasound-guided axillary FNAB has been carried out since 1997 (4, 5). US- guided FNAB emerged almost at the same time with SLNB, as an alternative technique. As it can be expected, through the technical development in ultrasound devices and introduction of high-resolution machines, the accuracy of FNAB has increased. It has been shown that lymph nodes

Table 2. Correlation between cytologic and histologic data

	Histology		
Cytology	**Benign**	**Malignant**	**n**
Inadequate	3/TN	1 /FN	4
Benign	18/TN	5 /FN	23
Malignant	0/FP	19 /TP	19
Total	21	25	46

TN: true negative; FN: false negative; FP: false positive; TP: true positive

Table 3. Correlation between FNAB results and axillary lymph node histopathology (n=46)

	Axillary histopathology				
Axillary FNAB	**Positive**	**Negative**	**Total**	**K[a]**	**p**
Positive	19	0	19	4.155	<0.001*
Negative	11	16	27		
Total	30	16	46		
Sensitivity		63.3%			
Specificity		100%			
Positive predictive value		100%			
Negative predictive value		59.3%			
Accuracy rate		76.1%			

[a]: Cohen Kappa analysis; *p<0.05. FNAB: fine needle aspiration biopsy

might be evaluated quite accurately with ultrasound (6). Many studies indicated that preoperative staging with axillary lymph node FNAB guides management rather correctly. Chang et al. (7) reported a considerably high positive and negative predictive value for US-FNAB as 98.7% and 81.8%, respectively.

If the preoperative axillary FNAB is positive then the decision for axillary dissection without SLNB can be straightforward. This technique also affects decisions on neoadjuvant chemotherapy, oncologic surgery and simultaneous reconstruction. Additionally, axillary lymph node sampling with US-FNAB performed before and after neo-adjuvant chemotherapy might be useful in the evaluation of treatment response (8).

Thanks to both comprehensive breast screening programs and the increased public awareness on breast cancer, the disease can be diagnosed at early stages in recent years. In such circumstances, a patient is less likely to have clinical or microscopic lymph node involvement on admission. Enlarged reactive LNs are another cause of clinically false positive evaluations. Size is not a useful criterion for distinguishing normal from abnormal axillary lymph nodes. Reactive or fatty lymph nodes may be large enough to be palpable and can be mistaken for metastatic disease (9).

Topal et al. (10) reported that the sensitivity of physical examination alone in axillary staging was 34-76%, and that of sonography was 36-92%. Nevertheless, Lumachi and colleagues suggested that by combining US with FNAB the specificity increased, the sensitivity remained unchanged, and a 100% specificity rate could be achieved in specialized breast centers (11). The ratio of false negative and false positive results on clinical examination is approximately equal to 1/3 (12). Similarly, the sensitivity rate was low while the specificity rate was pleasing in our study (Figure 1).

In a review published in JAMA, Rao et al. (1) advocated that axillary dissection was associated with more harm than benefit in women undergoing Breast Conserving Surgery (BCS) who do not have palpable, suspicious lymph nodes, have tumors 3.0 cm or smaller, and have 3 or fewer positive nodes on SLNB. In addition, the multi-disciplinary ACOSOG trial showed that completion of axillary dissection in clinical T1/T2, N0 tumors with a positive SLNB had no significant impact on local-regional recurrence and overall survival rates (13).

Factors Influencing Sensitivity and Specificity Rates

The number of involved lymph nodes is correlated with the sensitivity rate of US-FNAB. In case of involvement of two or more lymph nodes, the sensitivity increases from 47.1% to 80% (14). Deurloo et al. (15) suggested that the sensitivity and specificity rate of US-FNAB could be enhanced when lymph nodes with a cortical thickness of more than 2 mm were chosen for sampling.

The tumor size influences axillary lymph node involvement. As the tumor size grows, there is an increase in the number of involved nodes. The prognosis of small sized tumors that have axillary involvement is better than that of large ones (16). Especially, in primary breast cancer without axillary involvement, tumor location has prognostic value. Laterally localized tumors are more likely to metastasize to the axilla as compared to medially localized tumors. The tumor size means delayed diagnosis on the tumor dynamics. The tumors become more aggressive as they grow while more aggressive tumors grow faster.

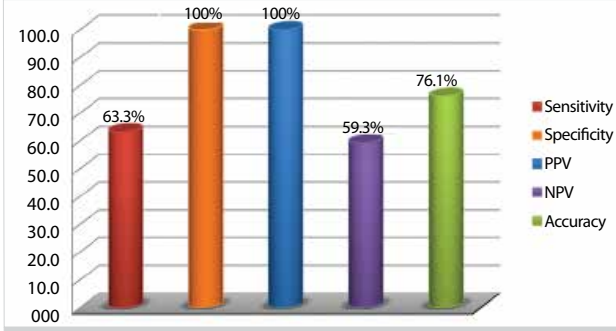

Figure 1. Diagnostic test results for fine needle aspiration biopsy
PPV: positive predictive value; NPV: negative predictive value

In our series, one patient had a sonographic negative axilla and was regarded as benign. The same patient's SLNB revealed negative findings for malignancy.

Even though FNAB is a less invasive, less expensive and rapid method for the evaluation of the axilla as compared to SLNB, the sensitivity of FNAB is not as high, and a negative result mandates SLNB. For this reason, the node positive group benefits most from axillary FNAB (17).

A review of the relevant literature, despite the methodologic differences in sampling and variability in patient populations, showed that unnecessary SLNBs were avoided in 1-28% of patients with preoperative axillary FNAB (18).

It is worth to consider that while the FNAB was negative in three cases and was positive in SLNB, none of them had metastatic lymph nodes in ALND.

The axillary lymph node FNAB produced false negative results in 19% of cases. It is difficult to explain all of them with micrometastasis. The biopsy should be repeated in case of non-diagnostic/insufficient cytology result since this group of patients has an extremely high proportion of positive nodes (19).

Various studies have reported the sensitivity and specificity rates of FNAB between 25-95% and 97-100%, respectively (8, 14, 20-30). False positive results has been reported around 1.4-1.6% (20, 23, 30), and false negative rates as 8-12% (15, 23, 24, 26, 29-31).

In our study, we found that the sensitivity and specificity of US-guided FNAB were 63.3% and 100%, respectively, with a negative predictive value of 59.3% and a positive predictive value of 100%.

The possible causes of false negative results may be the failure in imaging all the nodes, sampling error, micro-metastasis, mistakes in radiologic and pathologic assessment (30, 31).

Methods such as sampling more than one node, using immunohistochemical staining and imprint cytology have been proposed in order to increase sensitivity and accuracy in determining lymph node status with SLNB (32, 33).

In case of skip metastasis, it is clear that FNAB is more advantageous than SLNB. It is reported that metastatic disease could skip to level II nodes without involving level I nodes (34). With FNAB, not only the sentinel nodes but any lymph nodes that carry sonographic malignancy criteria can be sampled.

CONCLUSION

US-guided axillary lymph node FNAB has several advantages as well as disadvantages. The benefit of preoperative identification of axillary metastases is that it allows the surgeon to proceed directly to ALND, to avoid an unnecessary SLNB and a second surgical procedure involving the axillary nodes. Fine needle aspiration biopsy has almost no morbidity. The procedure is quick, minimally invasive and barely painful. Therefore, it is preferable in preoperative breast cancer staging.

Its false-negativity is especially detected in lymph nodes with partial involvement of micro-metastases or isolated tumor cells. However, the necessity of axillary dissection in such situations is also controversial. As for another disadvantage, US-guided axillary FNAB is a quite operator-dependent technique.

The sensitivity, specificity, negative and positive predictive value of axillary FNAB for assessment of axillary lymph node involvement in early breast cancer were determined in 46 breast cancer patients treated in January 2011-July 2013 in the General Surgery Clinic of Haseki Training and Research Hospital. We identified the sensitivity rate of axillary FNAB as 63.3%, positive predictive value of 100%, specificity of 100%, negative predictive value of 59.3% and accuracy of 76.1%.

Our sensitivity rate and negative predictive value of FNAB for axillary staging in early breast cancer was relatively lower than similar studies. The rates from specialized centers seem to be better. This study was the first experience in axillary staging with FNAB from our clinic with a limited number of cases. We think our study would be a modest contribution to the literature.

Since the sensitivity of US-guided FNAB is not satisfactory, FNAB cannot replace SLNB for the time being. As a minimally invasive technique, US-guided axillary lymph node FNAB should be evaluated by comprehensive clinical trials.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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Editorial Comment

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Re: Predictive value of fine needle aspiration biopsy of axillary lymph nodes in preoperative breast cancer staging

Can Atalay

Axillary management in breast cancer has evolved tremendously in the last decades. Sentinel lymph node biopsy (SLNB) has replaced axillary dissection in patients without any clinical and radiological involvement in the axilla. Although the complication rate of SLNB is lower than axillary dissection, the search for an accurate method to determine the axillary status in breast cancer with even lower complication rate is continuing. Fine needle aspiration biopsy (FNAB) is performed under ultrasonography guidance in case of suspicious lymph nodes in the axilla, especially in those with cortical thickening or decreased echogenecity in the hilum in addition to changes in size and shape of the lymph node. The accuracy of FNAB in predicting the status of the axilla is investigated in recent studies. Fine needle aspiration biopsy of the axilla helps the clinician in determining surgical approach and neoadjuvant chemotherapy. Nowadays, extent of axillary surgery has almost no definitive role in deciding the mode of adjuvant treatment. Obtaining information about the presence of metastatic disease in the axilla is enough to determine the prognosis of the patient. However, 30% of axillary metastases were detected with FNAB under ultrasonography guidance and additional 30% with SLNB whereas the axillary status of the remaining patients were determined by histopathologic examination (1). In addition to the information about the axilla, FNAB enables us to place clips into the metastatic lymph nodes to follow the results of neoadjuvant treatment.

Akinci et al. investigated this topic in the article entitled "Predictive value of fine needle aspiration biopsy of axillary lymph nodes in preoperative breast cancer staging" (2). This study aimed to determine the role of ultrasound-guided FNAB in axillary staging. Sensitivity, specificity, positive and negative predictive value, and accuracy of FNAB were studied. Sensitivity and negative predictive value showed moderate values (60%) whereas specificity and positive predictive values were 100%. Overall accuracy of axillary FNAB was reported as 76.1%. These results are in accordance with the results of the previous studies. Sensitivity of FNAB under ultrasound guidance changes between 45-95% and the specificity is almost 100% (3, 4). Microbiopsies using larger needles and addition of immunohistochemical examination increase the sensitivity and presence of micrometastases in the lymph node contributes to the false negative results (5). Small number of patients included in the study may be its limitation, however, prospective design of the study supports the results with higher reliability. Finally, this study encourages the clinicians to utilize ultrasound-guided FNAB more frequently to avoid unnecessary SLNB in breast cancer.

As a conclusion, randomized controlled trials including large enough number of patients are required to establish the value of FNAB in axillary staging of breast cancer. Sentinel node vs. observation after axillary ultrasound (SOUND) trial is an ongoing prospective randomized trial comparing SLNB and no axillary surgery in patients with normal axillary ultrasound (6). If a high predictive power of FNAB for axillary lymph node metastases could be proven, SLNB might be replaced by this method in the future. Detection of axillary metastases with FNAB might avoid performing SLNB and frozen section study decreasing time spent during surgery and total expenses in treatment.

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Original Investigation

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Laparoscopic resection for colorectal diseases: short-term outcomes of a single center

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ABSTRACT

Objective: Even though, laparoscopy is not accepted as the current gold standard in colorectal surgery, it can be performed as safely as open surgery. It is also widely accepted that the technique has many advantages. In this study, we evaluated the results of 33 patients with laparoscopic colorectal resection.

Material and Methods: Thirty-three patients who underwent laparoscopic colon surgery between January 2013 and September 2014 in the General Surgery Clinic at Marmara University Hospital were included in the study. Patients were evaluated in terms of their demographic and tumor histopathologic characteristics, type of surgery and early postoperative complications.

Results: Laparoscopic colorectal resection was performed for 33 patients who had malignant or benign lesions. The median age was 60 (35-70), and 18 (55%) were male patients. The majority of the patients (90%) were diagnosed with colorectal adenocarcinoma. Half of the patients were T3 and 67% had N0 stage. The median number of retrieved lymph nodes was 17 (4-28). Negative surgical margins were obtained in all patients. The postoperative hospital stay was 5 (4-16) days. Postoperative early complications were observed in only 5 patients. The majority of complications were treated without the need for surgery. No mortality was recorded in this series of patients.

Conclusion: This study showed that laparoscopic colorectal surgery could be performed safely based on its low complication rate, short length of hospital stay, providing sufficient surgical resection and lymph node dissection.

Keywords: Laparoscopy, colorectal surgery, colon resection

INTRODUCTION

Laparoscopic colorectal surgery provides less postoperative pain, better cosmesis, shorter hospital stay and earlier patient mobilization (1, 2). Jacobs et al. (3) performed the first laparoscopic colon resection in 1991 (3). However, it took time to be adopted due to its technical difficulties, lack of clinical evidence, the learning curve and fear of tumor seeding (4, 5). The recently published case series proved that there was no significant difference between open and laparoscopic colorectal surgery in terms of tumor recurrence, distant metastasis rates and disease free survival (6-8). Although laparoscopy is still not the gold standard in colorectal surgery, its advantages in experienced hands are acknowledged (9). In our study, we presented 33 cases who underwent laparoscopic colorectal resection for benign or malignant diseases.

MATERIAL AND METHODS

Thirty-three patients underwent laparoscopic colorectal surgery between January 2013-September 2014. An ethics committee approval was obtained from Marmara University. Our prospective database consisted of information on patient demographics, pathology reports (TNM stage, number of dissected lymph nodes), operation type, complications and length of hospital stay.

