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Analysis of the clinical features, treatment strategies, and results of borderline ovarian tumors

Borderline over tümörlerinin klinik özellikleri, tedavi stratejileri ve sonuçlarının analizi

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ABSTRACT

Aim: The objective of our study was to evaluate the preoperative circumstances, treatments, and postoperative states of patients at our university hospital.

Materials and Methods: This retrospective study used the Mersin University Hospital's gynecological oncology clinic database. Patient age, menopausal status, preoperative tumor markers, and preoperative ultrasonography features were collected from the hospital databases. After the initial procedure, information regarding the surgical method, histological classification, stage at the time of diagnosis, size of the tumor, status of the lymph nodes, and the ultimate pathological diagnosis were collected.

Results: This study has a cohort of 84 patients who underwent surgery between 2007 and 2023. The study groups had a median age of 41.5, ranging from 15 to 88. Out of the total patients, 71.4% were in the premenopausal stage. Final pathology revealed the presence of a malignant tumor in 10 patients, accounting for 11.9% of the total. Out of the total number of patients, six had serous tumors, while four had mucinous tumors. Out of the 83 people, a recurrence of the condition was found in 3, indicating a rate of 3.6%. The mean duration of progression-free survival for these individuals was 19 months. Only individuals in the early stage of the disease experienced a recurrence, and two exhibited micropapillary variants.

Conclusion: Ultimately, BOTs have a highly favorable prognosis. Patients who meet the criteria might consider undergoing fertility-preserving surgical procedures.

Keywords: Borderline ovarian tumors, ovarian cancer, gynecologic surgery

ÖZ

Amaç: Çalışmamızın amacı, üniversite hastanemizdeki hastaların ameliyat öncesi durumlarını, tedavilerini ve ameliyat sonrası durumlarını değerlendirmektir.

Gereç ve Yöntemler: Bu retrospektif çalışmada Mersin Üniversitesi Hastanesi jinekolojik onkoloji kliniği veri tabanı kullanıldı. Hasta yaşı, menopoz durumu, ameliyat öncesi tümör belirteçleri ve ameliyat öncesi ultrasonografi özellikleri hastane veri tabanlarından toplandı. İlk prosedürden sonra, cerrahi yöntem, histolojik sınıflandırma, tanı anındaki evre, tümörün boyutu, lenf nodlarının durumu ve nihai patolojik tanı ile ilgili bilgiler toplandı.

Bulgular: Bu çalışma 2007-2023 yılları arasında cerrahi uygulanan 84 hastadan oluşan bir kohortu içermektedir. Çalışma gruplarının ortanca yaşı 41,5 olup, 15 ile 88 arasında değişmektedir. Hastaların %71,4'ü premenopozal evredeydi. Nihai patoloji, hastaların %11,9'unu oluşturan 10 hastada malign tümör varlığını ortaya koymuştur. Toplam hasta sayısının altısında seröz tümör, dördünde ise müsinöz tümör vardı. 83 kişiden 3'ünde hastalığın nüks ettiği tespit edilmiş olup bu da %3,6'lık bir orana işaret etmektedir. Bu bireyler için ortalama progresyonsuz sağkalım süresi 19 aydı. Yalnızca hastalığın erken evresindeki bireylerde nüks görüldü ve ikisinde mikropapiller varyant göstermiştir.

Sonuç: Sonuç olarak, BOT'lar oldukça olumlu bir prognoza sahiptir. Kriterleri karşılayan hastalara fertilite koruyucu cerrahi prosedürler uygulanması düşünülebilir.

Anahtar Kelimeler: Borderline over tümörleri, over kanseri, jinekolojik cerrahi

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INTRODUCTION

Borderline ovarian tumor (BOT) was first described in 1929 as a semi-malignant ovarian tumor (1). Since the early 1970s, the World Health Organization (WHO) and the International Federation of Gynecology and Obstetrics (FIGO) have categorized BOT as a distinct group of ovarian tumors based on their appearance (specifically, the lack of invasion into surrounding tissue). BOT is characterized by moderate nuclear atypia and slightly increased mitotic activity but does not exhibit stromal invasion or rapid infiltrative growth (2).

