

# A diagnostic dilemma for solid ovarian masses: the clinical and radiological aspects with differential diagnosis of 23 cases

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## Summary

**Objective:** This study aimed to analyze the clinical characteristics and diagnostic features of ovarian fibromatous masses. **Materials and Methods:** The authors reviewed the records of 23 women who underwent laparotomic surgeries and whose final histopathological diagnoses were ovarian fibroma, cellular fibroma, or fibrothecoma from January 2005 to January 2013. The clinical, ultrasonographic, magnetic resonance imaging, tumor marker, therapeutic, and histologic data were analyzed. **Results:** The mean age of the patients was 50.9 years. Sixteen patients were menopausal. The preoperative ultrasonography examination incorrectly diagnosed seven lesions as uterine fibromas, and the magnetic resonance imaging examination incorrectly labeled three lesions as pedunculated subserous uterine fibromas. The cancer antigen-125 levels of 17 cases were measured, with four being abnormal. Twenty-three patients underwent a laparotomy. Twenty patients underwent a total hysterectomy with bilateral salpingo-oophorectomy, and three underwent a tumorectomy. The histological diagnosis was fibrothecoma in 21 cases, fibroma in one case, and cellular fibroma in one case. Histopathologic examination of the endometrium of seven of the 20 patients who underwent hysterectomy revealed simple endometrial hyperplasia without atypia. **Conclusion:** Ovarian fibromas and fibrothecomas are often misdiagnosed as uterine fibromas and occasionally mistaken for malignant tumors of the ovary preoperatively. As these tumors originate from ovarian stroma, they may be hormone-active tumors. Therefore, they may lead to premalignant changes in the endometrium. The preoperative evaluation of the endometrium is recommended.

**Key words:** Cellular Fibroma; Fibroma; Fibrothecoma; Magnetic Resonance Imaging; Ultrasonography.

## Introduction

Ovarian fibromas and fibrothecomas, which comprise 1-4% of all ovarian neoplasias, are the most common benign tumors of the ovarian stroma [1, 2]. They are included in the sex cord stromal tumors of ovaries and may present at any age. Ovarian fibromas/fibrothecomas are usually confused with uterine fibromas and rarely diagnosed preoperatively as they appear solid upon ultrasonography (USG) [3].

Ovarian fibromas are occasionally accompanied by ascites and cancer antigen 125 (CA-125) elevation in the serum; the clinical picture in that case may resemble that of a malignant ovarian tumor [4, 5]. The risk of Meig's syndrome, characterized by ascites and hydrothorax, increases, especially in tumors larger than ten cm. These lesions are generally asymptomatic and detected during routine gynecologic examinations [4]. As they originate from the stroma, they may secrete hormones (estrogen and rarely, androgens) and cause some clinical signs that depend on estrogen release.

This study examined 23 patients with ovarian fibromas or fibrothecomas with respect to their preoperative symptoms and USG and magnetic resonance imaging (MRI) results. As these tumors may be hormone-active, they may induce histopathological alterations in the endometrium.

## Materials and Methods

This retrospective study was approved by our hospital's local ethics committee. Informed consent forms were not needed. The study included 23 female patients who underwent operations for various gynecologic indications and were diagnosed with ovarian fibroma, fibrothecoma, or cellular fibroma by pathological examination between January 2005 and January 2013. The demographic data (age, height-weight index, parity, mode of delivery [spontaneous vaginal vs. caesarean section]), menopausal state (patients with amenorrhea for longer than one year after the last menstrual cycle, were accepted as menopausal), indications for operation, USG and MRI imaging findings, and tumor markers including serum CA-125 and carbohydrate antigen 19-9 (CA19-9) were analyzed. Two patients who presented to the present hospital with menometrorrhagia underwent endometrial biopsy before the operation, and one patient presenting with postmenopausal bleeding underwent fractional curettage before the operation.