All the patients were evaluated for presence of locoregional disease and distant metastasis with colonoscopy, computed thoracic and abdominal tomography and/or pelvic magnetic resonance imaging. Patients were informed on laparoscopic surgery and their consents were obtained. Locally advanced rectal cancers were treated with neoadjuvant chemotherapy and radiation therapy. Preoperative bowel preparation was achieved by sodium phosphate containing purgatives, and the antibiotic prophylaxis consisted of 2 gr Cefazolin and 500 mg Metronidazole. A second antibiotic dose was administered in operations lasting longer than 4 hours. Low molecular weight heparins were applied for thrombo-emboli prophylaxis with a dose adjusted for body weight 12 hours before the operation.

Under general anesthesia, a 1 cm supra-umbilical skin incision was done followed by Veress needle insertion for carbon dioxide insufflation up to 10-12 millimeter mercury (mmHg). Mesocolic excision was performed for colon tumors and total mesorectal excision was performed for rectal cancers. To avoid seeding and surgical site infection, a wound protector was used in all operations (Alexis® O™ Retrac-

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tor. Applied Medical Resources Corporation, Rancho Santa Margarita, CA; USA). Negative pressure drains were placed to the operative field after completion of surgical procedure. Postoperatively, peroral feeding was started either when the bowel movements were observed or with patient declaration of flatus. Early and late complications were recorded by weekly patient visits or by using radiologic assessment tools up to 1 month.

The surgical specimens were evaluated for tumor type, grade, lymph node number and metastasis, presence of perineural invasion and surgical margins. Staging was done according to the American Joint Committee on Cancer (AJCC) 2010 system.

Statistical Analysis

Data were analyzed using Statistical Package for Social Sciences for Windows version 17.0 (SPSS Inc; Chicago, IL, USA). Parametric data was given as mean±standard deviation, and nonparametric data as median with range (minimum-maximum).

RESULTS

Three hundred and sixty-six patients underwent colorectal surgery for either benign or malignant etiologies between January 2013-September 2013 36 (10%) of whom were operated laparoscopically. In the laparoscopy group, three surgeries were converted to open procedures; hence, 33 patients were included in the final analysis. The mean patient age was 60 (35-70) years, and 56% (n: 18) were male. Ninety percent of patients were diagnosed with colorectal adenocarcinoma. Anorectal cancer constituted 45% (n: 15), and 43% of them were treated with neoadjuvant chemotherapy and radiotherapy (Table 1). Patients with anorectal cancer were treated with abdominoperineal resection (n: 9) or low anterior resection (n: 6); loop ileostomy was performed in 5 patients in addition to coloanal anastomosis. All rectal cancers were operated by using the total mesorectal excision technique. Patients who were operated laparoscopically for benign diseases included one patient with Crohn's disease, one with familial adenomatous polyposis and one with villous adenoma (Table 2).

Co-morbid diseases consisted of diabetes mellitus (18%), hypertension (6%), chronic obstructive pulmonary disease (3%), and coronary artery disease (3%).

Histopathologic results are shown in Table 3. Two patients had in situ carcinoma, 1 T1, 3 T2, and 14 had T3 cancers. The median number of dissected lymph nodes was 17 (range: 4-28). The patient with 4 dissected lymph nodes in the final specimen was diagnosed as carcinoma in situ. 67% of the patients were lymphatic metastasis free, 23% (n: 7) had N1, and 10% (n: 3) had N2 disease. Surgical margins were negative in all patients. The median length of hospital stay was 5 (4-16) days.

15.2% of the patients had early postoperative complications. Superficial surgical site infection was observed in 1 patient who had right hemicolectomy and in 1 patient who had anterior resection. They both were treated with drainage and antibiotics. One patient with abdominoperineal resection had bowel obstruction, and he was treated by nasogastric decompression alone without requiring an additional operation. One patient who had laparoscopic right hemicolectomy was re-operated for long lasting bowel obstruction. An intraabdominal abscess was detected around the anastomosis, the abscess was drained. At the 3rd postoperative day, drains were withdrawn and the patient was discharged. Another patient who had a history of chronic obstructive pulmonary disease underwent laparoscopic right hemicolectomy. He had respiratory distress on the 2nd postoperative day and was followed up in the intensive care unit with noninvasive mechanical ventilation for 3 days. No further complications occurred. We did not have any fatal events in our series.

Table 1. Demographics and preoperative characteristics of patients (n=33)

Age [Median (Min-Max)]	60 (30-75)
Gender	
Male	18 (55%)
Female	15 (45%)
Preoperative diagnosis	
Adenocarcinoma	30 (91%)
Attenuated FAP	1 (3%)
Villous adenoma	1 (3%)
Crohn's disease	1 (3%)
Localization of the lesion	
Cecum	5 (15%)
Ascending colon	5 (15%)
Descending colon	2 (6%)
Sigmoid colon	6 (18%)
Rectum	12 (36%)
Anal canal	3 (9%)
Liver metastasis	2 (6%)
Neoadjuvant radiotherapy	13 (43%)

FAP: familial adenomatous polyposis

Table 2. Types of laparoscopic procedures performed

Laparoscopic procedure	Number of patients (%)
Abdominoperineal resection	8 (24.2)
Abdominoperineal resection +liver metastasectomy	1 (3)
Ileocecal resection	1 (3)
Sigmoid colon + small bowel resection	1 (3)
Low anterior resection	4 (12,1)
Low anterior resection + loop ileostomy	5 (16,2)
Right hemicolectomy	9 (27.3)
Sigmoid resection	3 (9,1)
Left hemicolectomy	1 (3)
Total	33 (100)

DISCUSSION

In this study, we presented our case series of 33 patients who underwent laparoscopic colorectal surgery. Laparoscopic sur-

Table 3. Histopathologic characteristics of patients with colorectal cancer (n=30)

Grade	Number (%)
1	3 (10)
2	8 (60)
3	1 (3)
Undetermined	8 (27)
T stage	
In situ carcinoma	2 (6)
1	1 (3)
2	3 (10)
3	14 (47)
4	6 (20)
No tumor	4 (13)
N stage	
0	20 (66.6)
1	7 (23.3)
2	3 (10)
Number of retrieved lymph nodes (median)	17 (4-28)
Lymphovascular invasion	10 (33)
Perineural invasion	8 (275)
Positive surgical margin	0 (0)

gery constitutes 10% of our colorectal operations. Therefore, the number of patients is low as compared to open surgery. Major limitations of this study are the small sample size, short follow-up period and the retrospective design of the study. In addition, the outcomes of this study group were not compared with that of patients with open surgery.

Nowadays, laparoscopic surgery is being widely used for the treatment of both malignant and benign colorectal diseases. It has advantages such as better cosmesis, shorter hospital stay, lower incisional hernia incidence and early mobilization as compared to open surgery. Grupta et al. found that systemic immunity appears to be preserved better in laparoscopic surgery as compared to open surgery (10). In our series, laparoscopic colorectal surgery constituted 10% of all colorectal cases and our rate of conversion to open surgery was 8%. The literature states the conversion rate to open surgery between 17-20% (11-13). Our low conversion rate may be due to patient selection.

The complication rate in laparoscopic colorectal surgery is not higher than in open surgery (14-16). In previous studies, the complication rates were found to be between 1.5–36% (17-19). Our complication rate was determined as 15%. The most common complication in our series was superficial surgical site infection (6%).

There are relative contraindications for laparoscopic colorectal surgery such as major cardiac or pulmonary disease, portal hypertension, coagulopathy, pregnancy, tumor obstruction and/or perforation, as well as T4 tumors (20). In our study, 6 (18%) patients had T4 disease and underwent laparoscopic resection.

In laparoscopic colorectal surgery, using a video processor with a magnification function aids the surgeon to visualize the hypogastric plexus, ureters and gonadal arteries. Direct visualization helps decreasing the risk of major injuries to these vital structures. Our follow-up period and study size are low to interpret its oncologic outcomes. The minimum number of dissected lymph nodes is reported as 12 for proper staging (21). Our mean number of lymph nodes in the final pathology specimens was 17, and all the resection specimens had tumor-free surgical margins.

CONCLUSION

Laparoscopy is currently not the gold standard in colorectal surgery. Nevertheless, it can be performed safely by colorectal surgeons and has advantages such as low complication rate, short hospital stay, sufficient extent of surgical resection and lymph node dissection.

Ethics Committee Approval: Ethics committee approval was obtained for this study from the ethics committee of Marmara University.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - W.A.; Design - W.A., A.C., Ö.G.; Supervision - Ö.G., M.Ü.U., S.Y., A.C.; Resources - W.A., S.Y., H.B.; Materials - W.A., S.Y., A.C., Ö.G.; Data Collection and/or Processing - H.B., W.A., M.Ü.U.; Analysis and/or Interpretation - W.A., S.Y., A.C., Ö.G.; Literature Search - W.A., S.Y., H.B.; Writing Manuscript - W.A.; Critical Review - A.C., M.Ü.U., Ö.G.

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Invited Review

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Evolution of management in peritoneal surface malignancies

Emel Canbay[1,2], Bahar Canbay Torun[3], Ege Sinan Torun[4], Yutaka Yonemura[1,2]

ABSTRACT

Management of peritoneal surface malignancies has gradually evolved by the introduction of cytoreductive surgery in combination with intraperitoneal chemotherapy applications. Recently, peritoneal metastases of intraabdominal solid organ tumors and primary peritoneal malignancies such as peritoneal mesothelioma are being treated with this new approach. Selection criteria are important to reduce morbidity and mortality rates of patients who will experience minimal or no benefit from these combined treatment modalities. Management of peritoneal surface malignancies with this current trend is presented in this review.

Keywords: Heated chemotherapy, peritoneal metastases, colorectal cancer, gastric cancer, ovarian cancer, mesothelioma

INTRODUCTION

Peritoneal surface malignancies (PSM) originating from the gastrointestinal tract organs, pseudomyxoma peritonei (PMP), ovaries and peritoneum have been considered as lethal diseases with dismal prognosis. The clinical course of tumors at this stage are characterized by a deterioration in quality of life and shortened life expectancy. Supportive care and systemic chemotherapy were the mainstay of treatment for these patients. However, continuous clinical research revealed that PSM treatment and even cure could be achieved with cytoreductive surgery (CRS) and hyperthermic intraoperative intraperitoneal chemotherapy (HIPEC). Appendiceal tumors or PMP (1, 2), and malignant peritoneal mesothelioma (3) have been treated successfully by CRS and HIPEC. Besides this, the role of CRS and HIPEC in the management of PSM that originates from ovary, stomach, colon and rectum is still under investigation. In this review, we summarized the results of CRS and HIPEC in the management of PSM as new treatment modalities.

Colorectal Cancer

Isolated peritoneal metastases develop in 8.5-25% of patients with colorectal cancer (CRC) (4, 5). Median survival is expected to be 6 to 12 months when peritoneal metastasis (PM) of CRC is treated with palliative intent. Systemic chemotherapy does not seem to provide better survival rates for these patients (6-8). It has been reported that prolonged survival was obtained with CRS and HIPEC in CRC patients with PM (9-17). A randomized controlled study from the Netherlands Cancer Institute supported these results (18). According to 8-years follow up results of this trial, when a complete cytoreduction was achieved, a 5-year survival rate was observed in 45% of these patients.

Completeness of cytoreduction, biological characteristics of the tumors and the extent of disease were found to be significant prognostic factors (19, 20). Similarly, a recent consensus statement on PM of CRC highlighted the importance of complete cytoreductive surgery in these patients (21). Therefore, CRC cases with PM have to be referred to a Peritoneal Surface Malignancy Center and assessed properly to evaluate the extent of the disease prior to CRS and HIPEC.

Besides the improved outcome of these patients with these combined new treatment modalities, the question that remains to be solved is whether CRS and HIPEC are the best options for CRC patients with PM. After oxaliplatin- and irinotecan- based chemotherapy, and anti- VEGF biological therapy were introduced as new treatment strategies for metastatic CRC, the overall survival and progression free survival were improved in these patients with solid organ metastases such as lung and liver (22-25). However, abdominal diffusion of systemic chemotherapy may not be sufficient to the intraperitoneal cavity and peritoneal surfaces in the presence of metastatic nodules on peritoneal surface. Plasma peritoneal barrier (PPB) is usually 90 µm and diffusion of systemic chemotherapy from subperitoneal mesothelial tissue to the peritoneum is very limited or not possible especially if the tumor nodules penetrate to the peritoneal surface deeper than 5 mm. A clinical study comparing new systemic chemotherapy with CRS and HIPEC were required to evaluate the effectiveness of this combined approach versus systemic che-

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motherapy. This study showed that the median survival was 64 months in CRS and HIPEC arm while it was 23 months in modern systemic chemotherapy arm. The 5-year survival rate was 51% with CRS and HIPEC, and 13% with modern systemic chemotherapy. According to this study, CRS and HIPEC can prolong survival in patients with limited peritoneal metastasis of CRC. This combined approach, however, carries a high morbidity and mortality risk even though it has promising results with respect to disease free survival and overall survival. Therefore, patient selection is important to tailor therapeutic plan in patients with short life expectancy.

Colorectal cancer patients with peritoneal dissemination might also have liver metastases. A recent systematic review and meta-analysis investigated the outcomes of liver resections combined with CRS and HIPEC in CRC patients with hepatic and PM (26). This study showed that CRC patients with isolated PM have a much longer overall survival as compared to patients with liver and PM. Besides this, the patients in this study demonstrated an increased median overall survival after CRS and HIPEC with hepatic resection as compared to treatment with modern systemic chemotherapy. Ongoing prospective randomized clinical trial results will clarify the necessity of HIPEC after curative resection in these patients (27).

Pseudomyxoma Peritonei

Pseudomyxoma peritonei is a rare condition resulting from the rupture of mucinous appendiceal or ovarian tumors, or tumors of primary peritoneal origin. Pseudomyxoma peritonei is characterized by widespread mucinous deposits within the peritoneal cavity. Serial debulking and systemic chemotherapy were conventional treatment options of PMP with a high recurrence rate (28). The 10-year survival was 63% with CRS and HIPEC in patients with PMP (29). High-grade tumor histology, and induction chemotherapy were found to be poor prognostic factors in PMP patients (30).

