Meigs' syndrome with elevated serum CA 125 level in a case of ovarian fibrothecoma

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Summary

Meigs' syndrome is the association of benign ovarian tumor, pleural effusion, and ascites. Meigs' syndrome with marked elevated CA 125 is a rare clinical entity and only 42 cases have been reported. Although there is difficulty in discerning the diagnosis of Meigs' syndrome from that of an ovarian malignancy, it should be considered in the differential diagnosis in postmenopausal patients with an ovarian mass, hydrothorax, ascites, and elevated CA 125. In this report, the authors present the case of a 52-year-old postmenopausal woman with ovarian fibrothecoma, pleural effusion, ascites, and elevated CA 125 (319.2 IU/ml). Exploratory laparotomy with total hysterectomy and bilateral salpingo-oophorectomy was performed, and the pathologic diagnosis was ovarian fibrothecoma. After the surgery, the pleural effusion disappeared spontaneously and the CA 125 became normal. The authors also summarized other cases of Meigs' syndrome with elevated CA 125, and reviewed the mechanism of elevation of CA 125, ascites, and pleural effusion.

Key words: Ascites; CA 125; Meigs' syndrome; Ovarian malignancy; Pleural effusion.

Introduction

Postmenopausal women with elevated serum CA 125, solid adnexal tumor, ascites, and pleural effusion are highly indicative of ovarian malignancy. However, the preoperative diagnosis is inadequate for accurate differentiation of benign lesions from malignant ovarian tumors. Thus, surgical exploration should be performed to confirm the pathologic results, since a small minority of patients with findings suggestive of ovarian malignancy have a benign condition, commonly known as Meigs' syndrome.

Meigs' syndrome is defined as the association of ascites, pleural effusion, and a benign solid ovarian tumor in which removal of the tumor results in complete resolution of symptoms and signs [1]. With elevated serum CA 125, Meigs' syndrome could be easily misperceived as an ovarian malignancy. The authors present a case of Meigs' syndrome due to ovarian fibrothecoma with elevated CA 125 in a postmenopausal woman, with a discussion of the clinical findings and review of the literature related to this unusual entity.

Case Report

A 52-year-old nulligravid woman presented to Ulsan university hospital in March 2012 with abdominal discomfort and progressive dyspnea for months. Menopause occurred at the age of 50 years. On physical examination, the abdomen was distended with ascites, and a hard mass was palpated in the whole abdomen. A chest x-ray showed the presence of a right-sided pleural effusion. A computed tomography (CT) scan of the abdomen-pelvis displayed a 18.5 x 17.5 x 17.3 cm sized solid mass suggesting a pedunculated uterine myoma with a moderate amount of ascites and a right pleural effusion (Figure 1-A). There was no evidence of lymphadenopathy or a metastatic lesion. Blood chemistry was within normal limits except for a high serum CA 125 level of 319.2 IU/ml. The other tumor markers were within normal limits (CA 19-9: 3.2 U/ml; CEA: 1.46 ng/ml; AFP:2.87 ng/ml; β-hCG 1.9 mIU/ml). Cytologic analysis of the pleural fluid was negative for malignant cells, and showed an exudative pattern (total protein 4.5 g/dl, WBC 280/μl, 44% lymphocytes), and was negative for gram and acid fast stains.

Under clinical suspicion of an ovarian malignancy, an explorative laparotomy was performed. Surgical findings showed serous ascetic fluid (1,400 ml), a well-demarcated left ovarian mass without excrescences which occupied the whole pelvis and abdomen. The uterus had a four-cm sized subserosal myoma, and the right adnexa appeared grossly normal (Figure 1-B). Total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed. On gross findings, the removed left ovarian tumor was uniformly solid, firm, and multi-nodular, weighed 1,464 g, and measured 17.5 x 13.4 x 7.0 cm. Intraoperative examination of the frozen section of the left ovarian tumor demonstrated spindle cell proliferation, favoring a benign fibroma. Ascitic fluid study showed only reactive mesothelial cells without malignant cells. The final pathologic report showed an ovarian stromal tumor consistent with a fibrothecoma.

