

Pseudo-Meigs Syndrome Caused by a Giant Uterine Leiomyoma with Cystic Degeneration: A Case Report

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Pseudo-Meigs syndrome is defined as secondary accumulation of ascites and hydrothorax associated with a pelvic tumor other than benign ovarian tumors such as fibroma, which usually resolve after surgical removal of the tumor. Here we report a case of pseudo-Meigs syndrome caused by a giant uterine leiomyoma, which was initially suspected to be ovarian cancer. A 37-year-old nulliparous woman presented with a 5-month history of abdominal distension and anorexia. Abdominal ultrasonography revealed a giant cystic lesion and solid mass in the peritoneal cavity, along with plentiful ascites. Chest X-ray images showed a small pleural effusion on the right side. The patient was referred to our hospital for treatment of suspected ovarian cancer and peritonitis carcinomatosa. Although serum CA125 level was elevated (up to 331.8 U/mL), magnetic resonance imaging showed a giant sub-serosal uterine leiomyoma with cystic degeneration (27 × 15 × 13 cm). A small dermoid cyst was also detected in the right ovary. Ascites was drained and the patient underwent myomectomy and ovarian cystectomy. The patient had a degenerated leiomyoma with no pathological evidence of malignancy. Because symptoms disappeared postoperatively and serum CA125 returned to normal, without recurrence of ascites, pseudo-Meigs syndrome was diagnosed. (*J Nippon Med Sch* 2020; 87: 80–86)

Key words: pseudo-Meigs syndrome, uterine leiomyoma, CA125

Introduction

Meigs syndrome is defined as the presence of ascites and pleural effusion in association with ovarian fibromas, ovarian thecomas, and granulosa cell tumors; ascites and hydrothorax resolve after tumor removal^{1,2}. On the other hand, pseudo-Meigs syndrome is a similar condition associated with pelvic tumors other than benign ovarian tumors described above, such as primary ovarian malignancies, ovarian metastasis of gastrointestinal malignancies, and uterine leiomyomas^{3–8}. Pseudo-Meigs syndrome is only rarely associated with uterine leiomyoma. Here we report a case of pseudo-Meigs syndrome caused by a giant uterine leiomyoma with cystic degeneration, which was initially suspected of being ovarian cancer.

Case Report

The patient was a 37-year-old woman, gravida 0, parity 0, with an unremarkable medical history and a regular menstrual cycle. She visited a clinic for treatment of progressive abdominal distension and anorexia of 5 months' duration. Ultrasound examination of the abdomen showed a giant intraperitoneal cystic lesion with substantial ascites, which led to her referral to the gastroenterology department. Because ovarian cancer and associated peritonitis were suspected, she was referred to our department.

A giant pelvic mass reaching the xiphoid process was palpable. Ultrasound examination of the abdominal area indicated that the mass (27 × 15 × 13 cm) was located above the uterus. The head side was cystic and the caudal side was solid. A papillary nodule was present on the

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https://doi.org/10.1272/jnms.JNMS.2020_87-205
Journal Website (<https://www.nms.ac.jp/sh/jnms/>)