Extent of the prior surgeries, high peritoneal cancer index (PCI) (31), elevated levels of CA19-9 (32) and CEA (33) were identified as poor prognostic factors by multivariate analysis. Peritoneal recurrence of PMP occurs as a result of the advanced stage of the disease at the time of initial diagnosis or as the consequence of relative chemoresistance to chemotherapy. Repeated CRS and HIPEC could be recommended to prolong survival in highly selected patients (34). Even though the treatment of PMP with CRS and HIPEC seems to provide promising results with low complication and mortality rates, the effects of this combined approach require further investigation to determine its potential benefits as a therapeutic procedure.

Gastric Cancer

Peritoneal metastases may be present in 5-20% of patients undergoing a potentially curative resection for gastric cancer (GC) at the time of initial diagnosis (35). Patients with PM that originated from GC have a poor prognosis and the estimated survival is 1-3 months without systemic treatment (36, 37). The median survival time does not exceed 9 months even with palliative systemic chemotherapy in these patients (38). Peritoneal involvement represents an independent risk factor for poor prognosis. Therefore, intraperitoneal chemotherapy has been proposed in GC patients with a high risk of peritoneal recurrence. Overall survival was prolonged in patients with intraperitoneal chemotherapy (39, 40). These results were also confirmed by a prospective randomized clinical trial (41). According to this study, even though the frequency of intraabdominal abscess and neutropenia were increased in surgery and HIPEC group, no statistically significant difference in morbidity was detected between radical surgery with HIPEC group and radical surgery group. Besides these improvements, the experience with CRS and HIPEC for PM of GC is still limited (42-45). Completeness of cytoreduction, PCI index less than 6, and response to systemic chemotherapy were found to be favorable prognostic factors in patients with PM of GC. Survival advantage with CRS and HIPEC can be obtained in patients with PM of GC (46). Recently, we reported that 152 of 194 (78.3%) PM of GC patients underwent CRS and HIPEC. In this group, the mortality was 3.9% and major complications occurred in 23.6% of patients. The median survival was 15.8 months and the 5-year survival rate was 10.7%. Multivariate analysis identified pathologic response to bidirectional intraperitoneal systemic chemotherapy, low tumor burden, and completeness of cytoreduction as prognostic factors (47). This study provides an important information in selection of cases who will benefit from this challenging combined approach.

Recent ongoing prospective randomized clinical studies will clarify the exact role of HIPEC and CRS in the management of PM of GC.

Ovarian Cancer

Standard management of patients with advanced stage ovarian cancer (OC) consists of optimal cytoreductive surgery followed by adjuvant systemic chemotherapy with taxane and platinum combination (48). However, despite the improved median overall survival with this regimen (up to 50 months), recurrence occurs in 75% of patients and 20-30% of these patients might have resistance to the platinum analogues (49). A survival benefit in patients treated with intraperitoneal chemotherapy and systemic chemotherapy as compared to systemic chemotherapy alone was also reported in a phase III trial (50). Intraperitoneal chemotherapy one dose prior to surgery yielded better survival rates than those who had only adjuvant systemic intravenous chemotherapy (51). Furthermore, the five-year survival rate can be increased from 17% to 58% with CRS and HIPEC in patients with recurrent ovarian cancer (52). Additionally, CRS with HIPEC might yield long-term survival in selected patients, especially in those with primary chemoresistance, and in recurrent advanced epithelial ovarian cancer patients (53). Complete cytoreduction was found to be a significant prognostic factor according to the results of this study. It has been reported that only 10% of patients with recurrent disease can undergo a complete resection, and the median overall survival can be only prolonged for 3 months according to the results of a recent meta-analysis (54). A clinical trial with a larger study group that addresses the role of CRS and HIPEC in recurrent ovarian carcinoma needs to be performed to determine the exact role of CRS and HIPEC in these patients.

Indeed, a phase III trial to examine the role of HIPEC in recurrent ovarian carcinoma was recently completed (55). In an 8-year period, the mean survival was 26.7 months in CRS with HIPEC and systemic adjuvant chemotherapy group, and was 13.4 months in patients treated with CRS and systemic adjuvant chemotherapy. The use of HIPEC, the extent of the dis-

ease, and the degree of cytoreduction have an important role in the survival of patients with recurrent ovarian cancer.

Diffuse Malignant Peritoneal Mesothelioma

Diffuse malignant peritoneal mesothelioma (DMPM) was considered as a fatal condition. Systemic chemotherapy and surgery showed limited benefit in this entity (56). Cytoreductive surgery with HIPEC showed a clear improvement in the outcome of DMPM as compared to traditional systemic chemotherapy (57-62).

A significantly prolonged survival was achieved in 405 patients with diffuse malignant peritoneal mesothelioma using CRS and HIPEC in a multi-institutional study (61). According to this study, the overall median survival was 53 months, and 5-year survival rate was 47%. Epithelial subtype, absence of lymph node metastasis, completeness of cytoreduction, and HIPEC were found to be independently associated with improved survival. A TNM staging for diffuse malignant peritoneal mesothelioma was recently proposed, and this classification is significantly correlated with survival advantages of this technique (62). CRS with HIPEC can be considered as a standard of care for patients with DMPM if optimal cytoreduction can be achieved.

The effect of new systemic cytotoxic agents such as pemetrexed prior to surgery in the treatment of peritoneal mesothelioma is gaining attention (63). If the patients are not suitable for an immediate surgery and intraperitoneal chemotherapy, they may be potential candidates for systemic chemotherapy with these new agents prior to surgery.

CONCLUSION

Peritoneal cavity needs to be considered as a specific organ consisting of two layers that cover the intraabdominal wall and serosal surface of intraabdominal organs. Peritoneal metastases can be treated with curative intent using CRS and HIPEC as a new evolving strategy. This approach achieves cure in many patients. The past three decades presented us sufficient information for patient selection and indications for the treatment of PM. HIPEC is the standard of care for PMP and PM of CRC, mesothelioma, and ovarian carcinoma while it is in the evaluation phase for GC. HIPEC is currently under investigation for treatment of PM of sarcoma, GIST, and small round cell desmoplastic tumors. Further studies will clarify the effectiveness of CRS in combination with HIPEC in PM of other intraabdominal solid organ tumors and primary peritoneal cancers.

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Case Series

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Fibroadenoma in the male breast: Truth or Myth?

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ABSTRACT

Truth or myth is seldom encountered in the practice of surgery, especially in cases of breast diseases. Yet, even after thousands of years of treating breast disease by surgeons/healers, fibroadenoma in the male breast seems to be a myth, due to the absence of fibro-glandular tissue. We wish to break this myth by our own experience as well as other studies by others all over the world, and unveil the truth that fibroadenoma in the male breast is a definitive entity and has a prevalence among the vast spectrum of breast diseases.

Keywords: Male, breast, fibroadenoma, tumour, benign lesion

INTRODUCTION

Diseases of the breast have influenced the world since ancient times. Fibroadenoma has almost always been associated with premenopausal female breast. A clinical diagnosis of fibroadenoma in the male breast is unexpected due to the lack of fibro-glandular tissue in normal males. Only a few cases of fibroadenomas in males have been reported in the literature; most of the reported cases involving male-to-female transsexuals (1, 2), or iatrogenic male fibroadenomas due to estrogen therapy for a medical condition in the elderly such as prostate carcinoma (3). Benign conditions such as gynecomastia, lipoma, epidermal inclusion cysts, and intraductal papilloma may mimic male breast cancer (4, 5). This article will attempt to highlight the truth behind the entity of fibroadenoma in males.

CASE SERIES

Over the last few years, we have come across 3 male cases with a breast lump. All patients were in the 18-23 years of age group. They were residing in different parts of the state of Madhya Pradesh and Chattisgarh. These patients presented with similar complaints of a lump in the breast (1: right subareolar, 2: right subareolar, 3: left subareolar) that has gradually been increasing in size since the last 1-2 years. The patients have ignored the lumps at first, and then consulted when the lump was large enough to be visible. There was no associated nipple discharge or ulceration in any of the cases. There was no history of any drug intake or other signs of any carcinoma, and no history of axillary swellings. The patients were born uneventfully after a full-term normal vaginal pregnancy. There was no family history suggestive of any other cardiac or cutaneous myxomas. The boys had attained sexual maturity at the ages of 14, 14 and 15 respectively. All other secondary sexual characters were normal and serum examination of hormonal profile was within normal limits.

These patients had soft, firm lumps in the breast measuring 2 x 2 cm, 4 x 3 cm and 2 x 1 cm, in the 1st, 2nd and 3rd patients, respectively, as described in the above paragraph. All the lumps were freely mobile and not fixed to the skin or underlying fascia. The surface of the lumps were lobulated.

Only the first patient underwent ultrasound that revealed a 2 x 2 cm solid, hypo-echoic, homogenous and well circumscribed mass (Figure 1). Fine needle aspiration cytology was done on all three patients on the lump which was suggestive of fibroadenoma (Figure 2).

Informed consent was obtained from all three patients, and they were subsequently investigated further and treated. Along with the regular information regarding their disease and the possible treatment options with benefits and risks, they were informed that we would be using their findings and treatment anonymously in some of our publications.

All three patients underwent simple nipple sparing subcutaneous mastectomy with lumpectomy by a periareolar incision (Figures 3, 4). This was done to rule any other possibilities of fibrocystic disease, for cosmetic purposes, and to differentiate between gynecomastia and fibroadenoma on histology.

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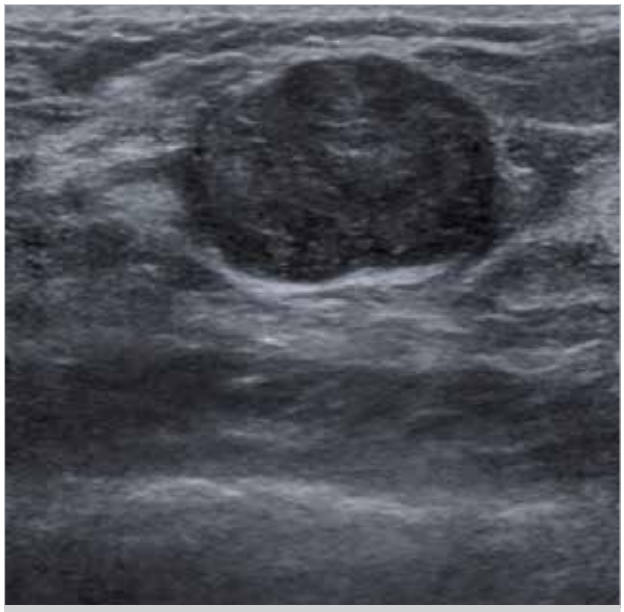

Figure 1. Ultrasonography showing fibroadenoma in the breast in the second patient

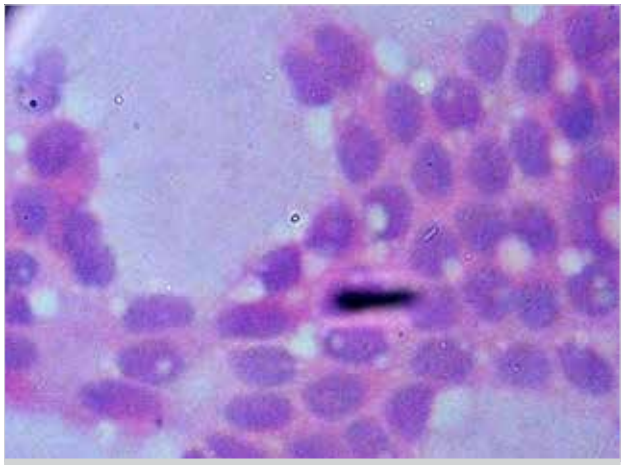

Figure 2. Fine needle aspiration cytology suggestive of fibroadenoma

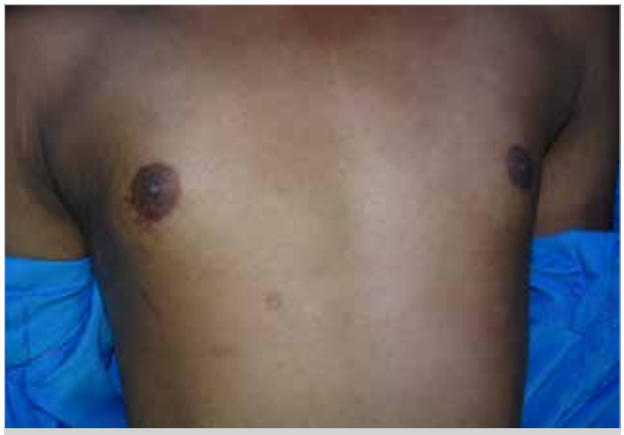

Figure 3. On operating table view of the 2nd patient showing a right breast lump

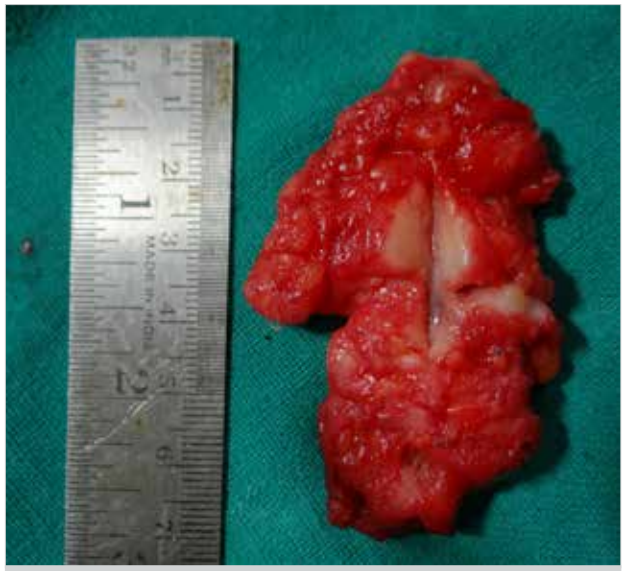

Figure 4. Gross specimen of the 3rd patient with a lump in the centre of gynecomastia