### Data collection and image interpretation

The medical records and images of the patients were accessed via the hospital registry (Hospital Information System: HIS, Picture archiving computed system: PACS). All patients were evaluated using B-scale USG, and 20 patients were also evaluated with color Doppler US. Fifteen patients underwent a pelvic MRI examination. The MRI examinations were performed using a 1,5 T device and an eight-spiral body coil. Intravenous contrast material

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(0.1 mmol/kg gadolinium diethylenetriaminepentaacetic acid) was administered to all patients during the examination. The images were consensually evaluated by two radiologists (A.S., B.G.) experienced in abdominal radiology. The mass's location, size (the two largest orthogonal diameters were evaluated in terms of millimeters), configuration, morphology, echogenicity relative to neighboring structures, and vascularization upon color Doppler ultrasonography (CDUS) (vascularization absent; avascular, vascularization present and close to the uterine myometrium; moderately vascular, vascularization less than the myometrium; hypovascular, more than myometrium; and hypervascular) were assessed.

Parameters similar to those examined in the ultrasonographic examination were investigated in the MRIs. In addition, the lesion's signal intensity relative to the uterus was examined in the T1- and T2-weighted examinations, and the contrast uptake pattern relative to the uterus and the capsule and the presence of necrosis were analyzed in the post-contrast images. Contrast uptake equal to, less than, and more than the uterus were interpreted as isovascular, hypovascular, and hypervascular enhancements, respectively. Both the USG and MRI were used to search for intra-abdominal fluid and pathologies of the uterus and other pelvic structures. Preoperative chest X-rays were re-evaluated particularly for the presence of pleural fluid.

#### *Pathological examination*

Operational materials of the patients were fixed with 10% formalin, and four-micron sections were obtained from paraffin-embedded blocks. Each slide was stained with hematoxylin and eosin (H&E), examined under a light microscope, and diagnosed based on the pathological properties of the tumors.

#### *Statistical analysis*

Statistical analyses were performed to examine the relationship of tumor size with age, the presence of ascites, and CA-125 levels. The data are expressed as the median and range. Frequency distributions were compared using rank correlation and the Chi-square test, and median values were compared using the Student *t* test or Mann-Whitney *U* test. A two-sided *p* value less than 0.05 was considered statistically significant.

## **Results**

#### *Clinical findings*

A total of 28 lesions were detected in the 23 female patients included in the study (lesions were bilaterally located in five patients). The age range of the patients was between 31 and 67 years. The mean presenting age was 50.9 years. Sixteen (69.6%) of the patients were considered to be in menopause. Twenty-one patients were multiparous, and two were nulliparous. The main symptoms were nonspecific abdominal pain (*n*=9), abdominal bloating (*n*=5), menometrorrhagia (*n*=2), and menopausal bleeding (*n*=1). Three patients presented with acute abdominal pain and underwent an emergency operation with the initial diagnosis of ovarian torsion. Three patients presenting with acute abdomen were in menopause. The largest tumor diameter was 16 cm and the smallest was 11 cm. One (6.25%) menopausal patient complained of postmenopausal bleeding.

The mean tumor diameter was 13.6 cm. There was no significant relationship between the tumor size and patient age (*p* > 0.05). However, three patients were asymptomatic

and underwent an operation after the detection of a mass in the ovary during a routine gynecologic check-up.