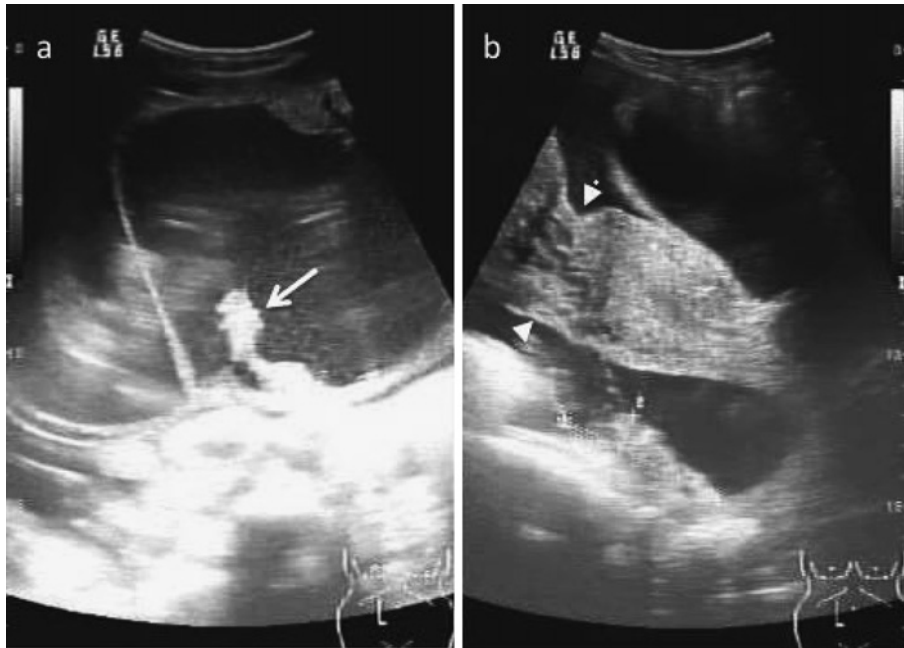


Fig. 1 (a) Ultrasonograms showing a papillary nodule on the cystic tumor wall (arrow) (b) and tumor attachment to the uterus by a pedicle (arrowheads).

cystic tumor wall (Fig. 1a), and a large volume of ascites was detected. Her uterus was anteverted, about the size of a hen's egg, and a 25-mm intramural leiomyoma was seen in the anterior wall. Endometrial thickness was normal. The tumor appeared to be attached to the uterus by a pedicle (Fig. 1b). Blood testing revealed acute inflammation: C-reactive protein concentration was 4.46 mg/dL (normal <0.14 mg/dL), fibrinogen was 716 mg/dL (normal 150-450 mg/dL), and CA125 was 331.8 U/mL (normal <35 U/mL), while the concentrations of other tumor markers, such as CEA, CA19-9, and SCC, were within normal ranges. Chest X-ray revealed limited pleural effusion on the right side.

MR imaging at low signal intensity on both T1-weighted images (T1WI) and T2-weighted images (T2WI) revealed a solid tumor on the caudal side. The cystic lesion appeared to be caused by accumulation of serous fluid (Fig. 2a). The solid mass seemed to be attached to the uterine fundus, and no bleeding was detected in the mass. Intensity on diffusion-weighted images was not diminished in the solid tumor or in the papillary nodules attached to the wall, which suggested that they were not malignant. Small intramural myoma-like tumors were also detected. A right ovarian tumor was suspected because of high signal intensity on T1WI (Fig. 2b) and low to iso-intensity on T2WI. In addition, fatty elements were identified on fat-saturated T1WI (Fig. 2c), which suggested a dermoid cyst. The left ovary was normal.

Lymph node swelling and peritoneal dissemination were not observed. Positron emission tomography-computed tomography (PET-CT) showed diffuse but weak uptake of F-18 fluorodeoxyglucose (FDG) in the solid part, but no uptake was detected in the cystic wall or nodules. Thus, we diagnosed uterine leiomyoma with cystic degeneration and determined that the tumor found in the right ovary was a dermoid cyst and that accumulation of ascites and pleural effusion was caused by pseudo-Meigs syndrome.

Exploratory laparotomy was performed. The ascites was drained (volume 8,050 mL), and the fluid was clear, yellowish, and negative cytologically. A giant tumor was attached to the uterine fundus by a pedicle (diameter 20 mm) (Fig. 3). The surface was smooth and did not adhere to surrounding tissues. The giant tumor (3.65 kg) was resected (Fig. 4a, b) and the uterine wall was repaired. Two small intramural myomas (3 cm each) and a right ovarian cyst (58 g) (Fig. 4c) were also removed. Although blood loss during surgery was moderate (270 mL), the patient developed hypoalbuminemia, and 5% albumin solution was perfused into the patient on postoperative day 1 to 2. Her postoperative condition was good and she was discharged on day 7. There was no pathological evidence of malignancy in any of the uterine tumor specimens or in the nodular lesions on the cystic wall. Although cystic and hyaline degeneration was observed, no atypical cells, necrotic tumor cells, or in-



Fig. 2 MRI imaging. (a) MRI (T2WI) revealing a giant tumor with cystic degeneration, small intramural leiomyomas, and massive ascites. Images of the right ovarian tumor (arrow) at (b) high signal intensity on T1WI and (c) low signal intensity on fat-saturated T1WI.