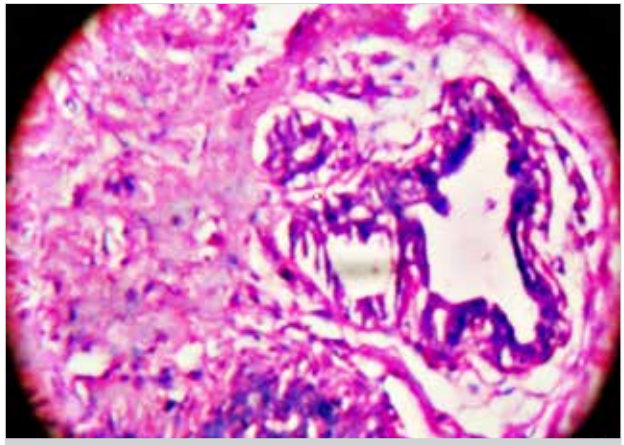

Figure 5. Histopathology suggestive of fibroadenoma in the 3rd patient

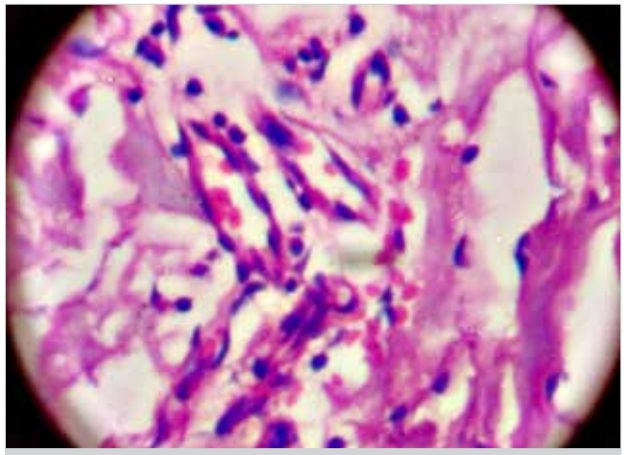

Figure 6. High magnification of histopathology evaluation suggestive of fibroadenoma in the 3rd patient

The histology showed florid ductal hyperplasia and focal secretory hyperplasia (Figures 5, 6). There were almost equal portions of epithelial and stromal components. The epithelial component of the rest of the breast specimen showed gynecomastia. The histopathology reports on all the patients were similar. Hence they were finally confirmed and diagnosed as male patients having fibroadenoma.

DISCUSSION

Fibroadenomas in the male breast are rare with only a few reported cases. Histologically, subareolar ducts are demonstrated in the normal male breast similar to those found in prepubertal girls (6). Holleb et al. (7) concluded that there was no true fibroadenoma of the male breast. It has been concluded by some authors that most of the reported lesions are poorly documented and nodular foci of gynecomastia have been reported as fibroadenomas (1). However, it is now apparent that fibroadenomas in the male breast are true events because there have been some reports in which fibroadenomas were well documented. Fibroadenomas have both estrogen and progesterone receptors (8). It has been discussed that proliferative changes in the male breast, like gynecomastia, lobular differentiation, and fibro-epithelial lesions are caused by hormonal imbalances and some medications. In the literature, fibroadenoma in the male breast appear to be always associated with gynecomastia. Shin and Rosen (9) could not find any reports of fibroadenoma in male patients who did not have concurrent gynecomastia. However, the presence of lobular differentiation with or without associated gynecomastia is less common (9). Lobular differentiation and fibroadenomas were found in two reported cases of male to female transsexuals who were undergoing demasculinization and feminization by hormonal therapy using ethinyl-oestradiol and cyproterone acetate and surgical treatment (10). Davis et al. (8) reported a case of a 19-year-old female with complete androgen insensitivity syndrome (CAIS) and a fibroadenoma of the breast. Four cases of male fibroadenomas have been reported in which gynecomastia with lobular differentiation was present in each case (11). One of the four patients had been treated with estrogens, whereas another patient had been treated with methyldopa and chlordiazepoxide. As Asscheman et al. (12) reported, there are genetic differences in estrogen sensitivity to dopaminergic regulation of prolactin secretion, and in the latter case, methyldopa was thought to play a role. For the other two patients, the possible causes of fibroadenoma formation remained elusive. In our cases, the presence of lobular differentiation was carefully sought; however, not found. In idiopathic pre-pubertal or senile gynecomastia, the increase in the plasma estrogen-to-androgen ratio usually will not induce acinar and lobular formation in the male breast. However, in transsexuals, in whom progestagenic antiandrogens, such as cyproterone acetate, are combined with feminizing estrogen therapy, then acini and lobular formation will occur (9, 13). The use of a luteinizing hormone-releasing hormone agonist to decrease testosterone levels for the treatment of advanced prostate cancer has contributed to the development of gynecomastia and fibroadenoma (9). Gynecomastia has also been associated with digitalis and spironolactone (14), which interfere with the production of testosterone and its conversion to the potent metabolite, 5-alfa-dihydrotestosterone (4, 10). Cimetidine is also a precursor of gynecomastia (15). Fibroadenomas in men without hormone treatment and with normal hormone levels are extremely rare. There is a report of single case of a man who had a fibroadenoma of the breast, gynecomastia, adenocarcinoma of the rectum, and polyposis coli, in which, the causative agent of the fibroadenoma was unknown and the development mechanism of the breast fibroadenoma was under question (16). Similarly, in all our cases, the patients did not have any causative factors as theorized until today and remains to be idiopathic. Leonard M Glassman, MD, had commented that "do not diagnose fibroadenoma in men even if it looks like fibroadenoma, and when you get such a biopsy result get another pathologist", but now we think that in the presence of very conclusive 3 cases, fibroadenoma in the breast can be seen in males and can be idiopathic.

CONCLUSION

In spite of the limited number of cases, taking the low prevalence of this particular pathology into consideration, it can be stated that idiopathic fibroadenoma in males is a possibility.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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Case Report

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Migration of mesh into gastric lumen: A rare complication of vertical banded gastroplasty

İlhan Ece, Hüseyin Yılmaz, Mustafa Şahin

ABSTRACT

The problem of revision of failed vertical banded gastroplasty (VBG) has become a common situation in bariatric surgery. Sleeve gastrectomy (SG) has been recently used to revise failed restrictive procedures. This study presents a patient that is treated with Roux-n-Y gastric bypass because of mesh migration after SG for revision of failed VBG.

Keywords: Vertical banded gastroplasty, revisional surgery, mesh migration

INTRODUCTION

Vertical banded gastroplasty (VBG) is a purely restrictive procedure in which the upper part of the stomach is partitioned by a vertical staple line with a tight outlet wrapped by a prosthetic mesh or silastic band (1). Weight regain following VBG may be related to staple-line dehiscence and stomal pouch dilation (2). Sleeve gastrectomy (SG) is a good alternative for revisional surgery. In this study, we present current treatment for the complication of an old method.

CASE PRESENTATION

A 32-year-old woman underwent open VBG for management of morbid obesity 11 years ago. Sleeve gastrectomy was performed for revisional surgery 3 years ago due to weight regain. The patient visited our outpatient clinic for epigastric pain that had persisted for the past 3 months. The physical examination was unremarkable except for mild tenderness in the epigastric region. Esophagogastroduodenoscopy demonstrated the gastroplasty mesh eroding into the stomach (Figure 1). Case was considered incomplete migration of VBG mesh (Figure 2, 3). Therefore, after taking the informed consent of patient, laparotomy was performed to confirm the mesh erosion. The mesh was removed, and Roux-en-Y gastric bypass was performed. Postoperative course was not eventful, and the patient was discharged on postoperative day 7.

DISCUSSION

Vertical banded gastroplasty a primarily restrictive bariatric surgical procedure, was first described by Mason (1). Weight loss occurs because of decreased caloric intake of solid food. Vertical banded gastroplasty has been documented as an effective operation for morbid obesity (3). However, the long-term results of VBG have been questioned by authors (4, 5). Several late complications have been described, including the need for revisional surgery in up to 56% of patients (6). Band erosion has been recognized as a potential late complication. The incidence of mesh or silastic ring erosion has been estimated at 0.4% to 3% (7). The average interval to mesh erosion has been reported at 3 to 4 years (7). Vertical banded gastroplasty has been replaced largely by other procedures and is rarely performed due to lack of sustained weight loss, as well as the high incidence of complications requiring revision (8). The most common cause of weight regain in VBG is staple-line disruption and pouch dilatation. Sleeve gastrectomy or Roux-n-Y gastric bypass could be selected according to the surgeon's experience, and patient's weight status for revisional surgery. In this study, we performed a sleeve gastrectomy 8 years after VBG. Sleeve gastrectomy was applied with open procedure because the patient had a laparotomy incision due to VBG.

Sleeve gastrectomy was improved as the first stage for biliopancreatic diversion and duodenal switch. However, SG was proved to be an effective bariatric procedure on a short-term basis. Restriction of passage for food through the stomach is the major mechanism for weight loss with this procedure. Another

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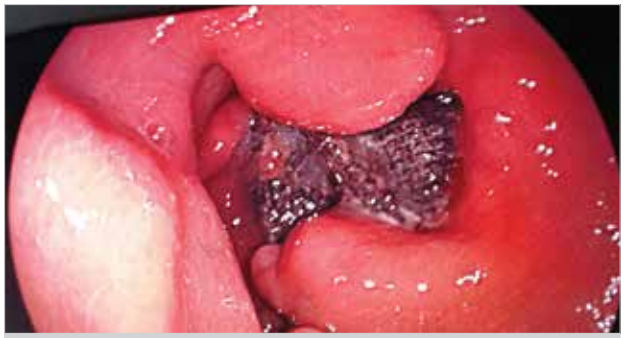

Figure 1. Image of the mesh in the stomach

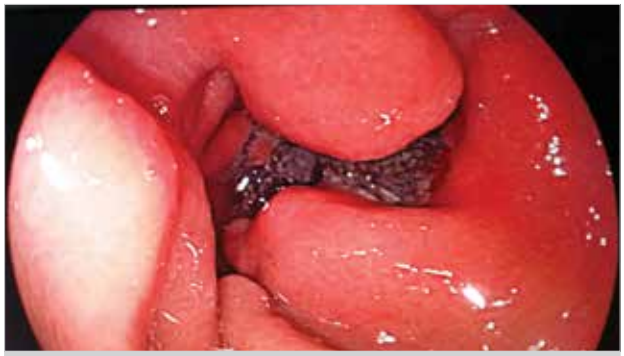

Figure 2. Incomplete migration of mesh

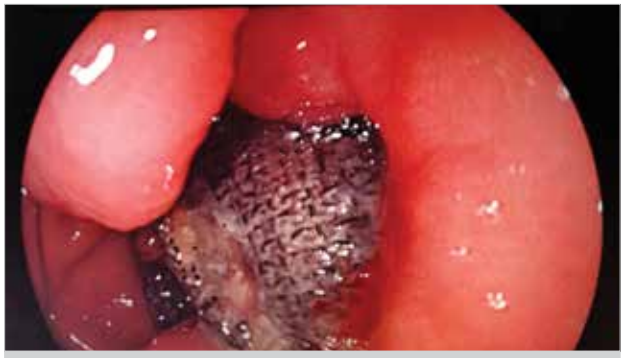

Figure 3. Mesh in the gastric lumen

widely investigated mechanism is reduction of ghrelin level by the excision of the gastric fundus (9). In the short-term follow-up, patients achieved severe weight loss. Most of surgeons widely performed this procedure due to its efficacy, technical simplicity, and low rate of morbidity. Furthermore, SG has been a preferred method for revisional surgery of failed VBG, also it should be noted that the remaining mesh could create serious problems in revisional procedures.

CONCLUSION

Revisional surgery that requires the release of the mesh can cause serious complications. Therefore, gastric bypass should be the first choice to prevent complications resulted from the remaining mesh for failed VBG.

Informed Consent: Written informed consent was obtained from patient who participated in this case.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - H.Y.; Design - İ.E.; Supervision - M.Ş.; Funding - M.Ş.; Data Collection and/or Processing - İ.E.; Analysis and/or Interpretation - İ.E.; Literature Review - İ.E., H.Y.; Writer - İ.E., H.Y.; Critical Review - M.Ş.

Conflict of Interest: No conflict of interest was declared by the authors.

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Case Report

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Incidental biliary cystadenoma mimicking liver metastasis in a gastric cancer patient

Pınar Yazıcı[1], Ünal Aydın[2]

ABSTRACT

Biliary cystadenoma represents a rare benign cystic hepatic neoplasm with premalignant potential. The diagnosis is usually difficult, and imaging methods may not be possible to clarify the pathology. It can be hard to determine, particularly in patients with a previous cancer history that has high metastatic potential in the liver. We presented a 53-year-old man with a newly diagnosed liver mass that was suspicious for metastasis 2 years after gastric cancer surgery and histological analysis confirmed the diagnosis of biliary cystadenoma.

Key Words: Gastric cancer, liver mass, biliary cystadenoma

INTRODUCTION

Biliary cystadenoma represents a rare benign cystic hepatic neoplasm with premalignant potential (1). The diagnosis is usually difficult, due to the similar clinical presentation as those of simple hepatic cysts. In addition, infected hepatic cysts, pyogenic abscess, degenerated liver tumor, Caroli disease, and post-traumatic or hemorrhagic cyst should be considered in the differential diagnosis. Radiological diagnostic methods for differentiating biliary cystadenoma from other malignant hepatic lesions may not be conclusive (2). Although this concern is not very important for the treatment approach to the management of focal liver lesions suspicious for biliary cystadenoma, it should be checked twice in a patient with a history of gastric cancer surgery, considering probable liver metastasis. Nevertheless, liver metastasis from gastric cancer is rarely cured, even by resection, with a 5-year survival rate of 11% (3). We presented a patient with gastric cancer which was complicated with a newly diagnosed liver mass that histological analysis confirmed the diagnosis of biliary cystadenoma.