#### *Radiological findings*

A total of 22 (22/28, 88%) lesions were detected by USG in 20 of 23 patients. Both lesions were observed on USG in two of the five patients with bilateral lesions, whereas only a single lesion was detected in the remaining three patients with bilateral lesions. Three patients were free of any pathology in the ovaries upon USG. The USG examination revealed that 11 of the lesions had a solid internal structure, seven had a mixed solid-cystic internal structural pattern, and two had hyperechogenic components suggestive of fatty tissue. Two tumors, in contrast, had a cystic appearance containing a dense, viscous fluid, due to prominent necrosis. On the Doppler scan, one of the hypervascular lesions (*n*=4) was found to have a low-impedance arterial flow suggestive of a malignancy. Three of these with an avascular masses (*n*=5) had ascites in the abdomen; the presence of severe abdominal pain suggested the presence of ovarian torsion. Seven lesions were reported as pedunculated subserous uterine myomas because they showed an echogenicity close to the uterine internal echo and a blood flow close to that of uterus. Six masses, however, exhibited much lower blood flow compared with the uterine parenchyma. A total of 16 masses were localized by MRI in 15 patients. The majority of the lesions (10/16, 62.5%) were iso- or hypo-intense in the T1-weighted imaging and hypo-intense in the T2-weighted imaging. The majority were homogenous in T1 (9/16, 56%) and heterogeneous in T2 (9/16, 56%). On the MRI examination, masses close to the midline and hypovascular relative to the uterus (*n*=3) were reported, with the initial diagnosis of a pedunculated myoma (Figure 1). In the other patients, the masses stained iso- (*n*=8) or hyper-intense (*n*=4) relative to the uterus were reported as ovarian benign solid tumoral masses. The MRI examination of the patient who had a suspicious malignancy on the Doppler scan showed similar contrast enhancement as the papillary projections, and thus the mass was reported as a borderline or malignant ovarian mass. Four (4/16, 25%) patients had areas of necrosis appearing hypointense in the T1-weighted images and hyperintense in the T2-weighted images. Two of these patients had ascites in the abdomen. Twelve (12/16, 75%) patients had a capsule with contrast uptake that surrounded the lesion and appeared isointense in the T1-weighted images and hypointense in the T2-weighted images. All patients had a normal preoperative chest X-ray, and no pleural effusion was evident. The patients' ages, symptoms, and radiological findings are summarized in Table 1.

#### *Laboratory findings*

The CA-125 levels were measured in 17 patients and were in the normal range (< 35 IU/ml) in 13 (13/17, 76.5%) patients. These levels were higher than the upper limit of

