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Original Article

Simultaneously with elevated tumor marker and hydrothorax in meigs' syndrome: a new clinical manifestation

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Abstract: Purpose: To report a new clinical manifestation of Meigs' syndrome accompanied with hydrothorax and elevated tumor marker but without ascites. Case: A 66-years old female patient, gravida 4, para 4, suffered a 15 cm neoplasm of right ovary and a massive hydrothorax without ascites. Lab exam revealed with CA125 in 2079 U/ml. With a primary diagnosis of malignant ovarian cancer, a surgery performed. The pathological biopsies confirmed of a benign ovarian fibroma and the patient made a good recover, and no recurrence was observed in the following 24 months. Conclusion: The clinical manifestation of Meigs' syndrome, compositing with elevated tumor markers and hydrothorax but without ascites, was never been reported before, and is easy to misdiagnose and mistreat. Meigs' syndrome should be considered in the diagnosis of malignant ovarian cancer and pathological biopsies are quite important.

Keywords: Ascites, hydrothorax, meigs' syndrome, pathology, tumor marker

Introduction

Normally speaking, an elevated serum tumor marker in postmenopausal women with solid adnexal masses, ascites and hydrothorax is highly revealing for malignant ovarian cancer. However, Meigs' syndrome is the exceptional one. In 1937, Dr. Meigs firstly reported a case of ovarian fibroma accompanied with ascites, and the ascites disappeared after removal of the mass. Thus, the term Meigs' syndrome was named [1]. In 1987, O Connell put forward that about 80% of the ovarian cancer patients got a higher CA125 level (>35 U/ml) [2]. However, Meigs' syndrome accompanied with an elevated tumor marker of CA125 is rarely seen, which only limited cases reported since the first one proposed in 1988 [3].

Here is a report of Meigs' syndrome accompanied with an elevated tumor marker and hydrothorax but without ascites. According to a MEDLINE search of the literature, this clinical manifestation has never been reported before, thus is easy to misdiagnose and consequently mistreat.

A 66-year-old Chinese patient, female, gravida 4 para 4, whose menopause occurred at the age of 45, was admitted to our hospital with a chief complaint of dyspnea and abdominal pain. This symptom had occurred over a period of 3 years and was accompanied with an 11 kg weight loss in recent 5 months. On physical examination, the patient got a reduced breathing sound and a mass of 15 cm in size was palpated in the hypogastrium without shifting dullness. Her uterus shrank in size. The remaining physical examination did not reveal any additional abnormalities. Trans-vaginal ultrasound and computed tomography (CT) scan revealed a neoplasm of size 15×15×10 cm in the right iliac region with arterial flow and without ascites. X-ray imaging suggested the presence of a moderate pleural effusion in the right side of the thoracic cavity. The concentration of serum CA125 was 2079 U/ml (normal level <35 U/ml). The human chorionic gonadotrophin β-HCG,