CASE PRESENTATION

A 53-year-old man was admitted to our clinic due to the detection of a new liver lesion, which was suspected for metastasis. His surgical history was notable for a gastric cancer treated with total gastrectomy and esophagojejunostomy 2 years ago. The histopathological examination revealed a moderate to poorly differentiated 'intestinal-type' gastric adenocarcinoma infiltrating the muscularis propria. Resection margins and 27 lymph nodes were free of tumor (T2, N0, M0). In the routine clinic visit in the follow-up, laboratory investigations revealed a mild elevation in cancer antigen 19-9 (CA 19-9) level (49.2 U/L, normal range ≤24), and Doppler ultrasonography of the liver was performed. It demonstrated a new liver mass 25 x 17 mm in size that was located next to the left branch of the portal vein, showing central hyperechogenicity and cystic margins. A follow-up positron emission tomography was recommended, and this confirmed a hypermetabolic focus in segment IV A of the left hepatic lobe, suspicious for metastatic disease (maximum standardized uptake value: 5.7) (Figure 1, 2). Informed consent was obtained, and he underwent explorative laparotomy.

Intraoperative ultrasonography findings demonstrated a 23-mm mass located between segment IVB and III, with evidence of venous invasion. With regard to these findings, left lateral hepatectomy was performed under selective intermittent inflow occlusion, delineating the resection line. No intraoperative or postoperative complication was observed, and the patient was discharged on postoperative day 5. Histopathological examination revealed benign biliary cystadenoma of the liver. There was no recurrence after 18 months of follow-up.

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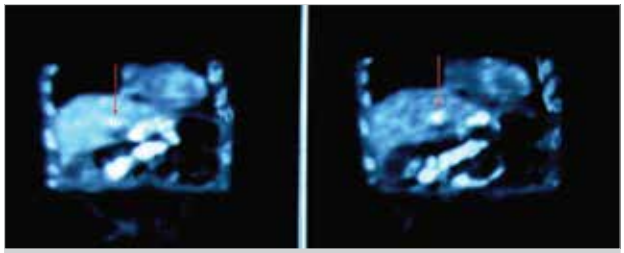

Figure 1. Hepatic mass (16 mm) located in the left lobe (arrow)

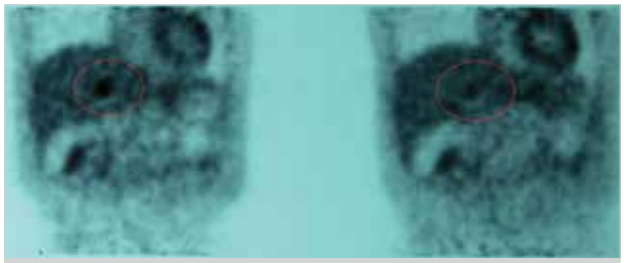

Figure 2. ^{18}F-fluorodeoxyglucose positron emission tomography, demonstrating metabolic hyperactivity of the hepatic nodule in the left lobe (red halo)

DISCUSSION

Biliary cyst tumors (cystadenoma or cystadenocarcinoma) account for 5% of all solitary cystic liver lesions. Although the initial diagnosis is usually made with abdominal imaging methods, they are not usually diagnostic despite being useful to characterize the lesion. Differential diagnoses include multiloculated or complicated biliary cysts, atypical hemangiomas, and hamartomas (4). It is hard to decide whether it is a new metastatic focus or another primary tumor, in the liver based on imaging or gross appearance, in a patient with a history of gastric cancer surgery. In our patient, elevated CA 19-9 level was considered as a marker of recurrence or metastatic disease.

Biliary cystadenomas are preoperatively misdiagnosed in 50% to 70% of cases, thus resulting in delayed and inaccurate treatment (5). The risk of recurrence is high if inadequate treatment is performed (6). Hence, the correct diagnosis is crucial. The preoperative radiological diagnostic accuracy may be as low as 30% for biliary cystadenoma, and therefore, a high index of suspicion is indicated (7). In the present case, Doppler ultrasound revealed a newly developed hypovascular liver mass containing cystic components and that was in close proximity to vascular structures and the lesion. Positron emission tomography also confirmed this lesion with increased metabolic activitiy. A history of gastric cancer surgery caused a diagnostic challenge for this patient and primarily raised the suspicion of metastatic liver disease. Although a histological examination usually offers the best differentiation, fine needle aspiration biopsy may not be helpful for the differential diagnosis of cystic liver tumors. Because the lesion was both single and easily accessible, instead of biopsy, we advocated surgical resection.

Complete surgical excision of the biliary cystadenoma is the optimal treatment approach to reduce the risk of both recurrence, with a rate of 10% (8, 9), and malignant transformation (5). Considering the malignant potential, radical resection remains the treatment of choice in patients with cystadenoma. In this patient, the main origin of the liver tumor was primarily considered metastatic due to a previous history of gastric cancer. Since the liver mass was small-sized, single, and appropriate for R0 resection, left lateral segmentectomy was performed.

CONCLUSION

This case emphasizes the infrequent manifestation of biliary cystadenoma, which can mimic metastatic liver disease in patients with previous gastric cancer. The prognosis for these two entities is very different, and accordingly, the proper diagnosis is important. However, diagnostic imaging methods may not be helpful. Hepatic resection and histological examination remain necessary to rule out metastasis in cystic tumors of the liver.

Informed Consent: Written informed consent was obtained from patient who participated in this case.

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Author Contributions: Concept - Ü.A.; Design - P.Y., Ü.A.; Supervision - Ü.A.; Funding - P.Y.; Materials - P.Y.; Data Collection and/or Processing - P.Y.; Analysis and/or Interpretation - P.Y., Ü.A.; Literature Review - P.Y.; Writer - P.Y.; Critical Review - Ü.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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Case Report

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Perineal rectosigmoidectomy for incarcerated rectal prolapse (Altemeier's procedure)

Mesut Sipahi, Ergin Arslan, Hasan Börekçi, Faruk Önder Aytekin, Bahadır Külah, Oktay Banlı

ABSTRACT

Perineal procedures have higher recurrence and lower mortality rates than abdominal alternatives for the treatment of rectal prolapse. Presence of incarceration and strangulation also influences treatment choice. Perineal rectosigmoidectomy is one of the treatment options in patients with incarceration and strangulation, with low mortality and acceptable recurrence rates. This operation can be performed especially to avoid general anesthesia in old patients with co-morbidities. We aimed to present perineal rectosigmoidectomy and diverting loop colostomy in a patient with neurological disability due to spinal trauma and incarcerated rectal prolapse.

Keywords: Altemeier's procedure, perineal rectosigmoidectomy, rectal prolapse

INTRODUCTION

Rectal prolapse is a rare disease with an increased frequency after the fifth decade. Rectoanal inhibitory reflex deterioration, high-pressure intermittent rectal motor activity, anorectal sensation disorders, and pudendal neuropathy have been suggested in its pathophysiology, but still its exact etiology is unknown (1). Clinically, it may present as mucosal prolapse (partial or pseudoprolapsus), internal prolapse (rectal intussusception), or full-thickness prolapse (2). Surgical treatment options can be abdominal and/or perineal approach. Despite the higher recurrence rate, due to its low complication rates and better patient tolerance the perineal approach is often preferred in elderly patients with comorbidities, and can be applied in irreducible cases requiring emergency surgery. In this article, a 60-year-old male patient who had had thoracic spine fractures and neurological sequela due to being trapped in a collapsed building twenty years ago, and who underwent perineal rectosigmoidectomy (Altemeier procedure) and protective sigmoid colostomy for incarcerated rectal prolapse is presented.

CASE PRESENTATION

A 60-year-old male patient with reduced sensation and muscle strength in both lower limbs and left drop foot sequela due to a traumatic injury twenty years ago presented to the emergency room with an irreducible mass and pain in the anal region that emerged during defecation 6 hours ago. He had experienced fecal incontinence, constipation, and a rectal prolapse that could be manually reduced for the past 6 months. He had hypertension, diabetes mellitus type 2, and was being treated for benign prostatic hypertrophy. The patient was conscious, cooperative, and oriented. On physical examination, his vital signs were normal except for sinus tachycardia (120/min). On anal inspection, he had 20 cm full-thickness prolapse of the rectum and sigmoid colon. The prolapsed segment was edematous and hyperemic. There were areas of ulceration up to 2 cm in diameter. Bowel sounds were normoactive, there were no signs of abdominal tenderness, defense or rebound tenderness. His neurologic examination revealed a left drop foot, and slightly atrophied muscles in both calves and lower limbs, more prominent on the left. Both lower extremity manual muscle strength was determined as 3/5. Although more pronounced on the left side, there was reduced sensation in both lower extremities. The pathologic values on laboratory investigations were a white cell count of 14.5 K/uL, hemoglobin 11 g/dL, and blood glucose level of 115 mg/dL. After adequate intravenous analgesia and sedation, a 20% mannitol impregnated laparotomy pad was applied on the prolapsed segment. Despite a slight decline in the edema, manual reduction failed. A written consent was obtained from the patient and his relatives after being informed on the planned surgery and its complications. The patient had emergency surgery. He underwent surgery in lithotomy position under general anesthesia (Figure 1). 1 gr of cefazolin sodium and 500 mg metronidazole IV infusion was used for antibiotic prophylaxis. An 18F Foley catheter was inserted into the bladder. Following preparation of the operation field, the rectum was circumferentially transected with electro-cautery approximately 1 cm proximal to the dentate line (Figure 2). The sig-

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İgure 1. View of incarcerated rectal prolapse

moid colon was exposed. The meso dissection was performed with Ligasure. Large arteries and veins of the sigmoid colon and rectum were ligated with 2/0 silk sutures, were cut and the meso dissection was completed (Figure 3). The resection was completed by circumferential transection of the sigmoid colon with electrocautery 2 cm proximal to the anal verge. Mucosal bleeding control was done. The anastomosis line was exposed with two overlapped rings of an outer anal canal and an inner sigmoid colon ring. The anastomosis was completed with continuous 2/0 Prolene suture in a single layer (Figure 4). The anastomosis line spontaneously reduced. On digital examination, the rectal anastomosis line was felt 6 cm proximal to the anal verge. Through an approximately 3 cm circular incision in the left upper quadrant, the skin and subcutaneous fat tissue were excised. The descending colon near the splenic flexure was pulled towards the incision. The protective sigmoid colostomy was matured in accordance with the technique. His postoperative follow-up was uneventful. Stool discharge was observed from the colostomy on postoperative day 1. Oral intake was started. The patient was discharged on postoperative day 3 following proper wound healing, adequate food intake, acceptable pain control with oral nonsteroidal anti-inflammatory analgesics, and ostomy care training.

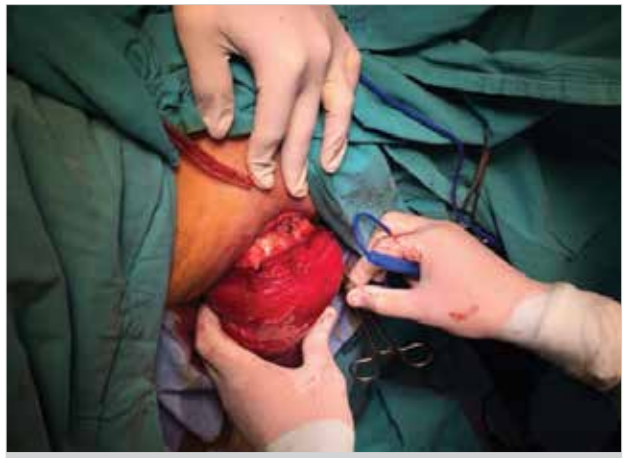
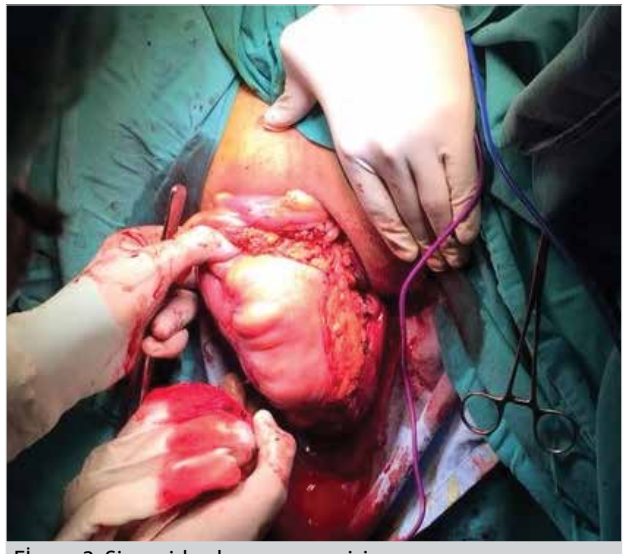


Figure 2. Rectal incision line



İgure 3. Sigmoid colon meso excision

Figure 4. Anastomosis line

DISCUSSION

The prevalence of external prolapse in the general population is less than 0.5% (3). 80-90% of patients with rectal prolapse are women over the age of 50. Although the etiology of rectal prolapse is unknown, the most accepted theory, as shown by defecation proctography, is rectorectal intussusception (1). Its incidence is higher in elderly patients, those with vaginal birth, chronic psychiatric disorder, and Ehlers-Danlos syndrome type IV (1). Defecation is a complex mechanism in which several

muscles and nerves participate. The anorectal and pelvic autonomic innervation is controlled by both the autonomic and somatic nervous systems. The levator ani and puborectalis muscles are innervated by sacral 2-5 nerves, while the external anal sphincter muscle is innervated by pudentalis inferior-rectalis inferior nerve. Parasympathetic innervation is supplied by sacral nerves 2-4, and sympathetic innervation by the pelvic plexus. The sensory innervation of the anal region and distal rectum is also supplied by the pudendal nerve (4, 5). We believe that our patient's prolapse etiology was associated with the previous trauma-related spinal injuries that have led to both motor and sensory deficits. Our patient has been complaining of fecal incontinence and constipation for the past 6 months.