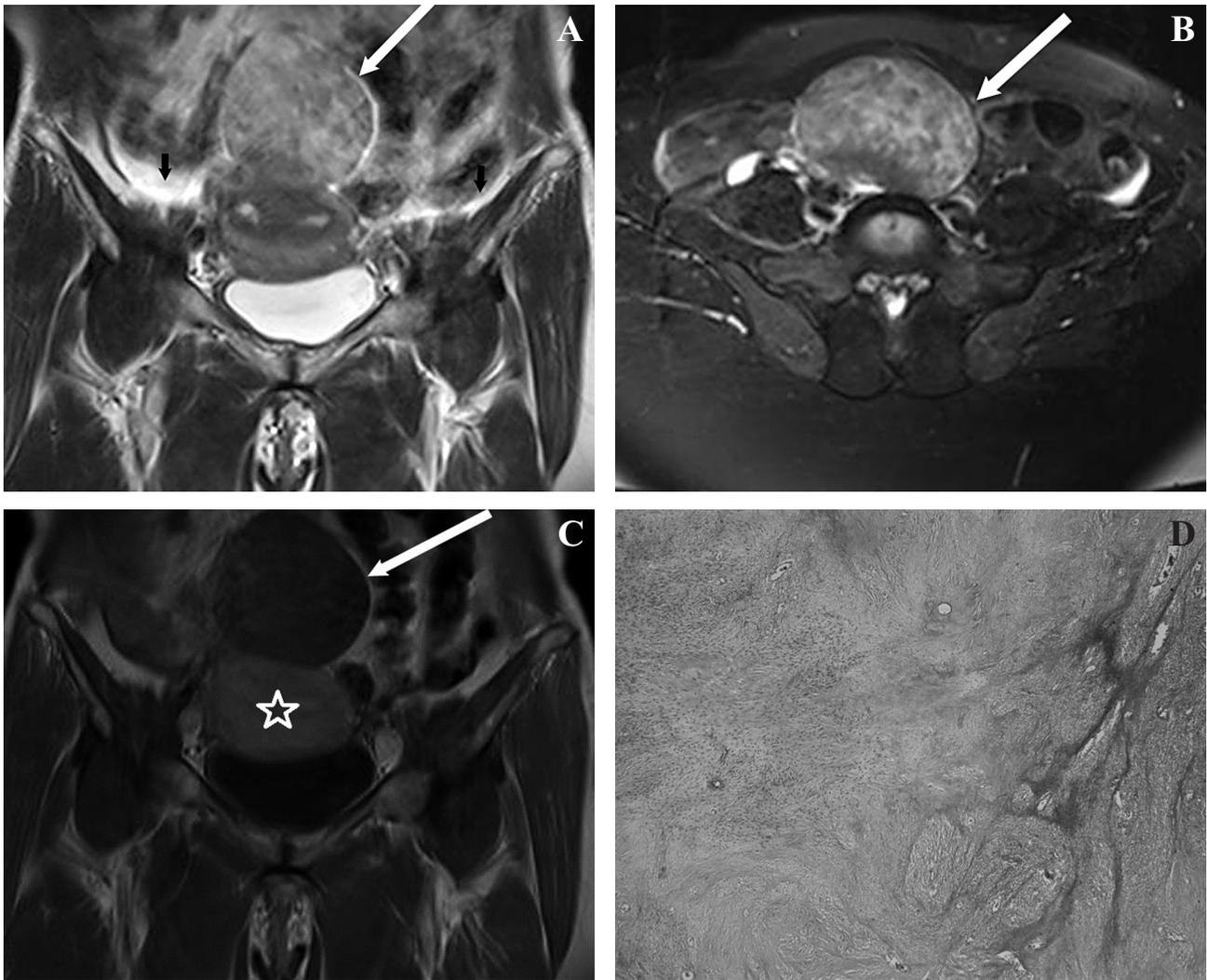


Figure 1. — A 51-year-old female patient with abdominal pain. The ultrasonographic examination revealed an 8x7 cm solid avascular mass with a myoma-like internal structure and diffuse ascites in the abdomen. (A) A subsequent MRI showed an 8x7x6 cm hyperintense mass-like formation (white arrow) at the midline, which had a close relationship with the uterus. There is also free fluid in the abdomen (black arrows). (B) In post-contrast fat suppression axial sections, the lesion shows no contrast uptake (white arrow), and (C) a normal contrast uptake is evident in the uterus (star). (D) The lesion was reported to be a torsioned myoma, but the histopathological examination revealed a torsioned fibrothecoma. The microscopic specimen shows dense, spindle-shaped cellular structures with round nuclei that do not contain cellular atypia and mitosis. The presence of neighboring foci of necrosis and hemorrhage suggested torsion (H&E x40).

normal (65, 68, 73, and 80 IU/ml) in only four patients (4/17, 23,5%). There was no relationship between the tumor size and CA-125 elevation ( $p > 0.05$ ).

All five patients in whom the CA 19-9 levels were measured had normal CA 19-9 levels ( $< 40$  IU/ml). Three of the four patients with elevated CA-125 levels had abdominal ascites both on USG and during the operation. In contrast, the patient with a CA-125 level of 64 IU/ml had no free fluid in the abdomen in both preoperative imaging examinations and during the operation. The largest diameter of the tumor was measured as eight cm.

#### Operative findings

Twenty of the patients who were operated on underwent a total abdominal hysterectomy and bilateral oophorectomy, and simple mass resection was performed in three patients. Five patients had bilateral lesions, and the remaining patients had a unilateral lesion (left ovary: eight, right ovary: ten). The tumor size ranged between two and 17 cm, and the mean diameter was 8.7 cm. Nine (39.1%) patients were diagnosed with abdominal ascites. The tumor size ranged from eight to 17 cm (mean 11.8 cm) in the patients who had ascites in the abdomen. Five of the patients