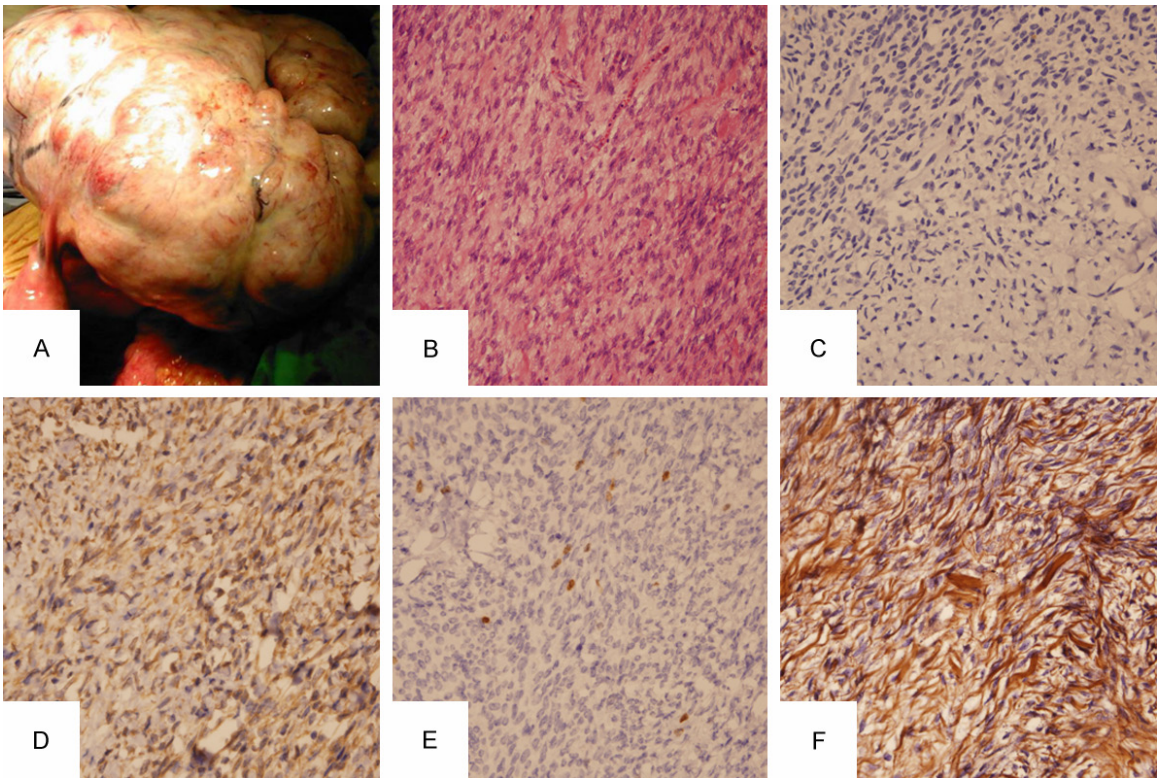

Figure 1. A. The enlarged right ovary is under removed in the operation. B. Hematoxylin and eosin staining, ×200. Abundant spindle fiber cells are visible. C. The IHC result of Desmin, ×400. The cell cytoplasm staining was positive, suggesting the tissue could be originated from stroma. D. The IHC result of Vimentin, ×400. The cell cytoplasm staining was negative, eliminating muscle originated. E. The IHC result of Ki-67, ×400. Ki-67 is used to stain the cells in proliferation, and the cell nucleus can be stained in brown. In the picture, the positive cells were in less than 1%, and cannot be a malignant tumor. F. The IHC result of Foot, ×400. It is used to stain reticular fiber. In benign tumor tissues, the fiber center on single tumor cell, while in malignant tumor tissues, it is center on group of tumor cells. In the picture, fibers surrounded each tumor cell respectively.

CA15-3, CA19-9, CEA levels andanti-nuclear antibody (ANA), anti-Scl-70 antibody, and anti-double-stranded-DNA antibody and anti-centromere antibody were within normal ranges. In order to remit her polypnea, the patient underwent a thoracocentesis and about 670 ml serous hydrothorax was drained from the right side of the thoracic cavity. With a suspicion of malignant ovarian cancer, a surgery then arranged.

At the explorative laparotomy, the right ovary appeared pale, smooth and enlarged, 15 cm × 15 cm × 14 cm in size, with serous layer completed (**Figure 1A**). The left ovary and uterine were shrinking. The fallopian tubes, liver, diaphragm, bowel, and omentum were free of the disease. No evidence of intra-peritoneal implants or enlarged lymph nodes were noted, and no necrosis presented. A surgery of total hysterectomy and bilateral salpingo-oophorectomy was performed.

The cytology of exudate was negative for malignant cells. Frozen sections and final histopathology confirmed of ovarian fibroma (**Figure 1B**). Subsequent immunohistochemical staining indicated DES (-) (**Figure 1C**), SMA (+), Inhibin-A (+), VEGF (-), VIM (++) (**Figure 1D**) and Ki-67 <1% (**Figure 1E**), and the argentaffin staining (**Figure 1F**) result revealed fibers surrounding each tumor cell. The patient made an uneventful recovery. About 2 weeks later, the pleural effusion disappeared and the CA125 level began to decrease, returning to normal 3 months later. The patient underwent further clinical examination over a period of 2 years. During this time, the levels of serum CA125 ranged from 4 U/ml to 13 U/ml, and chest radiography presented no hydrothorax.