Youthful women are diagnosed with them at an early stage and have a more favorable prognosis compared to malignant ovarian tumors (3). The 5-year survival rates range from 95% to 97%, with around 70% of these cancers being diagnosed in stage I (4). A thorough examination of the abdominal and pelvic cavities is necessary to accurately determine the stage of the disease and ensure its complete eradication. Surgical staging often involves several essential procedures, including cytologic washings, tumor resection, infracolic omentectomy, and peritoneal biopsies. It is not advisable to perform routine lymphadenectomy (5). While recurrences are higher in cases where the ovary is preserved, there is no significant adverse effect on survival. This is because the majority of recurrences are of the borderline type and can potentially be salvaged with surgical intervention (6,7).

This study aimed to describe and analyze the clinical characteristics, tumor histology, and treatment approaches for women diagnosed with BOT at Mersin University from 2007 to 2023.

MATERIALS AND METHODS

This retrospective analysis involved patients who were diagnosed with borderline ovarian tumors at the Department of Obstetrics and Gynecology, Mersin University Faculty of Medicine, from 2007 to 2023. The project received approval from our university's Clinical Research Ethics Committee (18/10/2023, approval number 2023/706). Pertinent information regarding the patient's age, menopausal state, preoperative tumor markers, and preoperative ultrasound features were acquired from hospital databases. After the pre-surgery, we collected data on the surgical method, histological classification, stage at the time of diagnosis, size of the tumor, lymph node condition, and ultimate pathological diagnosis. Gynecologic pathology specialists examined tissue samples. Furthermore, the study evaluated supplementary therapies, the duration of postoperative monitoring, and potential instances of relapse. It examined them for staging using the 2014 FIGO staging criteria. Patients with incomplete data were not included in the analysis.

The statistical studies were conducted using IBM SPSS Statistics 22 software developed by IBM et al. in the United States. The data distribution was assessed for normalcy using the Kolmogorov-Smirnov Test. The data were presented as percentages, mean ± standard deviation, and median. A significance level of $p \leq 0.05$ was used to determine statistical significance.

RESULTS

The mean age at diagnosis time was 42.29 ± 16.06 years, 71.4% of the patients were premenopausal. Histopathologically, 39 patients had serous (54.9%), 23 patients had mucinous (32.4%), five patients had seromucinous (7.0%), three patients had endometrioid (4.2%), and one patient had Brenner (1.4%) type BOT. Stage 1a was seen in 45 cases (53.6%), stage 1b in 1 case (1.2%), stage 1c in 36 cases (42.9%), stage 3a in 1 case and stage 3c disease in 1 case.

The median preoperative CA 125 value was 26 U/l (2-5842), 31 (36.9%) patients had high levels of CA 125 (35 U/mL). In individuals with serous pathology, the median CA 125 level was 31.5 U/mL, while in those with mucinous type, it was 20.5 U/mL. No statistically significant difference was observed between the two groups (p=0.379). The CA 125 level was significantly greater in nulliparous patients compared to multiparous ones (p=0.032).

The maximum tumor size was 8.89 ± 5.43 cm in the serous type, 15.17 ± 6.65 cm in the mucinous type, 7.58 ± 3.60 cm in the ceruminous type, and 4.63 ± 1.89 cm in the endometrioid type. Tumor size was significantly larger in nulliparous patients (p=0.012). When comparing premenopausal and postmenopausal individuals, no statistically significant difference was found between the two groups (p=0.196).

In unilateral tumors, 52.6% were serous, and 35.1% were mucinous histopathologic types. In bilateral tumors, 64.3% were serous, and 21.4% were mucinous. 87.0% of mucinous tumors were unilateral, whereas 23.1% of serous tumors were bilateral.