Table 1. — *Clinical characteristics of the women.*

Characteristics	Median (range)
Age (years)	50.9 (31-67)
Parity (%)	
Multiparity	21 (91.3)
Nulliparity	2 (8.7)
Postmenopausal women (%)	16 (69.5)
Body mass index (kg/m <sup>2</sup> )	27.8
Associated symptoms n (%)	
Acute abdomen	3 (13)
Pain	9 (39.1)
Palpable abdominal mass	5 (21.7)
Postmenopausal hemorrhage	1 (4.3)
Menorrhagia	2 (8.7)
Asymptomatic	3 (13)
Preoperative diagnosis (%)	
Myoma uteri	7
Benign Ovarian tumors	12
Malign ovarian tumors	1
Mass diameter in women with ascites (mm)	12.1 (8-17)
Location of fibrothecoma/fibroma (%)	
Right	10 (43.4)
Left	8 (34.7)
Bilateral	5 (21.7)
Histopathological results (%)	
Fibroma	1 (4.3)
Fibrothecoma	21 (91.3)
Cellular fibroma	1 (4.3)
Treatment (%)	
HT+BSO	20 (87)
Tumorectomy	3 (13)
Endometrial pathology in total hysterectomy (%)	
Endometrial hyperplasia	7 (35)
Proliferative endometrium and myoma uteri	11 (55)
Adenomyosis	2 (10)

with abdominal ascites had a left ovarian tumor, and four had a right ovarian tumor. None of the patients with bilateral fibrothecomas had abdominal ascites.

### *Histopathological findings*

In seven patients, the masses of ovarian origin were sent for frozen examination during the operation, and the results were negative. One of the two patients presenting with menometrorrhagia had a preoperative endometrial curettage result consistent with simple endometrial hyperplasia without atypia, whereas the other had a result consistent with an irregular proliferative endometrium. The patient who presented with postmenopausal bleeding had a preoperative curettage that showed endometrial superficial epithelium. The results of the pathological examination of the cases revealed fibrothecoma in 21 patients, cellular fibroma in one patient, and fibroma in one patient. In the patients, five fibrothecomas originated from both ovaries, six originated from the left ovary, and ten originated from the right ovary. Cellular fibroma and fibroma originated from the

Table 2. — *Distribution of hyperplasia in the endometrium histopathology of patients undergoing hysterectomy.*

	Menopausal patients	Premenopausal patients
Total patient number (n)	16	4
Number of patients with simple hyperplasia without atypia (%)	5 (31.3)	2 (50)

Table 3. — *Distribution of the ovarian histopathology of patients whose endometrial histopathological examination revealed simple endometrial hyperplasia without atypia.*

	Total	Fibrothecoma	Fibroma	Cellular fibroma
Number of patients with simple hyperplasia without atypia (%)	7 (100)	6 (85.7)	1 (14.3)	0

left ovary. Five of the 16 patients who were in menopause and underwent a total abdominal hysterectomy and bilateral salpingo-oophorectomy had an endometrial histopathology consistent with simple endometrial hyperplasia without atypia (Table 2). Two of the four patients who were premenopausal and underwent a total abdominal hysterectomy and bilateral salpingo-oophorectomy had an endometrial histopathology consistent with simple endometrial hyperplasia without atypia. Out of the seven patients with an endometrial pathology consistent with simple endometrial hyperplasia without atypia, six were diagnosed with a fibrothecoma in the ovary, and one had a fibroma in the ovary (Table 3). Ovarian torsion was observed in three women, all of whom were menopausal (Figure 1D).

USG examinations three months and one year after the operation did not show abdominal ascites in any patient. The follow-up laboratory results showed normal CA-125 levels. The present authors continue to follow-up these patients in an asymptomatic state.

### **Discussion**

Ovarian fibromas/fibrothecomas are the most common benign tumors of the ovary, which are included in the group of sex cord stromal tumors of the ovary. They are almost always benign and curable by surgical excision. This tumor is usually seen in postmenopausal women [2, 6]. The mean age of the women in the present study was 50.9 years, and 16 (69.6%) of the patients were in menopause.