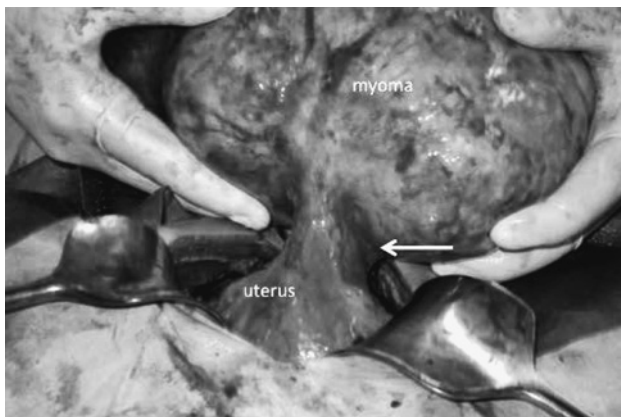


Fig. 3 Photograph showing a leiomyoma attached to the uterus by a pedicle (arrow).

creased mitosis were seen in any of these specimens. Our final diagnosis was therefore large benign uterine leiomyoma with cystic degeneration (Fig. 5). Examination of the right ovarian tumor revealed skin-like squamous epithelial cells, hair follicles, and sebaceous or sweat glands, but no immature tissue was identified. These features are compatible with mature cystic teratoma. After surgery, pleural effusion was no longer visible on chest radiographs. No additional ascites accumulation has been observed, and serum CA125 level returned to normal within 6 months. Our final diagnosis was pseudo-Meigs

syndrome.

The patient provided written informed consent for the publication of this case report and the accompanying images.

Discussion

Meigs syndrome is a benign clinical condition that was first described as a combination of ovarian fibroma, ascites, and pleural effusion. Benign ovarian tumors classically comprise fibroma, thecoma, and granulosa cell tumor, and ascites and pleural effusion resolve after tumor removal¹. In 1954, Meigs proposed that the term “Meigs syndrome” be restricted to benign, solid ovarian tumors accompanied by ascites and pleural effusion². Conditions that were similar but caused by other benign and malignant pelvic tumors have thereafter been referred to as pseudo-Meigs syndrome or atypical Meigs syndrome³. A number of studies have reported cases of pseudo-Meigs syndrome associated with struma ovarii, mature teratoma, uterine myoma, ovarian cancer, and ovarian metastasis of malignancies. Pseudo-Meigs syndrome is often diagnosed after close examination, typically during follow-up appointments after treatment of other malignant tumors⁴⁻⁸.

The pathogenesis of ascites and pleural effusion in patients with Meigs syndrome or pseudo-Meigs syndrome

