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CASE REPORT

Meigs Syndrome Caused by Fibrothecoma of the Ovary

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Huge or enlarged solid ovarian tumor, elevated serum CA-125 levels, massive ascites, and even pleural effusions are common features of ovarian cancer which have the worst outcome of gynecological malignancy. Here, we report a 53-year-old woman with fibrothecoma-associated Meigs syndrome mimicking ovarian malignancy, whose symptoms resolved gradually, and subsequently, serum CA-125 level declined to normal range after surgical intervention. The pathological diagnosis revealed fibrothecoma of the ovary compatible with Meigs syndrome containing the triad of benign ovarian tumor, ascites, and pleural effusion. Therefore, Meigs syndrome should be considered one of the clinical differential diagnoses for a large ovarian tumor with ascites, pleural effusion, and elevated CA-125.

Key words: Fibrothecoma, Meigs syndrome, ascites, CA-125, ovarian malignancy

INTRODUCTION

Ovarian tumors could occur among women of all ages. More than 30% of them may be malignant, especially in patients with perimenopausal or menopausal status. Around 60%–80% of patients with ovarian cancer present with huge ovarian tumors, ascites, elevated serum CA-125 levels, or pleural effusion.[1] Therefore, ovarian malignancy is highly suspected if an enlarged ovarian tumor appears with these clinical features. However, there is a rare condition, called Meigs syndrome characterized by a unique group of pathological benign lesions, which could mimic gynecological malignancy with the abovementioned clinical presentations. Here, we report a patient with Meigs syndrome who was diagnosed initially with ovarian cancer and had spontaneous resolution of symptoms after primary surgical intervention with tumor resection.

CASE REPORT

The patient is a 53-year-old married woman without significant prior medical history. She suffered from progressive shortness of breathing for 6 months. In August 2020, she visited the local medical department due to her persistent symptoms. At the thoracic medicine outpatient department, physical examination revealed absent breath sounds on the right hemithorax and decreased breath sounds on the left hemithorax. Shifting dullness with an enlarged pelvic mass was also noted. Chest X-ray showed bilateral massive pleural effusion. Thoracocentesis was done with appropriately 150 ml of pleural fluid collected. The pleural fluid cytology showed mesothelial cells with lymphocytes and neutrophils but was negative for malignant cells.

Thoracic and abdominal computed tomography (CT) scan with intravenous contrast material injection showed bilateral pleural effusion with a huge right adnexal mass, measuring 21 cm, along with massive ascites [Figure 1]. Based on the results of these investigations, ovarian malignancy was suspected, and the patient visited our hospital for a second opinion.

Chest X-ray was prescribed, and bilateral pleural effusion was noted with the dominance of the right side. Pelvic sonography revealed a large, solid, homogeneous, hyperechoic mass, about 21 cm × 13 cm in size [Figure 2]. The level of CA-125, checked at our hospital, was 920 U/ml.

Laparotomy was performed few days later. A large amount of ascitic fluid (approximately 1500 ml) was aspirated and a huge

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lobulated solid mass was observed. The mass was carefully freed from the surrounding adherent structures with a total abdominal hysterectomy and bilateral salpingo-oophorectomy [Figure 3]. The frozen section revealed ovarian benign fibrothecoma and the definite histopathological result revealed fibrothecoma of the ovary composed of the fibrous area with spindle cells and luteinized area. The cells in the luteinized area were immunoreactive for α-inhibin and melan-A but negative for cytokeratin. Mitotic figures were <5/10 high-power field and proliferative activity is <5% [Figure 4]. Three weeks later, the patient recovered with the resolution of ascites and pleural effusion and the level of serum CA-125 gradually decreased to the normal range. The therapeutic and course timeline of this case and the clinical conditions were also listed in Table 1.

DISCUSSION

Meigs syndrome, a triad of benign ovarian tumor, ascites, and pleural effusion, was first described in 1937 by Dr. Meigs, and its symptoms resolve after primary resection of the tumor. The prevalence of Meigs syndrome begins to increase in the third decade and the average age at presentation is in the fifth decade. Although these patients are usually diagnosed with ovarian malignancy before surgical intervention, a good prognosis with a total resolution of ascites and hydrothorax after surgical removal of the tumor is commonly noted.[2]