Microscopically, ovarian fibromas are solid tumors originating from fibroblastic cells [2, 7, 8]. Ovarian fibromas are solid tumors consisting of cellular bundles and intersecting strips of hyaline-appearing collagen and fibrous tissue. Fibroblastic cells are spindle-shaped and do not possess signs of atypia. Fibrothecomas comprise lipid-

laden theca cells forming thecomas and some other cells forming fibromas; this terminology is used when the distinction between these two forms is not clear [8]. Cellular fibromas, which are a rare form of ovarian fibromas, can also occur. A tumor containing cells with closely packed nuclei with absent or minimal nuclear atypia in addition to one to three mitoses per ten high-powered fields is classified as a cellular fibroma [9]. These tumors are benign despite reports of local recurrence after surgery. A tumor showing moderate nuclear atypia and three mitoses per ten high-powered fields has malignant potential and is designated as a fibrosarcoma.

The symptoms are generally non-specific and include pelvic pain and menometrorrhagia [4]. However, three of the patients in this series presented with acute abdomen and underwent an operation with the diagnosis of ovarian torsion; the histopathological examination revealed a fibrothecoma in the ovary. The largest diameter of the fibrothecomas in the torsioned ovaries was 16 cm, and the smallest was 11 cm; the mean diameter was 13.6 cm. Son *et al.* reported torsions with a rate of 6.4% [6]. This study also detected a mean tumor diameter of 11 cm. Vijayaraghavan *et al.* reported a patient presenting to the hospital with acute abdominal pain who was diagnosed with right ovarian torsion; after undergoing a laparotomy, this patient was found to have a fibroma with a diameter of 16 cm accompanied by a torsioned ovary [10].

Misdiagnosing ovarian fibromas as uterine fibromas in the preoperative period is common [3, 11]. The present authors also operated six patients with an initial diagnosis of uterine fibroma as a result of imaging examinations during the preoperative workup. Due to their fibrous content, ovarian fibromatous masses can be confused in the radiological examinations with subserous, pedunculated uterine fibroids that extend especially into a broad ligament. In a study assessing 35 patients with ovarian fibromas and fibrothecomas by MRI, Shinagore *et al.* compared their findings with nine uterine fibroids in the same patient group and stressed that neither the signal properties of the mass in the T1- and T2- weighted sequences nor the contrast uptake were radiological distinguishing features from uterine fibroids [12]. Fibromas and fibrothecomas can be distinguished from uterine fibroids only by demonstrating the relationship of the lesion with the ipsilateral ovary. The presence of a follicle or capsule surrounding the lesion increases the possibility of a fibroid. Ovarian fibroids actually lack a capsule, but they considerably slenderize the ovarian stroma they originate from, forming the pattern of a capsule. Oh *et al.* observed a capsule surrounding the lesion on MRI with a rate of 67% in a 24-patient series [13]. The present authors also noticed a capsule surrounding the mass in 75% of the patients; however, they did not encounter any cystic pattern consistent with an ovarian follicle in the area surrounding the mass.

The present authors observed a serous cystadenoma in addition to a fibrothecoma in the right ovary of one of the

patients who had bilateral fibrothecomas and a serous cystadenoma in the same ovary as the fibroma in another patient. In a 38-year-old woman with bilateral fibrothecomas, the right ovary had changes consistent with endometriosis. The histopathological examination of the uteri of 20 patients who underwent a total abdominal hysterectomy revealed adenomyosis in two patients, uterine fibroma and proliferative endometrium in 11 patients, and simple endometrial hyperplasia without atypia in seven patients. The authors' search of the English literature did not reveal any studies reporting the development of endometrial hyperplasia in patients with fibrothecoma/fibroma as frequently as in this study (7/20, 35%).

Five (21.7%) women in the present study had bilateral fibrothecomas. Son *et al.* [6] reported a rate of 4.3% for bilateral tumors, and Paladini *et al.* [3] reported a rate of 6%. Previous studies reported a bilateral tumor incidence of zero to 11.76% [1, 2, 4, 11]. The present authors found a bilateral tumor rate of 21.7%, which was higher than in previous studies. Ten of the patients had right ovarian tumors, six had left ovarian tumors, and five had bilateral fibrothecomas. Cellular fibromas and fibromas were of left ovarian origin. They also found that, unlike Sivanesaratnam *et al.* and Leung *et al.* [4, 11] but in agreement with Son *et al.* [6], the possibility of having a right ovarian fibroma was higher.