The postoperative course was uneventful. The pleural effusion resolved nearly completely on the fifth postoperative day (Figure 1-C). The serum CA 125 decreased to 79.0 IU/ml on the eighth postoperative day. The patient was discharged on the ninth postoperative day. After 3 months, there were no signs of pleural effusion on the chest X-ray and serum CA 125 had fallen to 11.2 U/ml.

Discussion

Meigs' syndrome is a triad of benign ovarian tumors accompanied by ascites and pleural effusion. When other ovarian tumors (metastatic or primary malignant tumors or fallopian tube tumors) are found in association with the cri-

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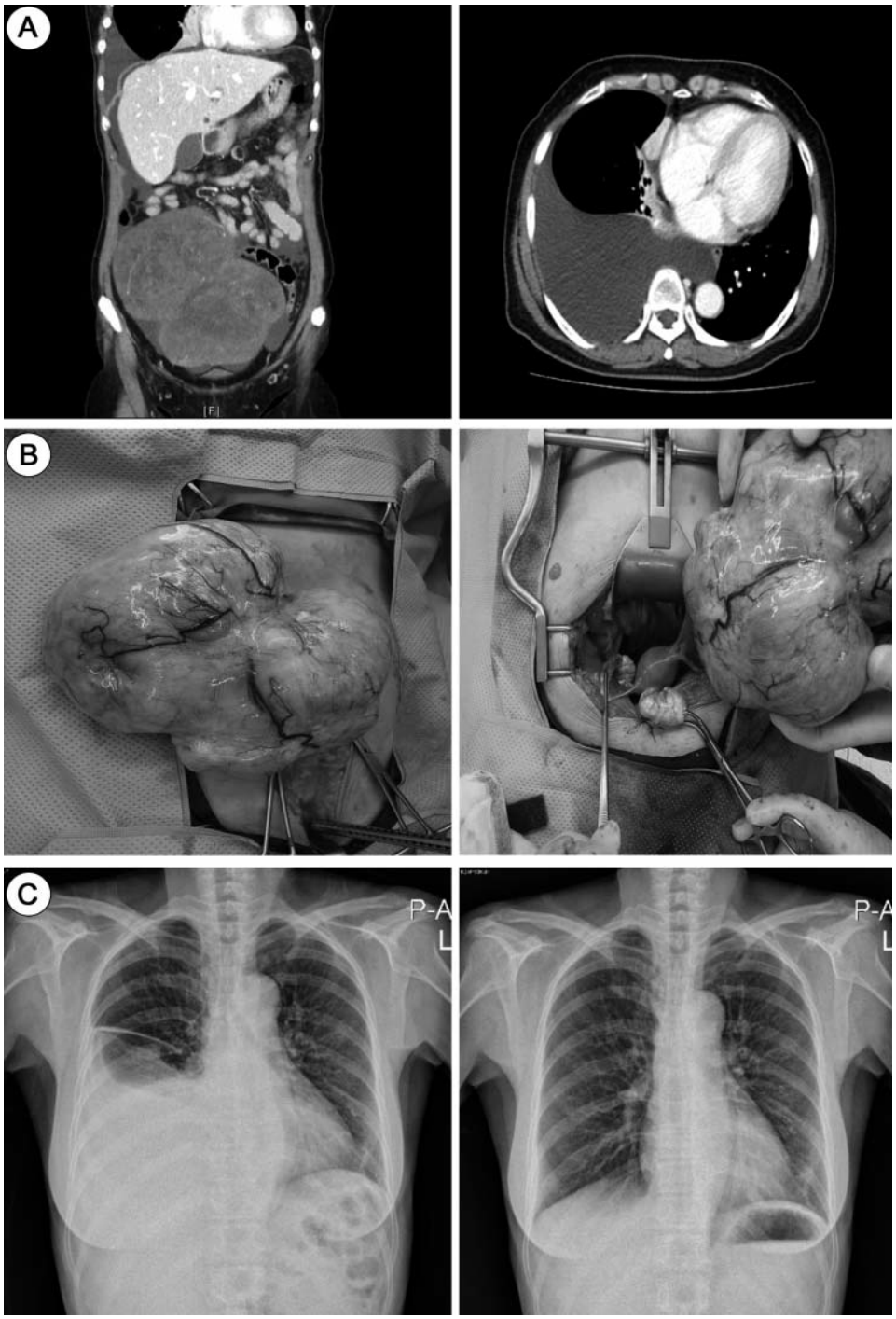