Table 1. Reported cases of Meigs syndrome with the level of CA125

Author	Age	Chief complain	φ	Ascites	Hydrothorax	BO-CA125	PO-CA125	Operation	Pathology
Jones [3]	70	Pelvic mass	11	1200	Not refer	226	32	①	Fibroma
Hoffman [5]	32	Increasing abdominal girth	11	600	Positive	498	11	①	Thecoma
Walker [6]	52	Increasing abdominal girth	16	4500	Positive	>5000	8	①	Cellular fibroma
	67	Abdominal pain	18	3000	Not refer	104	Not refer	①	Cellular fibroma
Williams [7]	74	Chest pain	15	300	Negative	329	7.4	②	Thecoma
Lin [8]	74	Increasing abdominal girth	20	7000	Not refer	2120	20	①	Fibroma
	72	Increasing abdominal girth	14	6000	Positive	7000	26	①	Fibroma
Turan [9]	63	Increasing abdominal girth	18	Positive	Positive	743.6	14.6	①	Thecoma
Timmerman [10]	71	Anhelation	30	1000	Massive	485	6.2	②	Fibroma
Siddiqui [11]	73	Dyspnea	15	Positive	Not refer	1780	8	①	Fibroma
Abad [12]	51	Abdominal pain	6	5000	Not refer	577	243	①	Fibroma
Chan [13]	13	Abdominal mass	20	2000	Not refer	970	Not refer	③	Fibroma
Patsner [14]	62	Not refer	10	300	Not refer	185	Not refer	Not refer	Fibroma
	52	Not refer	16	1500	Not refer	520	Not refer	Not refer	Fibroma
	58	Not refer	18	100	Not refer	80	Not refer	Not refer	Fibroma
	60	Not refer	14	100	Not refer	64	Not refer	Not refer	Fibroma
	72	Not refer	18	1500	Not refer	1200	Not refer	Not refer	Fibroma
Buttin [15]	67	Increasing abdominal girth	11	3500	Positive	759	Not refer	①	Brenner tumor
Huang [16]	31	Abdominal distension	7	1300	Not refer	396	Not refer	①	Sclerosing stromal tumor
Vieira [17]	65	Dyspnea and weight loss	14	Positive	Positive	319	53.7	①	Thecoma
Bildirici [18]	17	Pelvic pain	25	400	Not refer	193	Not refer	Not refer	Sclerosing stromal tumor
Choi [19]	69	Abdominal distension	12	2500	650	82.49	Normal	①	Granulosa cell tumor
Jung [20]	50	Chest discomfort	19	Positive	Moderate	1476.8	Normal	①	Sclerosing stromal tumor
Mendoz [4]	46	Dyspnea	25	500	Positive	1808	11	Not refer	Fibroma
Kaur [21]	12	Abdominal pain	10	Positive	Positive	708	22.32	③	Granulosa cell tumor
Liou [22]	17	Abdominal fullness	15	9000	Not refer	4208	Normal	③	Sclerosing stromal tumor
Lanitis [23]	56	Breast lump	13	Positive	Positive	59	15	④	Fibroma
Benjapibal [24]	56	Dyspnea	13	2500	Not refer	1064	22	①	Fbroma
Costa [25]	63	Abdominal distension	4.2	8000	Positive	2168	Normal	①	Sclerosing stromal tumor
Loué [26]	35	Abdominal pain and mass	40	4500	500	1835	Normal	①	Fibro-thecoma

Footnotes: φ, Tumor diameter; ①, total abdominal hysterectomy (TAH) and bilateral salpingo-oophorectomy(BSO); ②, bilateral salpingo-oophorectomy and partial omentectomy; ③, unilateral salpingo-oophorectomy; ④, ovarian mass excis.

The incidence of Meigs' syndrome is quite low, accompanying with ascites in only 10-15% of patients, and based on above, approximately 1% accompanied with hydrothorax [4]. Based on an English literature review of MEDLINE, there were 32 cases, which got an elevated CA125 associated with Meigs' syndrome, reported previously during the past 26 years, and all the patients suffered ascites (**Table 1**). The present one got a new clinical manifestation.

The pathogenesis of ascites and hydrothorax are largely unknown. According to the distribution of lymphatic vessels in diaphragmatic, pleural effusion may secondary to the ascites [8, 10]. Alper Sevinc *et al*. considered that the degree of elevation of CA125 level is related to the amount of ascites present, and reported when the ascites was more than 3 liters, it was commonly about 978 U/ml [27]. All the reported cases were along with either ascites or both of ascites and hydrothorax. Meanwhile, this patient was only coupled with hydrothorax and got a level of CA125 higher than 978 U/ml. Although CA125 has been demonstrated to be elevated in some benign conditions, the level in this case was the highest one than typically seen, making it more like as the malignant cancer. We highlight this feature sincerely, for its interesting presentation may interest others who will encounter a similar situation in the future.

In conclusion, when a pelvic mass, pleural effusion, and an elevated CA125 were coordinated in a female patient at a same time, Meigs' syndrome should be taken into consideration, although the clinical manifestation could suggest of malignancy. Surgery treatment is the priority method. Follow-up always has no obvious abnormalities.

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Disclosure of conflict of interest

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