Ovarian fibroma, the most common ovarian stromal tumor, is also the most common tumor of Meigs syndrome, accounting for 1% of the total incidence. Fibroma found in Meigs syndrome is usually seen as a simple nonsecreting tumor. Fibroma may also contain thecoma elements which form estrogen secreting and form fibrothecoma, which is a rare ovarian tumor of the thecoma–fibroma group.[3] It is rare for fibrothecoma-related Meigs syndrome to have elevated serum CA-125. According to a previous study, fibrothecoma-related Meigs syndrome, with a serum CA-125 level of more than 35 U/mL, accounts for only 0.1% of all ovarian tumors.[4] There are only 16 of these cases reported in the past 10 years according to a literature review [Table 2].[5-11] All these patients had tumors larger than 10 cm, ascites no less than 4 liters, and

Table 1: The therapy and course timeline of this case and all detailed clinical conditions

2020/01 - 2020/08	• The patient visited the local medical unit with progressive shortness of breath and abdominal fullness for 6 months ○ Physical examination revealed decreased bilateral breath sounds with a huge palpable pelvic mass ○ Chest X-ray: Massive bilateral pleural effusion (more on the right side) ○ Pleural fluid cytology showed mesothelial cells with lymphocytes and neutrophils but was negative for malignant cells • Computed tomography of the chest and abdomen were performed ○ A large irregular tumor arising from pelvic region with ascites was revealed on abdominal computed tomography ○ Bilateral pleural effusion was noted on chest computed tomography but no mass lesion over bilateral lung parenchyma
2020/08	• The patient was transferred to our hospital due to a suspicion of ovarian cancer • CA-125 was analyzed: 920 U/ml • Transabdominal total hysterectomy and bilateral salingo-oophorectomy were performed ○ Frozen diagnosis: Fibrothecoma ○ Final pathology diagnosis: Compatible with fibrothecoma
2020/10	• CA-125 returned to the normal range 2 months later • Pleural effusion also resolved on chest X-ray

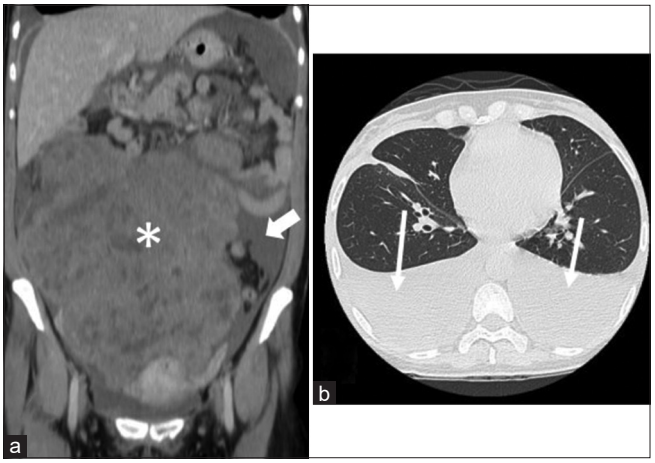

Figure 1: Abdominopelvic computed tomography demonstrated a huge ovarian tumor with an irregular surface (*) and ascites (arrowhead) (a) Chest tomography revealed bilateral pleural effusion (b)

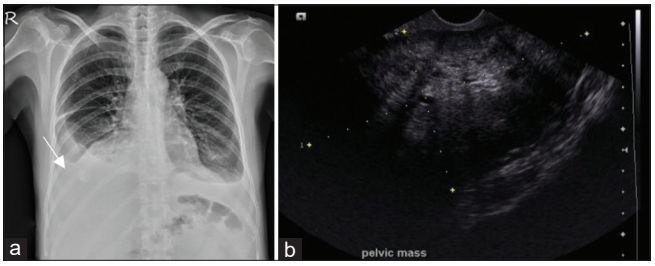

Figure 2: Chest X-ray revealed blunting of bilateral costophrenic angels which was more dominant on the right side (arrow) (a): transvaginal sonography revealed a hyperechoice mass lesion over cul-de-sac (yellow dotted line) (b)

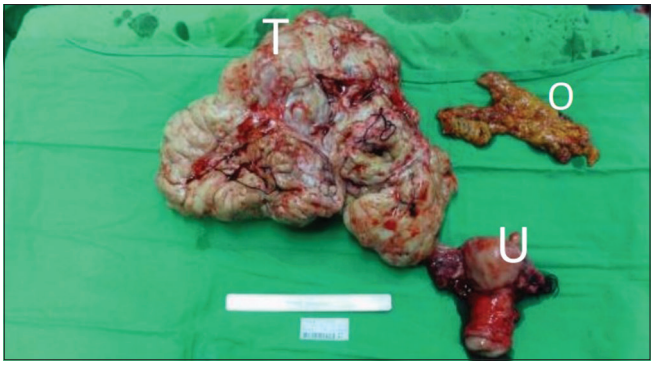

Figure 3: Huge right adnexal tumor (T) with the uterus and left ovary (U) and a part of the omentum (O)