Figure 1. — (A) Computed tomography reveals a 18.5 x 17.5 x 17.3 cm sized solid mass with a moderate amount of ascites and a right pleural effusion. (B) Intraoperative gross appearance of the left ovarian tumor. (C) Comparison of the chest X-ray of before (left) and after removal of the tumor (right). Complete remission of the pleural effusion was observed on the fifth postoperative day.

teria of Meigs' syndrome, the term pseudo-Meigs' syndrome is used [1]. This clinical condition was first described by Demons in 25 October 1902. However, Demons did not limit the association of these effusions to fibroma alone, but widened it to all benign tumors of the ovary and fibroma of the broad ligament. In 1937, Meigs rediscovered Demons syndrome, using seven cases, highlighting the importance of being familiar with the combination of fibroma of ovary, ascites, and hydrothorax. Thus, this clinical combination is called Demons-Meigs syndrome or Meigs syndrome [2]. Ovarian fibroma accounts for two to five percent of surgically removed ovarian tumors, and Meigs' syndrome is found in about one percent [3]. About 91.4% of ovarian tumors associated with Meigs' syndrome are fibromas [4]. Pleural effusion is found in one percent of those with ovarian fibroma and ascites is present in 10-15% [5, 6].

Table 1. — *Published cases of Meigs' syndrome with elevated CA 125 level.*

Author	Year	Patient age	Histopathology	Tumor size (cm)	CA 125 (U/ml)	Ascites (ml)
Jones and Surwit [10]	1989	70	Fibroma/thecoma	11 x 9 x 8	226	1,200
Hoffman [11]	1989	32	Thecoma	11 x 11 x 7	498	NR
Martin *et al.* [12]	1990	NR	Granulosa cell tumor	NR	307	NR
Walker *et al.* [13]	1990	52	Cellular fibroma	16 x 4 x 8	> 5,000	4,500
		67	Cellular fibroma	18 x 15 x 10	104	3,000
Le Bouedec *et al.* [14]	1992	66	Fibroma/thecoma	15	645	NR
		76	Fibroma/thecoma	12	286	NR
Williams *et al.* [15]	1992	74	Luteinized thecoma	15 x 10 x 9	329	300
Lin *et al*. [8]	1992	74	Fibroma	20 x 12 x 12	2,120	7,000
		72	Fibroma	14 x 8 x 7	7,000	6,000
Turan *et al*. [16]	1993	63	Thecoma	18 x 9 x 5	744	NR
Timmerman *et al.* [17]	1995	71	Fibroma	30 x 20.5 x 10	484.5	1,000
		73	Fibroma	19 x 17 x 9	42.3	500
Aoshima *et al.* [18]	1995	33	Brenner tumor	NR	71	NR
Siddiqui and Toub [19]	1995	73	Cellular fibroma	15 x 13 x 10	1,780	NR
Abad *et al*. [5]	1999	51	Cellular fibroma	6 x 5	577	5,000
Chan *et al.* [6]	2000	13	Fibroma	20 x 19 x 10	970	2,100
Patsner [20]	2000	62	Fibroma	10	185	300
		57	Fibroma	14	850	1,000
		52	Fibroma	16	520	1,500
		60	Fibroma	14	64	100
		72	Fibroma	18	1,200	1,500
		58	Fibroma	18	80	100
Bretelle *et al.* [21]	2000	71	Fibrothecoma	7 x 6.6	2,610	NR
Buttin *et al*. [22]	2001	67	Brenner tumor	11 x 9 x 6	759	3,500
Massoni *et al*. [23]	2001	33	Fibrothecoma	17.5 x 11.5	752	3,200
López *et al.* [24]	2002	78	Fibroma	22 x 8.5 x 20	498	NR
		68	Fibroma	18 x 14 x 10	265	NR
Huang *et al.* [25]	2003	31	Sclerosing stromal tumor	7 x 6 x 6	396	1,300
Vieira *et al.* [26]	2003	65	Thecoma	14 x 12 x 8	319	NR
Bildirici *et al.* [27]	2003	17	Sclerosing stromal tumor	25 x 18 x 15	193	400