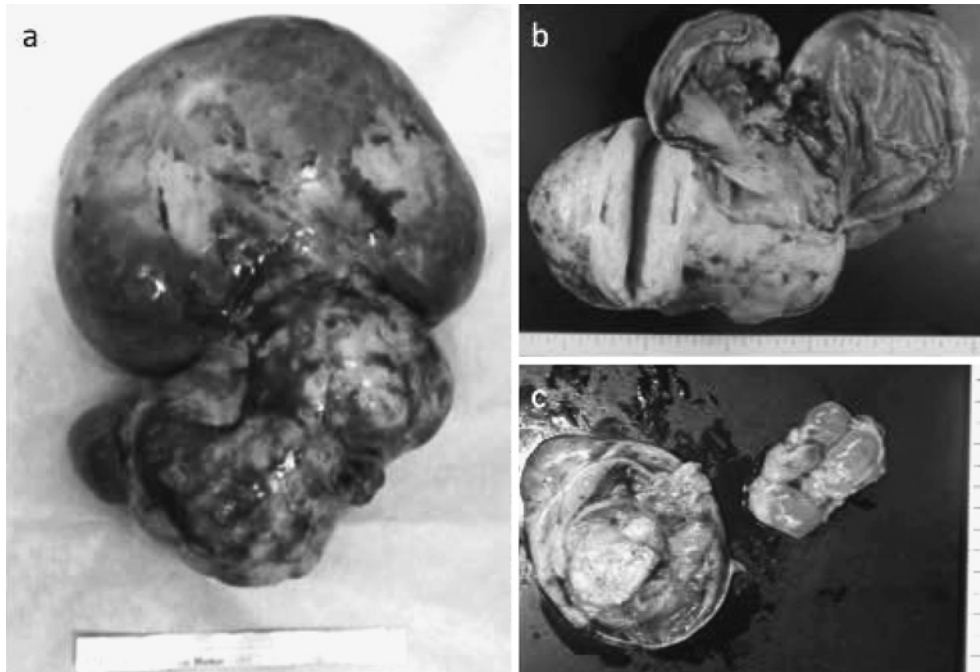


Fig. 4 Macroscopic findings of the patient specimen. (a, b): A giant leiomyoma (3.65 kg) with cystic degeneration. (c) Right ovarian cysts including fatty tissue, hair, and skin.

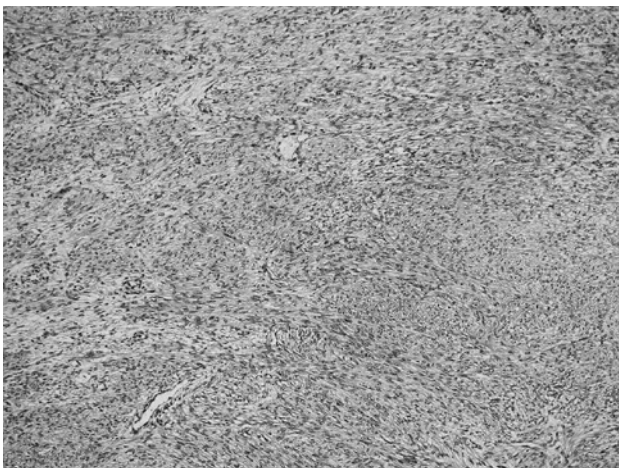


Fig. 5 The pathologic characteristics of the mass were consistent with a uterine leiomyoma (original magnification $\times 100$; hematoxylin-eosin stain).

remains uncertain. Meigs suggested that irritation of the peritoneal surfaces by a solid ovarian tumor could stimulate ascites production. Samanth and Black reported that peritoneal fluid might be secreted from the tumor, after observing that large tumors (>10 cm) containing a myxoid component within the stroma were often associated with ascites⁹. Tissue fluid may leak from tumor surfaces, which undergo edematous change due to lymphatic or venous obstruction, which causes intermittent torsion or tumor compression^{10,11}. Other mechanisms, such as inflammatory reactions, hormonal stimulation,

toxin release, and low serum protein levels, have also been suggested¹¹. In addition, release of various mediators from tumors might promote capillary permeability, leading to ascites^{12,13}. In our patient, a myoma the size of a human newborn's head was connected to the uterus by a narrow pedicle and exhibited substantial cystic degeneration. Intermittent twisting of the tumor stem or compression of lymphatic and blood vessels might also contribute to ascites formation. Pleural effusion is thought to be secondary to ascites accumulation. Ascites flows into the pleural cavity through the vena cava opening, via small pores in the diaphragm area and through the draining lymphatic vessels. Pleural effusion usually occurs in the right pleural cavity. Nearly 60% of patients presenting with Meigs or pseudo-Meigs syndrome have fluid accumulation in the right pleural cavity only¹⁰.

Serum, ascites, and pleural fluid from a patient with Meigs syndrome or pseudo-Meigs syndrome have high levels of growth factors such as vascular endothelial growth factor (VEGF) and fibroblast growth factor^{12,13}. Elevated expression of cytokines such as interleukin (IL)-1 beta, IL-6, IL-8, and tumor necrosis factor (TNF)-alpha are characteristic of ascites accumulation and pleural effusion¹⁴. Pathological examination showed that VEGF was strongly expressed on the epithelium of benign fallopian tubes in patients with advanced colorectal cancer but was not expressed on the primary cancer or metastatic ovarian tumors¹⁵. These findings suggest that ascites