Positive peritoneal cytology was detected in 9 (16.7%) patients. High CA 125 levels were detected in 66.7% of patients with positive cytology results. There was no significant difference in CA 125 levels between the two groups, as indicated by a p-value of 0.546. Of the patients with positive cytology, 83.3% were serous, and 16.7% were mucinous histopathologic type.

Out of the 83 people, a recurrence of the condition was found in 3, indicating a rate of 3.6%. The mean duration of progression-free survival for these individuals was 19 months. Only individuals

Table 1. Demograghic and statistical characteristics of borderline ovarian tumors

Age	
Median (n, range in years)	41.5 (15-88)
≤ 40	39 (46.4%)
> 40	45 (53.6%)
Menopausal status (n,%)	
Premenopausal	60 (71.4%)
Postmenopausal	24 (28.6%)
Histology (n,%)	
Benign	3 (3.6%)
Malign	10 (11.9%)
Borderline	71 (84.5%)
Serous	39 (54.9%)
Mucinous	23 (32.4%)
Seromucinous	5 (7.0%)
Endometrioid	3 (4.2%)
Brenner	1 (1.4%)
Tumor markers (U/mL) Ca125	MEDİAN 26.0 2-5842 U/mL
Median size (range in cm)	10.00 (1-28)
Stage in diagnosis (n,%)	
1A	45 (53.6)
1B	1 (1.2)
1C	36 (42.9)
3A	1 (1.2)
3C	1 (1.2)
Surgery (n,%)	
Cyctectomy	30 (35.7%)
Bilateral cyctectomy	7 (8.3%)
Unilateral salpingo-oopherectomy (USO)	27 (32.1%)
Hysterectomy	40 (47.6%)
Omentectomy	6 (7.1%)
Pelvic lymph node dissection	23 (27.4%)
Paraaortic lymph node dissection	22(26.2%)
Appendectomy	25 (29.8%)
Treatment after recurrence Carpoplatine/paclitaxel combination	3 (3.6%)
Recurrence (n,%)	3 (3.6%)

in the early stage of the disease experienced a recurrence, and two exhibited micropapillary alterations. One patient experienced a recurrence in the opposite ovary after relapsing following oophorectomy, while the remaining patients experienced recurrence after cystectomy. The presence of micropapillary variations and the performance of cystectomy have been recognized as the most significant risk factors for the recurrence of the disease. The histological subtypes detected in the recurrences were serous and mucinous.

Patients who have advanced disease or have lost their ability to reproduce are treated with a comprehensive surgical procedure. This procedure includes cleaning the peritoneal cavity, removing the uterus and fallopian tubes, removing the ovaries, removing the fatty tissue in the lower abdomen, completely removing visible lesions in the peritoneum, or taking multiple tissue samples from the peritoneum. In cases of mucinous borderline ovarian tumors, patients also undergo an appendectomy. Unilateral salpingo-oophorectomy was performed in 27 patients, and cystectomy in 30 patients who wanted to preserve early-stage fertility.

DISCUSSION

This study involved a retrospective review of 84 individuals with BOT who underwent surgery at our clinic. The age distribution of patients diagnosed with BOTs exhibits significant variation across different studies, indicating a broad range of ages. Within a particular study, the average age at which the condition was diagnosed was 41.77 years, with the age range spanning from 19 to 84 years. The majority of patients, precisely 70%, were in the premenopausal stage (8). Another study reported a mean age of mean age 40 years , with patients ranging from 15 to 84 years, and noted that 71.1% of patients were premenopausal (9). A third study revealed that the average age of diagnosis was 40.6 years, with patients spanning from 17 to 78 years. Furthermore, 51.9% of instances were individuals under 40 years (10). In a larger cohort, the median age at initial diagnosis was 47 years, with a range from 13 to 85 years, and the age distribution was divided into three groups: 114 patients aged 13-39 years, 100 patients aged 40-50 years and 138 patients over 50 years (11). Finally, another study reported a mean age at diagnosis of 40.1 years, ranging from 14 to 80 years (12). Collectively, these studies suggest that although BOTs can occur at any age, they are most commonly diagnosed in women in their 40s, and a significant proportion of cases occur in young, premenopausal women. In our study, the median age of the patients was 41.5 years, ranging from 15 to 88 years. Similarly, in our study, most patients were in the premenopausal period.