Cisse *et al.* [28]	2004	25	Fibroma	15 x 11 x 9.8	482	NR
Choi *et al*. [29]	2005	69	Granulosa cell tumor	12 x 10 x 6	82	2,500
Jung *et al.* [30]	2006	50	Sclerosing stromal tumor	19 x 13 x 10	1,476	NR
Moran-Mendoza *et al.*[31]	2006	46	Fibroma	25 x 23 x 19	1,808	500
Kaur *et al.* [32]	2009	12	Juvenile granulosa cell tumor	10 x 10	708	NR
Benjapibal *et al.* [33]	2009	56	Fibroma	13 x 10 x 10	1,064	2,500
Lanitis *et al.* [4]	2009	56	Fibroma	13.5 x 10 x 8	59	NR
Amorim-Costa *et al.* [34]	2010	63	Sclerosing stromal tumor	6	2,168	8,000
Boufettal *et al.* [35]	2011	51	Fibrothecoma	7	412	1,000
Liou *et al.* [36]	2011	17	Sclerosing stromal tumor	14.5 x 13 x 9.5	4,208	9,000
Rousset *et al.* [37]	2011	72	Fibroma	17	41	NR
Current report	2012	52	Fibrothecoma	17.5 x 13.4 x 7.0	319	1,400

The process of forming ascites is not fully understood. Meigs suggested that the fluid in the abdomen is formed by leakage from edematous fibroma. Limited venous and lymphatic drainage might contribute to stromal edema and transudation, and pressure on the lymphatics in the tumor itself might cause the leakage of fluid through the lymphatics on the surface [7]. Other causes have been suggested that produce mechanical irritation of the peritoneum by the tumor or peritoneal fluid production [8]. Vasoendothelial and fibroblast growth factors and cytokine secretions may also play a role in the third-space fluid accumulation [9]. The cause of pleural effusion was suggested to arise from ascitic fluid transferred via the transdiaphragmatic lymphatic channels [5]. Some authors have suggested that the mesothelium is the main factor in the production of ascites [8].

Meigs` syndrome with elevated serum CA 125 level has been described in the literature in only 42 cases (Table 1). An immunohistochemical study on CA 125 suggested that elevation of CA 125 in patients with Meigs' syndrome was mainly caused by mesothelial expression of CA 125 in the peritoneum and omentum rather than by the tumor bed [8, 17, 22]. The quantity of ascites might be correlated with a rise in the level of CA 125: when the volume of ascites is less than 1 litre, the expected CA 125 level is 125 U/ml;

when the volume is from one to two litres, 325 U/ml; when greater than two litres, above 789 U/ml [36].

Despite Meigs' syndrome being regarded as a benign disease, this condition can be fatal if untreated. Some cases of death associated with Meigs' syndrome have been reported in the literature. The main cause of death is lung collapse due to a large pleural effusion [38, 39].

In conclusion, a huge solid adnexal mass, abdominal ascites, and pleural effusion with elevated CA 125 is highly predictive of an ovarian malignancy in postmenopausal women. However, it is important to remember that this ominous finding does not always predict a lethal condition, but a benign adnexal lesion associated with Meigs' syndrome is also a possible diagnosis in a small number of women.

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