There are various surgical treatment options for rectal prolapse. Surgery can be performed by either abdominal or perineal approaches (6). The morbidity and recurrence rate of each operation varies. Abdominal surgeries have less recurrence and higher mortality rates than perineal surgery (6, 7). Additionally, abdominal surgeries have a higher risk of impotence and infertility (8). Abdominal approaches include suture rectopexy (mortality 0%, recurrence 0-3%), suture rectopexy + resection (mortality 0 to 6.7%, recurrence 0-5%), posterior mesh rectopexy (mortality 0-3%, relapse 3%), anterior sling (Ripstein procedure) rectopexy (0 to 2.8% mortality, recurrence 0-13%), laparoscopic rectopexy (0% mortality, recurrence 0-10%) (7). In the laparoscopic approach, length of hospital stay and mortality rates are low while relapse is more common, especially because of inadequate dissection during the learning curve (6). This operation also requires laparoscopic surgical knowledge and experience. Nevertheless, laparoscopic rectopexy is a good treatment option with acceptable recurrence and low mortality rate. Perineal approaches mainly refer to two operations including Delorme's operation (mortality 0-4%, 4-38% recurrence), and perineal rectopexy (mortality 0-5%, 0-16% recurrence) (7).

The choice of surgery must be decided according to the patient and surgical experience. Abdominal surgery may be preferable for curative intent in especially a young patient without comorbidities, those with high intellectual and cultural status, and in patients who can deal with the morbidity burden. Poylin et al. (6) reported that abdominal surgery in elderly rectal prolapse patients is as safe and effective as in the young. Laparoscopic rectopexy is a good treatment option with low recurrence and mortality rates. This procedure requires advanced laparoscopic knowledge and experience. Perineal surgery may be especially preferred in debilitated patients with co-morbid diseases and older age groups (7). The applicability of perineal rectosigmoidectomy under spinal anesthesia provides another advantage in the choice of surgery.

Surgical options are more challenging in case of incarceration, due to the increased risk of performing surgical anastomosis because of bowel edema. Initially, reduction should be tried to reduce edema and the consequent risk of surgical complications, as well as to schedule for an elective surgery. Methods such as mannitol, elastic compression, hyaluronidase and sugar application can be used for reduction (1). The rate of anastomotic leak is 2-6% in elective rectosigmoidectomy in contrast to the 25% in incarcerated prolapse. Stapled methods and the two-stage approach have been tried to reduce the leakage rate, but the most common application is protective ileostomy or colostomy (9). Perineal rectosigmoidectomy and protective loop colostomy surgery through one incision is a less invasive surgical option with less risk of contamination as compared to open prolapse surgery. The length of hospital stay is also shorter in perineal approaches as compared to abdominal procedures (10). Compared with abdominal rectopexy, this surgery has disadvantages such as the need for bowel resection, the requirement for an anastomosis, an ileostomy or colostomy, and a second surgery for ostomy closure. Although rectal prolapse is a rare disease, it can be encountered in clinical practice. Perineal rectosigmoidectomy is a reasonable surgical option in selected cases.

CONCLUSION

The type of surgery for patients with rectal prolapse should be selected by taking the patient's overall condition and the surgical experience into account. Although its recurrence rate is higher as compared to abdominal rectal prolapse procedures, perineal resection may be the preferred surgical option in incarcerated rectal prolapse, especially those requiring resection, in debilitated, elderly patients with co-morbid diseases, and in whom general anesthesia is contraindicated.

Informed Consent: Written informed consent was obtained from patient who participated in this case.

Peer-review: Externally peer-reviewed.

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Case Report

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Primary squamous cell carcinoma of the stomach

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ABSTRACT

Primary squamous cell carcinoma of the stomach accounts for less than 1% of all gastric malignancies. Less than 100 cases were reported in the literature. Therefore, knowledge about management and prognosis of the disease is limited. Surgical approach is the basic form of treatment. In this study we confirmed a case of primary gastric squamous cell carcinoma with the aim of contribution to the literature, which is seen rare, and the diagnosis was confirmed pathologically.

Keywords: Squamous cell carcinoma, stomach, pathology

INTRODUCTION

Adenocarcinoma accounts for 95% of primary gastric carcinomas. The incidence of primary squamous cell carcinoma (SCC) of the stomach is less than 1% of all gastric malignancies (1). It is first described by Rörig et al. in 1895 (2, 3). It is more commonly seen in men and incidence increase in sixth decade (2, 3). Squamous cell carcinoma of the stomach is not involved in the formation of Lauren and World Health Organisation (WHO) classification of gastric cancer. Squamous cell carcinoma may arise from tertiary syphilis, corrosive acid intake and prolonged cyclophosphamide treatment. These tumors may originate from undifferentiated mucosal stem cell that arise from squamous metaplasia and ectopic squamous epithelial background (4). Here we present an unusual case of primary gastric squamous cell carcinoma.

CASE PRESENTATION

Forty-nine years old man applied to our clinic with the symptoms of nausea, vomiting and epigastric pain. The patient had a history of 4 kg weight loss in last three months. His sister had died because of gastric cancer. The patient's physical examination was unremarkable. Laboratory tests were normal, except anemia (Hgb: 7.2 g/dL). There was a prepyloric antral wall thickening and multiple lymphadenopathy around celiac trunk, hepatoduodenal ligament and perigastric area. Then, we made an endoscopy to the patient. In endoscopy there was an ulcerovegetative mass from antrum toward pylorus (Figure 1). Pathology result was squamous cell carcinoma. There was no adenoid component. The patient was taken for screening whole-body positron emission tomography (PET). We saw irregular wall-thickening and mass lesion that has intense fluorodeoxyglucose (FDG) standardised uptake value (SUVmax: 20.3). Besides that there were multiple lymph nodes around lesser curvature, gastroduodenal area and hepatic hilus which have less FDG uptake (SUVmax:3.4). The patient was operated on July 2013, there was a tumoral mass of 10 x 5 cm involving all layers of gastric wall. Total gatrectomy and Roux-en-Y esophagojejunostomy (D2 dissection) were done. The patient was discharged after 7th day of the operation.

Specimen including stomach, omentum and lymph nodes was sent for histopathologic examination. When the incision through lesser curvature was done there was an ulcerovegetative mass located on posterior antral wall which has 6 cm proximal and 1.8 cm distal margin (Figure 2). Macroscopically the tumor has reached serosal layer.

Microscopic examination of tumoral area revealed that there were atypical bizarre epithelial cells including keratin plugs with eosinophilic cytoplasms, prominent nucleoli and intercellular bridges. These findings resemble us squamous cell carcinoma of other parts of the body. Examined numerous samples did not prove adenoid component. The tumor cells were stained strongly positive by p63, CK 5/6 and CK7 immunohistochemically, that means squamous neoplasia (Figure 3).

Tumor was extending into the subserosal layer. There was no invasion in perigastric, paraaortic, celiac mesenteric lymph nodes, but 5 of the regional lymph nodes were invaded. Proximal and distal surgical margins were clear. There was a widespread intestinal metaplasia around the tumor. The tumor was accepted as pT3N2 according to the TNM classification.

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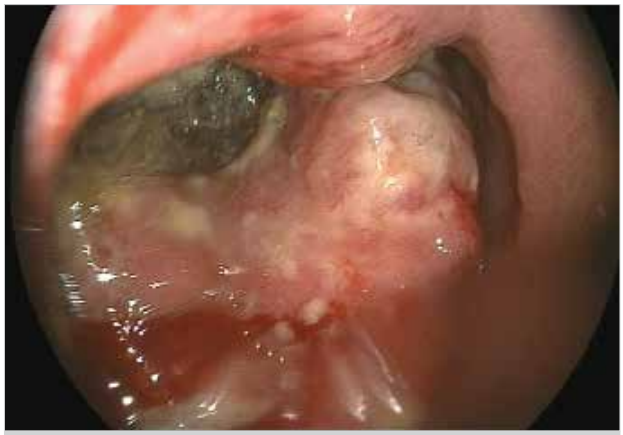

Figure 1. Endoscopic appearance of the tumor

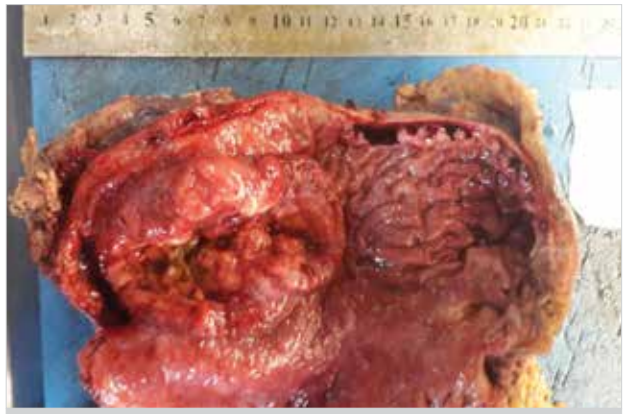

Figure 2. Macroscopic appearance of the tumor. Stomach is incised through lesser curvature.

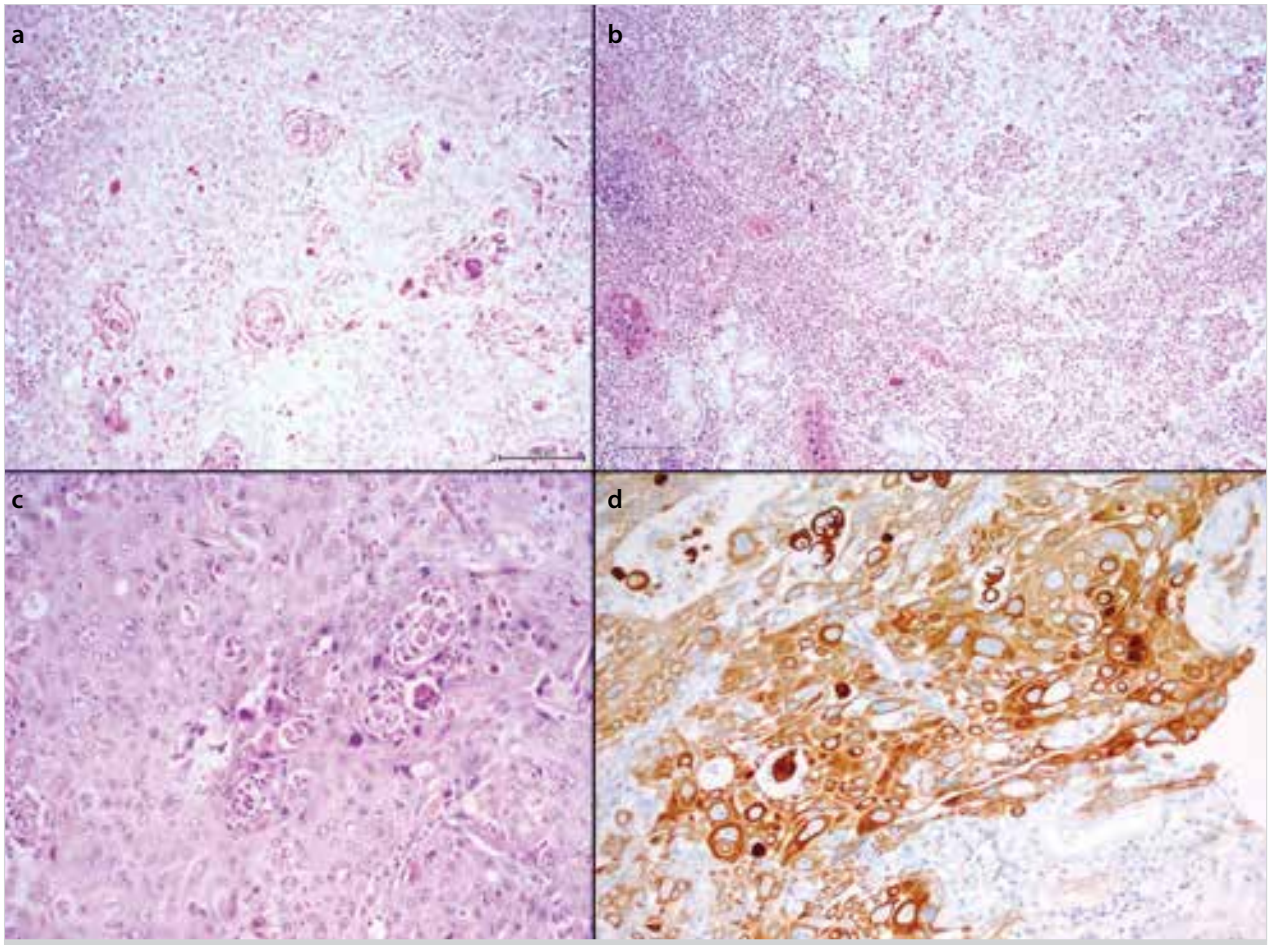

Figure 3. a-d. Neoplastic cell infiltration next to the gastric cells (x10) (a). Keratin plugs supporting squamous neoplasia (b). Atypical squamous epithelial cells with eosinophilic cytoplasm with large, prominent nucleoli (c). Tumor cells displayed (d) CK5/6 immunoreactivity. A;X10, B;X10, C;X20 (H&E). D;X20 (CK5/6)

A month after the operation the patient was taken to the oncological treatment program. Cisplatin (60 mg/m^2/day) one dose and capecitabine (2000 mg/m^2/day) 14 day combination chemotherapy was administered. After chemotherapy, 45 Gy in 25 fraction radiotherapy and capecitabine (1650 mg/m^2/day) were applied concurrently. This protocol was administered 5 days a week for 5 weeks. Than initial chemoterapy was repeated, thus oncological treatment was terminated.

DISCUSSION

Primary gastric squamous cell carcinoma (SCC) accounts 0.04-0.07% of of all gastric malignancies. It is first descibed by Rörig et al. in 1895 (2, 3). Since then only about 100 cases have been published (4). It is five times more common in males. When compared to adenocarcinoma, it is more aggressive and more prone to make lymphovascular invasion (5). For the diagnosis of gastric squamous cell carcinoma, the tumor must be completely in gastric mucosa and the esophageal mucosa should be spare of the tumor. For this reason Parks et al. (6) described

3 criteria for the diagnosis: 1) The tumor should not be localized in cardia. 2) The tumor should not invade esophagus. 3) The tumor should not be elsewhere in the body. Beside these criteria Boswell and Helwig (7) had defined 4 histopathological criteria: 1) Keratinized cell masses lined up like pearls. 2) Mosaic pattern cells that have sharp scheme. 3) Intercellular bridges (In high concentration sulphydril and disulfide groups) 4) Containing keratin.