In the present study, the tumor diameter in nine patients (39.1%) with abdominal ascites ranged between eight and 17 cm. The average tumor diameter was 11.8 cm in patients with abdominal ascites. However, those patients with no ascites had a tumor diameter ranging from two to 11 cm, with an average size of 6.6 cm. In the present study, the tumor size was not proportional to ascites ( $p > 0.05$ ). The relationship between fibromas and ascites is explained by the observations showing that the cortex layer of the ovary, the origin of the fibroma, does not have lymph vessels, making the tumor form a transudate [2, 6, 7].

Abdominal ascites disappear after tumor resection [2, 14]. Nine patients in the present study who had abdominal ascites at the preoperative period also had no signs of ascites at the three-month and one-year follow-ups. The CA-125 elevation and presence of abdominal ascites were correlated with each other in the present study ( $p < 0.05$ ). Three of nine (33.3%; 3/9) patients with abdominal ascites had CA-125 elevation, whereas six (66.7%; 6/9) had subnormal CA-125 levels (CA-125 35 IU/ml). The present results are consistent with those reported by Pastnerand *et al.* and Son *et al.* [5, 6].

The CA-125 levels normalized three months later in the patients with a preoperative elevation of these levels. Previous studies also reported rare CA-125 elevation that normalized after the operation [14]. Surgery is the recommended mode of treatment in fibromas/fibrothecomas. Although radical surgery has been recommended in perimenopausal and postmenopausal women, simple excision of the mass has been recommended in younger patients [2].

Ovarian fibromas/fibrothecomas may be confused with uterine fibromas due to their echogenicity, which is similar to the internal echo of the uterus, and due to a similar blood flow as the uterus. They may also be confused with malignant ovarian tumors due to the accompanying free abdominal fluid, elevated tumor marker level, and solid tissue pattern [4, 5]. The initial diagnosis of ovarian fibromas may be misleading until the surgical therapy is performed and the diagnosis is confirmed by definitive histopathological examination. As fibromas/fibrothecomas originate from the ovarian stroma, they may actively secrete hormones, including estrogen and androgens. They may also cause premalignant changes in the endometrium, such as endometrial hyperplasia due to unopposed estrogen release at the premenopausal and postmenopausal periods [15, 16]. Therefore, evaluating the endometrium for estrogen exposure with ultrasonography and histopathological examination is beneficial, especially in premenopausal and postmenopausal patients scheduled to undergo salpingo-oophorectomy or tumor excision. Myoma uteri, irregular proliferative endometrium, and simple endometrial hyperplasia without atypia, which the present authors observed in the histopathological examination of the patients who underwent hysterectomy in this study, are conditions that are observed when the endometrium is exposed to estrogen. Therefore, evaluating the uterus using ultrasonography with regard to endometrial thickness and using endometrial biopsy with regard to histopathological diagnosis at the preoperative period will be useful to guide the selection of the operation type.

The main limitations of this study were its retrospective nature and the small sample size. The authors believe that future studies with larger sample sizes examining various pathologies (e.g., torsioned uterine fibroids) are clearly needed.

## Conclusion

Ovarian fibromas and fibrothecomas are common solid tumors of the ovaries. Due to diagnostic challenges, gynecologists and radiologists should consider ovarian fibromas in differential diagnoses, especially in patients with ovarian solid masses at a postmenopausal age. This tumor may be confused with uterine fibromas in radiological imaging studies. In postmenopausal patients presenting with acute abdominal torsion, ovarian fibromas/fibrothecomas should be considered as possibilities among the potential gynecological etiologies. These tumors may occasionally be confused with malignant ovarian tumors due to abdominal ascites, elevated CA-125 levels, and their solid structure. However, it should be noted that these tumors are benign and may be completely cured with surgical therapy. They may also be hormone-active and thus may lead to premalignant changes in the endometrium due to unopposed estrogen release. The endometrium should be thoroughly

evaluated before and after the operation. A more radical therapy would be appropriate in patients who have a preoperative diagnosis suggestive of fibroma or fibrothecoma and no concerns regarding fertility.

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