The most common histopathological type of BOTs is serous, as consistently reported in multiple studies. In a study by J. Ren et al., serous histology was the most common, accounting for 101 of 234 cases (43.2%) (12). Similarly, another study found that serous BOTs accounted for 61.6% of cases (9). This trend is also supported by data showing that serous BOTs are the leading histological type in bilateral tumors, with 91% of such cases being serous (10). In addition, a study investigating the relationship between tumor markers, tumor size, and histopathology found that serous histopathology was more frequent in unilateral tumors (41.1%) and even in bilateral tumors (85.2%) (13). Another research paper confirmed these findings by reporting that serous BOTs accounted for 59.3% of cases in stage IA and 66.7% in stage IIIC, further

emphasizing its prevalence at different stages of the disease (8). These studies emphasize that serous histology is the most common type of BOT, followed by mucinous, and other types such as endometrioid, clear cell, and Brenner are significantly less frequent. Our study found the most common serous subtype and the second most common mucinous subtype.

CA 125 levels are an essential biomarker in the diagnosis and management of BOTs, with variations observed according to histopathology and tumor stage. A study analyzing CA 125 levels in patients with BOTs found that serous borderline ovarian tumors exhibited higher CA 125 levels than mucinous tumors, with a statistically significant difference (13). Specifically, mean CA 125 levels in serous histopathology were markedly elevated at 372.8 U/l, while mucinous tumors showed lower levels (13). In addition, the distribution of CA 125 levels varied according to the stage of the tumor. For example, in stage IA, 65.9% of patients had CA 125 levels below 35 U/mL, whereas in more advanced stages such as IIIC, 85.7% of patients had levels above 35 IU/ml, indicating a correlation between higher CA 125 levels and advanced disease stages (8). This trend underlines the utility of CA 125 as a marker for disease progression. The median CA 125 level of the patients in our study was 26. There was no significant difference between CA 125 levels when comparing histopathologic types (p=0.211).

In the study by Güngör et al., 80.3% of the patients were stage 1A (10). In a study by Güvenal et al. in 539 patients, 73.5% of the patients were found to be 1A (9). In our study, stage 1A was the most common stage with 53.6%.

In a study by Ren et al. investigating the factors affecting recurrence in patients with BOT, recurrence was found to be 16.8% in patients who underwent conservative surgery and 5.2% in patients who underwent radical surgery (12). In a single-center study conducted by Güngör et al. with 183 patients, the recurrence rate was 2.7%. In this study, adjuvant chemotherapy was administered to 8.1% of the patients. In the same study, 91 patients (49.7%) underwent comprehensive surgery, and USO was the most common fertility-preserving surgery. Unilateral cystectomy was performed in 15 patients (16.8%) (10). In the Turkish Gynecologic Oncology Group study by Güvenal et al. evaluating 539 patients, the recurrence rate was 5.4%. In the same study, the recurrence rate was 8.3% in patients who underwent conservative surgery and 3% in patients who underwent radical surgery (9). In a study by Ayhan et al. evaluating recurrence and prognostic factors in Borderline ovarian tumors, 13 of 100 patients received chemotherapy, and the recurrence rate was found to be 3% (8). Our study found the recurrence rate to be 3.6% and the rate of patients who received chemotherapy to be 3.6%. We thought that the low recurrence rate and the low number of patients who received chemotherapy may be due to the higher number of patients who underwent radical surgery compared to other studies. In our study, cystectomy was the most common procedure, and USO was the second most common procedure in patients who underwent fertility-preserving surgery.

In conclusion, BOTs have an excellent prognosis with low recurrence rates. Fertility-sparing surgery options should be considered for appropriate patients. Larger studies with well-staged patients are needed for the management of BOTs and treatment options.

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