There are some processes for the explanation of pathophysiology of primary SCC of the stomach. Most popular of them is malignant transformation from squamous metaplastic background. SCC is associated with chronic inflammation in the absence of metaplasia (8). Outside of these processes have been reported by Strauss et al. (9): 1) Squamous differentiation in adenocarcinoma. 2) Squamous metaplasia in endothelial cells or gastric vessels. 3) Squamous cell islets in gastric mucosa. 4) Differentiation ability of totipotent stem cells to other cell types.

Our knowledge about the management and prognosis of SCC of stomach is restricted because it is seen rarely. Primary treatment of the disease is surgery (10). Schmidt et al. (3) have reported 5 years survival without symptoms of the disease by the treatment composed of surgery, radiotherapy and chemotherapy (5-fluorouracil, leucovorin, cisplatin and etoposide). Yıldırım et al. (4) had achieved a 3 year remission in the SCC of stomach that had nearby organ invasion with the 5-fluorouracil and cisplatin protocol.

Due to the inadequate number of reported cases, the efficacy of neoadjuvant chemotherapy and radiotherapy is unknown. Hovewer, as SCC of any other part of the body adjuvant chemotherapy and radiotherapy are primary mainstay treatment of the SCC of stomach.

CONCLUSION

The prevalence of SCC of the stomach is very low and it is an aggressive neoplasm as it metastasizes to the lymph nodes and the liver. We know that primary gastric SCCs are aggressive tumors due to higher incidence of lymphovascular and serosal invasion which are responsible for poor prognosis. Clinicians must be aware of all these.

Informed Consent: The patient's consent form of all treatment levels including medical and surgical treatment steps was taken routinely, however this article is written after all treatment and discharge of patient from the hospital. Thats why we did not need to prepare special consent form for the article.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - A.S., K.Ö.; Design - O.B.G.; Supervision - F.Ç., C.E.; Funding - E.Y.; Materials - K.Ö., F.Ç.; Data Collection and/or Processing - C.E., H.Y.; Analysis and/or Interpretation - S.A.; Literature Review - A.S.; Writer - O.B.G., A.S.

Conflict of Interest: No conflict of interest was declared by the authors.

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Case Report

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The development of pneumobilia after blunt trauma

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ABSTRACT

Pneumobilia is the detection of gas within the biliary system. It usually develops after bilioenteric anastomosis, percutaneous or endoscopic biliary interventions, infections and abscesses. The treatment is surgical, especially in cases with no prior interventions to the biliary system. The development of pneumobilia is quite rare after blunt trauma. Therefore, both the diagnosis and management are challenging for surgeons. Herein, we present the diagnosis and conservative management of a patient with pneumobilia after blunt trauma.

Keywords: Blunt trauma, pneumobilia, conservative management

INTRODUCTION

Pneumobilia is defined as the presence of gas in the biliary system. It may be detected after biliary-enteric anastomoses, percutaneous (PTC) and endoscopic (ERCP) procedures (1). The presence of air in the biliary tract without any intervention suggests infection, abscess, or an abnormal connection between the biliary-enteric system and may require immediate treatment. Emphysematous cholecystitis, and pyogenic cholangitis are accepted as causes of infectious pneumobilia (2). Pneumobilia due to blunt abdominal trauma is a clinical situation that is encountered very rarely (3). Herein, we present a patient with blunt abdominal trauma-related pneumobilia that was detected by abdominal tomography, and was treated non-operatively.

CASE PRESENTATION

An 18-year-old male patient was admitted to the emergency department after falling from a tractor and the tractor's rear wheels crushing his hips. He had no additional diseases and drug use. The patient's abdominal examination was normal except minimal suprapubic tenderness. The pelvis was tender on compression. On abdominal computed tomography (CT), there were no signs of solid or hollow organ injury or intraabdominal free air; however, diffuse air was detected in intrahepatic bile ducts (Figure 1a, b). Computed tomography of the pelvis revealed multiple fractures in the sacrum, right acetabulum, right pubic rami and diastasis in multiple joints. The patient did not have a history of gallstone disease, and there were no stones in the gallbladder either on abdominal CT or ultrasound images. He was previously not exposed to any surgical or endoscopic procedures directed to the bile ducts. The patient was operated on by orthopedic surgery. He was followed-up by our clinic during his hospital stay, and his physical examination and laboratory findings remained normal. He was discharged uneventfully. The patient is under follow-up for the past 3 months without any complications.

DISCUSSION

Pneumobilia is a rare condition indicating a passage between the gastrointestinal and biliary systems. This is often perceived as a serious intra-abdominal pathology that requires laparotomy. The most common causes are gallstone disease and consequent biliary-enteric fistula, and biliary tract surgery. In the literature, the incidence of gallstone-induced biliary-enteric fistula has been reported as 0.4-3.5%, and it is stated that pneumobilia can be detected in about 50% of these patients (1). Pneumobilia may also be associated with ERCP, emphysematous cholecystitis, pyogenic cholangitis, and incompetent Oddi sphincter. The most common cause of pneumobilia in the absence of previous biliary surgery or biliary-enteric fistula is an incompetent Oddi sphincter.

A case of retrograde pneumobilia due to intestinal obstruction in a patient without any history of previous surgery or biliary-enteric fistula has also been reported in the literature (4). Pneumobilia due to blunt abdominal trauma is extremely rare (2, 5, 6). Only a limited number of such cases have been reported in the literature. The pathophysiology was described as the passage of air within the proximal enteral loops to the sphincter of Oddi and biliary system in a retrograde manner with increased intra-abdominal pressure, by Gering et al. (5). Besides blunt abdominal trauma, Ladurner et al. (3) reported a case of pneumobilia after cardiopulmonary resuscitation (CPR). In that patient, CPR has been performed for 3 minutes for sudden cardiac arrest in a patient who had been followed-up due to trauma. There was no pneumobilia on the

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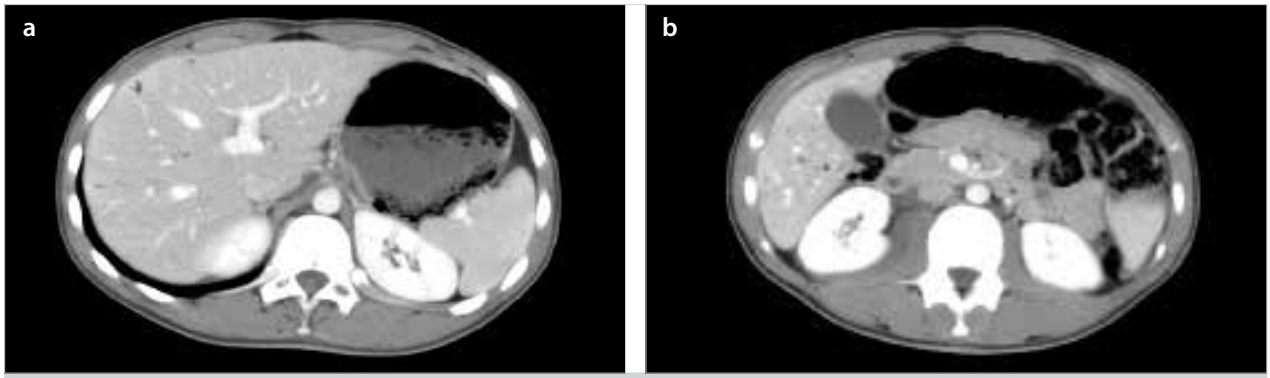

Figure 1a,b. Image of diffuse air within intrahepatic bile ducts

abdominal CT images obtained prior to the cardiac arrest, while pneumobilia was identified in the second CT image set after the CPR. This situation was thought to be due to the retrograde passage of air into the the biliary system due to the increased intra-abdominal pressure during CPR.

Pneumobilia may be detected in plain X-ray, but CT and magnetic resonance imaging (MRI) views are more selective (2, 6). The diagnoses of patients presented in the literature were all made by CT images (7, 8). Similarly, in our case, the presence of diffuse air within intrahepatic bile ducts was observed on abdominal CT images.

It is difficult to make a definite treatment recommendation due to the limited number of cases. In the study containing the maximum number of cases reported in the literature, Barnes et al. (6) reported that they had a different approach in all 3 cases of pneumobilia due to blunt abdominal trauma. They performed laparotomy due to pneumobilia to the first case, and the intra-abdominal organs were found to be intact. In the second patient, they performed duodenoscopy to rule out a possible duodenal injury and have determined that the duodenum was normal. They managed the third patient conservatively, and reached the conclusion that isolated pneumobilia can be treated conservatively. Bautista et al. (4) have found that pneumobilia due to high proximal small bowel obstruction regresses spontaneously with non-operative management by nasogastric decompression. We believe that in our patient the pneumobilia resulted from retrograde Oddi sphincter dysfunction due to increased intra-abdominal pressure.

CONCLUSION

Conservative management without surgery seems to be the most appropriate method in the treatment of pneumobilia in hemodynamically stable patients with isolated pneumobilia and those without additional radiologic findings and clinical signs.

Informed Consent: Verbal informed consent was obtained from patient who participated in this case.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - İ.O., Z.Ö., B.A.; Design - S.T., Ç.D.; Supervision - Z.Ö., E.Y.; Funding - E.Y.; Analysis and/or Interpretation - M.Ş., H.A.K.; Literature Review - Z.Ö., E.Y.; Writer - Z.Ö.; Critical Review - M.Ş., H.A.K., İ.O.

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Case Report

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Tubulopapillary adenoma of the common bile duct presenting with jaundice

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ABSTRACT

In this report, an adult patient with tubulopapillary adenoma of the common bile duct that manifested with jaundice is presented. Diagnostic challenges were analyzed. Although adenomas of the common bile duct are rare, they should be kept in mind in the differentiation of lesions of this region. It should be remembered that these lesions radiologically could mimic carcinoma and choledocholithiasis. Endoscopic resection should be considered as the primary method for treatment. Histopathology is the gold standard in diagnosis.

Keywords: Adenoma, tubulopapillary, common bile duct, histopathology, endoscopic resection

INTRODUCTION

Villous/tubulovillous adenomas are benign epithelial tumors usually detected in the colon. They often present by polyps elevated form the mucosa. These, mostly sporadic detected lesions can sometimes be a component of diseases such as familial adenomatous polyposis, Gardner's syndrome and Peutz-Jeghers syndrome (1, 2). Villous/tubulovillous adenomas are rare in the common bile duct, and similar lesions of this localization are called papillary/tubulopapillary adenoma. General symptoms are bile duct obstruction and jaundice. They may be confused with common bile duct stones and malignant tumors during pre-operative evaluation (3, 4). Thus, unnecessary extensive surgical procedures can be applied in some cases. The definite diagnosis is only made by postoperative histopathologic examination of the surgical specimen. Herein, an adult male patient who presented with jaundice and had common bile duct tubulopapillary adenoma was presented with emphasis on diagnostic challenges.

CASE PRESENTATION

A 51-year-old male patient was admitted to the clinic with persistent jaundice and pain in the right hypochondriac region for the past week. On physical examination, the skin and mucosal surfaces were icteric. The right hypochondriac region was mildly tender on palpation. The laboratory examinations were characteristic for obstructive jaundice. The magnetic resonance cholangiopancreatography (MRCPG) showed intra- and extra-hepatic bile duct dilatation and a mass in the distal portion of the common bile duct causing obstruction that was compatible with a stone. The patient was prepared for endoscopic retrograde cholangiopancreatography (ERCPG). Informed consent was obtained from the patient and his relatives prior to the procedure. A polypoid lesion was observed in the ampulla of Vater during duodenoscopy. The lesion was extracted with snare polypectomy method after 1: 10000 diluted adrenaline injection to its base. The common bile duct was then cannulated by the ERCPG catheter and the contrast material was injected. The widest portion of the common bile duct dilatation was observed to be 2.0 cm in diameter and a filling defect was detected in the distal portion. A balloon catheter was inserted to the common bile duct and the lumen was cleared by expanding the proximal portion with air. Meanwhile, a short-pedicled, dark pink polypoid lesion that was 1.5 x 1.0 cm in size was seen to move towards the intestinal lumen and was removed by applying snare polypectomy again (Figure 1). After the procedure, the patient's symptoms quickly regressed. Three days after the operation the patient's biochemistry tests were within normal limits. On histopathologic examination, the lesion was composed of villous and tubular structures consisting of a stroma of spindle cells lined with dysplastic single-layer columnar epithelium (Figure 2). Based on these findings, the patient was diagnosed as tubulopapillary adenoma of the common bile duct with mild dysplasia. Any recurrence or complication was not observed during the six-month follow-up period. Magnetic resonance cholangiopancreatography obtained four months after the procedure was normal. On follow-up duodenoscopy, ampulla of Vater appeared normal.

DISCUSSION

Adenomas are benign tumors composed of epithelial tissue, and are the most common lesions of the digestive tract. Generally, they appear as single, well-defined polypoid lesions. According to the World Health Organization classification there are five types of adenoma in the gallbladder and extrahepatic bile ducts: tubular, papillary, tubulopapillary, biliary cystadenoma, and papillomatosis (adenomatosis).