Table 2: Fibrothecoma-related Meigs syndrome with elevated serum CA-125 level reported in the past 10 years

Author	Year	Case number	Age	Ascites volume (ml)	Pleural effusion volume (ml)	Tumor size (cm)	CA-125 (U/ml)
Loué *et al*.[11]	2013	1	35	4500	500	23.3×20	1835
Yazdani *et al*.[6]	2014	1	50	NA	NA	12×10	>600
Danilos *et al*.[5]	2015	1	50	4000	NA	13×9	2310
Shen *et al*.[10]	2018	6	NA	NA	NA	NA	>35*
Ziruma *et al*.[7]	2019	1	19	12000	200	8×10	125
Stabile *et al*.[8]	2021	1	62	20000	NA	20	1744
Shang *et al*.[9]	2021	4	54**	NA	NA	>10†	346‡

*CA-125 level of six cases were above 35 U/mL; **Average age of four cases; †Tumor size of four cases were all above 10 cm; ‡Average CA-125 level of four cases. NA=Not available

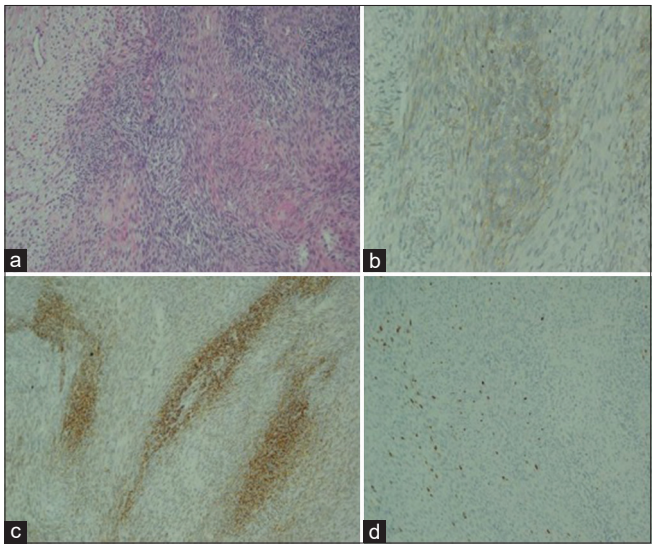

Figure 4: Pathologic findings of the ovarian fibrothecoma. The tumor cells are composed of fibrous spindle cells and luteinized area, H and E ×100 (a). The luteinized areas are immunoreactive for α-inhibin (b) and melan-A (c). The proliferative activity is <5% by Ki-67 stain (d)

pleural effusion amounting to 200–500 mL on each side. Larger tumor size, massive ascites, and hydrothorax also correlated with elevated serum CA-125 levels.[9] However, there was no age-specific prevalence.

CA-125, first described in 1983, is a high-molecular-weight glycoprotein recognized by a monoclonal antibody and utilized as a clinical diagnostic marker with an increased value seen in 80% of gynecological malignancies. Although this value varies by age, it can also be elevated in 30% of patients with benign conditions such as endometriosis, peritonitis, and ascites.[5]

The cause of ascites in Meigs syndrome is not well established so far. One hypothesis proposes that irritation of the peritoneum by a solid mass could stimulate mesothelial cells to produce several cytokines such as vascular endothelial growth factor, tumor necrosis factor-α, interleukin (IL)-1b, IL-6, and IL-8. Another is that tumor transudation to the surface is greater than the peritoneum capacity of reabsorption or tumor obstruction of the lymphatic vessels of the peritoneum. The right-sided hydrothorax occurs in 75% of all cases of Meigs syndrome; left sided only is rare but can be bilateral. The cause of hydrothorax remains unknown, although it is now generalized that the passage of ascitic fluid through the diaphragm or diaphragmatic lymph vessels to the pleural space may be a cause of pleural effusion.[11]

CONCLUSION

The clinical presentation of a huge ovarian mass, massive ascites, and pleural effusion along with elevated serum CA-125 usually indicates an ovarian malignancy. However, Meigs syndrome should be considered one of the differential diagnoses if body fluid cytology is negative for malignant cells and all symptoms resolve spontaneously after primary optimal resection of ovarian tumor with definite pathological confirmation that does not require further clinical treatment.

Ethical approval

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of the Tri-Service General Hospital, National Defense Medical Center for agreement of the study (B202215106, approved on 16 April 2022).

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published, and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

Data availability statement

All data generated or analyzed during this study are included in this published article.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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