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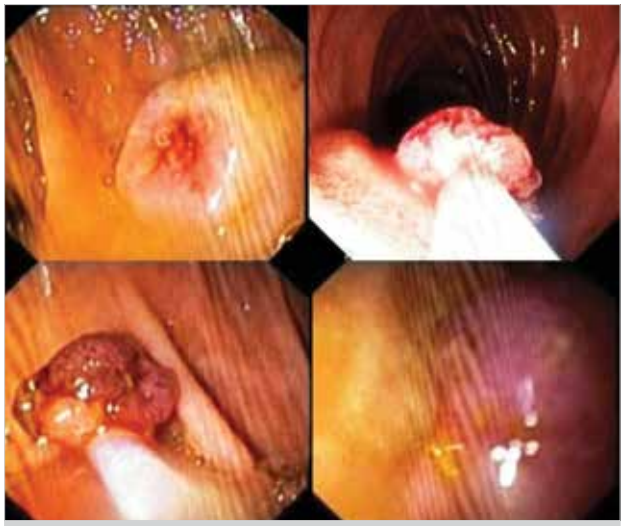

Figure 1. Polipoid lesion and its resection within the common bile duct on endoscopic evaluation

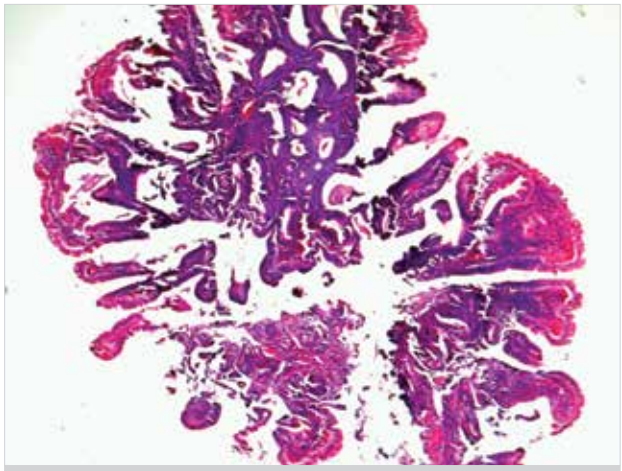

Figure 2. Microscopic view of tubulovillous adenoma in the common bile duct (hematoxylene eosin; x40)

Adenomas are more common in the gallbladder than in the common bile duct. Adenomas are detected in 0.3-0.5% of cholecystectomy materials performed for chronic cholecystitis and cholelithiasis. Tubular adenomas are more common in the digestive system, while papillary/tubulopapillary adenomas are less frequent (5). These have the same morphologic characteristics as intestinal villous/tubulovillous adenomas, and have a high risk of malignancy (6, 7). The first papillary (villous) adenoma of the common bile duct in the English literature has been reported by Saxe et al. (9) and a total of 27 cases have been reported so far (3, 8).

Adenomas of the gallbladder and extrahepatic bile ducts are more common in women. Conversely, approximately 70% of common bile duct papillary/tubulopapillary adenomas are detected in men. The age range of cases presented in the English literature is 27-84, with an average age of 63.6 years (3). Adenomas usually present with jaundice, abdominal-especially right upper quadrant- pain, dyspepsia, nausea and vomiting symptoms similar to other lesions that cause common bile duct obstruction. Although the majority of adenomas in the ampullary region are found sporadically, they can sometimes manifest as a component of polyposis syndromes (1, 2).

The preoperative diagnosis of common bile duct adenomas is very difficult. The radiologic suspicion of malignancy in adenomas has been reported several times (4). Sometimes, as in our case, the adenoma could be perceived as a common bile duct stone in radiologic evaluations. Likewise, endoscopic examinations are insufficient in terms of ruling out malignancy. Malignancies can be correctly evaluated only in procedures performed by very experienced biliary endoscopists. In such cases, what makes endoscopic examination superior to radiologic evaluations is the possibility of obtaining biopsy for histopathologic examination. Histopathologic evaluation is the most reliable method in the diagnosis of adenoma. Histopathologically bile duct adenomas are composed of a dysplastic epithelium and stroma consisting of connective tissue such as their gastrointestinal tract counterparts. In situ carcinoma component was also determined in some biliary adenomas (3).

There is no consensus on the optimal treatment method of common bile duct adenomas of the ampullary region and the distal portion of the common bile duct (3). The implementation of endoscopic resection in patients with common bile duct adenoma with high-risk of malignancy has been first proposed in 1992 by Sturgis et al. (10). However, it was emphasized that the recurrence risk was high.

Similarly, local endoscopic resection (papillectomy) of ampullary region adenomas can be successfully carried out. The same method can be applied with sphincterotomy in distal intra-ductal adenomas, particularly in patients with suspected malignancy (11). Ariche et al suggested common bile duct resection along with hepatoduodenal ligament lymph node dissection in suspicious lesions of the middle portion of the common bile duct (7).

The prognosis of common bile duct adenomas is good. Nevertheless, the anatomical structure of this region restricts surgical procedures, which in turn leads to insufficient resection and recurrence in some cases. Careful histopathologic examination of the resection material is very important in terms of predicting prognosis.

CONCLUSION

Although common bile duct adenomas are rare, they must be kept in mind in the differential diagnosis of lesions of this region. It should be considered that they resemble carcinoma or common bile duct stones on radiological examinations in many cases. Endoscopic local resection should be considered as the main treatment method, and histopathologic evaluation is the gold standard for diagnosis.

Informed Consent: Written informed consent was obtained from patient's parents and patient who participated in this case.

Peer-review: Externally peer-reviewed.

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Conflict of Interest: No conflict of interest was declared by the authors.

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Letter to the Editor

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New developments in bariatric and metabolic surgery and HIPER-1 study

Alper Çelik

Dear Editor,

Metabolic syndrome and type 2 diabetes, which is the most important component of this syndrome, has become a pandemic creating a global health problem (1). Approximately 8-10% of the global health expenditure is being spent for obesity, and these numbers are increasing every day (2). Taking the modern diet and environmental conditions into consideration, it is evident that obesity will become a more serious health problem in the near future (3).

Although it is expressed in many recognized guidelines that the preferential treatment of obesity is diet and lifestyle modifications, it is impossible to obtain the desired results with this treatment method in majority of the patients (4). In fact, even in individuals with insulin resistance and without pre-diabetes or with non-morbid obesity, this approach fails to achieve clinical goals (5).

Currently the most effective and long-term results in the treatment of obesity can be achieved with Metabolic and Bariatric Surgery (6). Bariatric surgical procedures not only treat obesity but also provide better results than medical treatment, although varying according to procedure type, through neurohumoral mechanisms independent of weight loss in the treatment of accompanying diseases -especially- type 2 diabetes (7, 8).

However, we still do not exactly know the details of the road that leads to this success. Restrictions on calorie intake, changing gut-brain axis, absorption alterations, modifications in the microbiota are some of the factors that we know partially; while especially the change in the level of small intestine derived hormones, when these levels have to be changed, which procedure results in what extent of alterations are still unknown. However, the surgical community acts as if we have found all the answers and have forgotten the actual problem. The concern that this attitude will lead to adverse consequences in the future obliges every surgeon to review their practice. Several significant reasons for such concerns have recently revealed themselves in written, social and visual media. Over the past 3 months, the negative consequences of obesity surgery along with mortalities have been covered in all aspects of the media and our community has been affected from this situation.

Who should perform such procedures, under what conditions, and after what type of training are the contents of another discussion. Nevertheless, why only the negative consequences of obesity surgery are being covered by the media is interesting.

Obesity is a dynamic, psychogenic-based, multi-component heterogeneous illness that is being treated with multiple surgical, medical and paramedical methods. Thus, disputes between disciplines on current clinical practice is inevitable. However, this situation does not necessitate publicizing the extreme downsides of a particular treatment method. The lesson learned from this situation is to realize where the negative results of the treatments we implement can lead to. Because the real problem will arise once the individuals we operate will start regaining weight or the diseases they got rid of will re-appear in the near future.

The problems currently being experienced is only the small part of the iceberg that is visible above the water, the real issue will arise once it will be implied that the treatment we are applying is not as effective as we think it is. In combat with this problem, not a single surgeon should think "I will re-operate again if he/she gains weight" or "will perform bypass if he/she gains weight". Because as each failing medical treatment affects patient compliance, patient compliance and expectations with respect to the operation are affected negatively by the undesirable consequences of any surgical procedure. More im-

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portantly, some anatomical changes that occur after the initial surgery may make it impossible to apply additional surgical techniques appropriate for that patient. Perceiving malabsorption procedures as a savior only indicates our desperation on the subject. The first reason for this is that malabsorption itself is a disease that is described by the World Health Organization. Secondly, the patients with 'created' malabsorption will have limitation in their exercise capacity due to deficits in trace elements, calcium, and particularly iron, and will find their selves in the vicious circle before their operation, if not worse.

Every physician who provides services for Bariatric and Metabolic Surgery should think: "How is it that gastric bypass patients with 30 mL pouch and those with sleeve gastrectomy of 100-150 mL volume can be equivalent in terms of weight loss rate in the long-term, and how do these patients start to gain weight again after 3 years?". The reply to this question alone should be able to show that long-term success cannot be achieved by mechanical restriction.

Looking at the medium and long-term (5 and> 10 years) data, we see from the literature that effective and permanent weight loss is possible with techniques such as proximalising the ileum, bilio-pancreatic diversion (BPD) and duodenal switch (DS), ileal transposition (IT) and transit bipartition (TBI) (9-11). Although BPD, and to a lesser extent DS, cause serious malabsorption, this risk is acceptable for IT while it is minimal for TB. We need to identify to which patient, under which conditions, which type of surgery should be applied, immediately.

In order to overcome these problems, a multi-center, prospective study with international participation (Turkey, Australia, Netherlands, USA) is planned in our Foundation. The study named "HIPER-1" (Human Intestinal Peptides Evaluation & Research) aims to measure the activities of small intestine induced neuropeptides in healthy adults, in individuals with various metabolic disorders who did not undergo surgery, as well as in patients with different types of surgical procedures, and to establish a rating system based on these results. Detailed and current information on our study, which has completed the registration process to the Clinical Trials (www.clinicaltrials.gov) that is the official clinical trials database of the United States Federal Government, will be announced from the Foundation's website. The first part of this study that is planned to continue for a long period is called HIPER-1, and we hope that the initial and following stages will be completed with contributions of the surgical community. Through this and similar studies, by acting together, we can offer important contributions both to our patients and our clinical practice, as well as the future of Bariatric and Metabolic Surgery.

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Comment: Leiomyosarcoma of the retrohepatic vena cava: Report of a case treated with resection and reconstruction with polytetrafluoroethylene vascular graft

Kamuran Cumhur Değer, Mustafa Duman, Erdal Polat, Sinan Yol

To the Editor,

We read with interest the paper titled "Leiomyosarcoma of the retrohepatic vena cava: Report of a case treated with resection and reconstruction with polytetrafluoroethylene vascular graft" by Yankol et al. (1). In this case report, the authors describe a successful treatment of a retrohepatic vena cava leiomyosarcoma with resection and polytetrafluoroethylene vascular graft reconstruction. As mentioned in the manuscript surgical resection with negative margins is the gold standard treatment. But after resection, in conjunction with inferior vena cava (IVC) reconstruction options, there also stands another choice which is ligation without reconstruction, which is not discussed in the manuscript. Regarding to this case report, we aimed to present a patient (S.Ö,prot:806/59,F) from our clinic to whom we performed segmented IVC resection and ligation for diagnosed level 2 vena cava leiomyosarcoma. IVC was ligated above aortoiliac bifurcation and below renal veins. Because of the high graft thrombosis risk this approach was preferred instead of anastomosis. Intermittent pneumatic compression was applied and low dose fractioned heparin was given at therapeutic dosage in order to protect from deep venous thrombosis risk and lower-extremity edema. On postoperative day 3, the patient had underwent a second laparotomy because of intraabdominal bleeding. Perioperative exploration revealed an oozing type bleeding from the proximal caval stump. After hemostasis the patient sent to intensive care unit for close follow-up. On postoperative day 8, chylous drainage was encountered and oral feeding was stopped following total parenteral nutrition (TPN) support. 2 weeks after TPN treatment the drainage was turned to serous character and oral feeding was restarted with abolishment of TPN support. Finally the patient was discharged with compression stocking and 5-mg. coumadin tb./day orally one month after surgery and she did not suffer from renal failure or lower extremity edema during her hospitalization. Pathologic findings revealed a grade 2 leomyosarcoma with negative margins. Immunohistochemistry panel showed that SMA: (+), Desmin: (+), S-100: (-) CD117: (-) Ki-67 index: 30%. Six cycles of chemotherapy was given to the patient following discharge from our clinic. Now the patient is on postoperative 8th month and there is no documented recurrence or metastasis.

The proper technique following IVC resection in the literature is lacking. Caval reconstruction is associated with longer operative time and has its own morbidity and mortality rates. On the other hand in the absence of sufficient collateral venous flow or in cases of interruption of vital organ vasculature, it is necessary to make a vascular reconstruction (2).

Daylami et al. (3) claimed in their paper that reconstruction of the IVC was not necessary for resection of tumors below the level of the hepatic veins in most if not all cases. They also mentioned lower-extremity edema and acute renal failure as an albeit transient and early postoperative complication. According to their series with 6 patients, 2 of them developed chylous leak and 1 of them was treated with dietary modification and percutaneous drainage and the other with a Denver shunt.

We wonder if the authors have checked the patency of graft during follow-up because as Hirohashi et al. (4) suggested in their case report, thrombosis may occur as a late complication in an inferior vena caval graft. In conclusion, we believe that whenever possible, primary IVC resection without reconstruction in the management of lower IVC leiomyosarcoma should be preferred due to its benefits by means of shorter operation time and acceptable morbidity and mortality rates.

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Author's Reply

To the Editor,

We thank to Değer et al. for their interest and comments with complementary contributions regarding our case report " Leiomyosarcoma of retrohepatic vena cava: Report of a case treated with resection and reconstruction with polytetrafluoroethylene vascular graft".

Değer et al. also presented their case without reconstruction which is the one of the alternative treatment option in the literature with success. As they also mentioned every treatment techniques have their own complication risks after surgery.

As we mentioned in our conclusion; treatment at a center experience in liver resection and transplantation allows better opportunity for safe resection and reconstruction with shorter operation time and acceptable mortality and morbidity rates. The additional time for reconstruction with PTFE graft was only 15-20 minutes which was not very important for this case.

We have been checking the patency of the PTFE vascular graft during the follow-up period with clinical and radiological findings. By the time no thrombosis has been occurred.

We believe that both techniques have their own serious risks after surgery. We preferred to treat this case with most physiological treatment option which was applied many times in the literature with successful results.

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