Table 1

Author	Year	Age	Tumor size (cm)	Ascites	Side of pleural effusion	CA125 (U/mL)	Operation	Recurrence
Frank et al	1973	66	18 × 16 × 13	Yes	Right	NS	Removal of tumor	NS
Rush	1976	47	20	Yes	Left	NS	TAH, BSO, colon polypectomy	NS
Handler et al	1982	35	9 × 9	Yes	Right	NS	Removal of tumor	No, 1 year
Buckshee et al	1990	46	20 × 20	Yes	Bilateral	NS	TAH, myomectomy, RSO	No
Ollendorf et al	1997	31	27 × 18 × 13	Yes	Right	301	Myomectomy	No, 8 months
Brown et al	1998	31	17 × 11.5 × 8.5	Yes	Right	83	Myomectomy	No, 18 months
Domingo et al	1998	46	20	Yes	Bilateral	317	TAH, BSO	NS
Dunn et al	1998	46	30 × 18 × 15	Yes	Right	254	TAH, BSO, OM, lymph node sampling	NS
Migishima et al	2000	51	12 × 24 × 12.5	Yes	Left	820	TAH, BSO	No, 4 months
Amant et al	2001	39	30 × 30 × 15	Yes	Left	785	TAH	NS
Kebapci et al	2002	38	9 × 10 × 10.5	Yes	Left	281	Myomectomy, Appendectomy, OM	NS
Weise et al	2002	27	7 × 8 × 6	Yes	Right	1,854	Myomectomy	No, 3 months
Weinrach et al	2004	40	19 × 11 × 10	Yes	Right	734	TAH, BSO	No, 6 months
Landrum et al	2008	47	20 × 22	Yes	Bilateral	475	TAH, BSO, PEN, PAN	NS
Ricci et al	2009	35	15 × 10 × 8.5	Yes	NS	231.4	Myomectomy	No, 3 years
Chourmouzi et al	2010	41	13 × 16	Yes	NS	436.7	Myomectomy	NS
Makris et al	2012	26	11 × 8 × 10	Yes	NS	93.9	Myomectomy	No, 2 months
Yip et al	2013	41	12 × 11 × 8	Yes	None	939.7	Myomectomy	NS
Oguma et al	2014	50	14 × 8 × 7	Yes	Right	218	TAH, BSO	NS
Seo et al	2014	22	9 × 5	Yes	None	450	Myomectomy	No, 5 years
Dong et al	2015	37	20 × 18 × 10	Yes	Bilateral	920.4	TAH	No, 82 months
Gibbons JA	2019	35	29	Yes	NS	272.9	Removal of tumor, division of adhesions, TAH, BSO, OM	NS
Present case		37	27 × 15 × 13	Yes	Right	331.8	Myomectomy, ovarian cystectomy	No, 6 months

NS: Not specified, TAH: Total abdominal hysterectomy, BSO: Bilateral salpingo-oophorectomy, RSO: Right salpingo-oophorectomy, OM: Omentectomy, PEN: Pelvic lymphadenectomy, PAN: Para-aortic lymphadenectomy

and pleural fluid result from VEGF hypersecretion by oviducts, which is caused by stimulation by the metastatic ovarian tumor. Interestingly, concentrations of these cytokines are significantly higher in ascites than in serum, which suggests that the growth factors driving hyperpermeability in the ovary or peritoneal vessel are released locally rather than systemically^{14,16}.

Because CA125 is expressed in various tissues and an increase in CA125 serum levels is observed in a variety of clinical conditions, this tumor marker does not necessarily indicate malignancy. Pseudo-Meigs syndrome was previously described in relation its association with elevated serum CA125. Peritoneal mechanical stimulation exerted by the uterine myoma itself or by the presence of substantial ascites also increases CA125¹⁷. Finally, cytokines released from necrotic or degenerative tissues can cause peritoneal inflammation and increase CA125^{14,18,19}. In fact, after removal of ascites and myoma, serum CA 125 level rapidly decreased in our patient.

Uterine leiomyoma or fibroids are the most common benign tumors of the female reproductive system. When leiomyoma and ascites and/or pleural effusion occur simultaneously, a diagnosis of pseudo-Meigs syndrome should be considered. This condition is clinically important because it might be confused with malignant tumors concomitant with peritonitis carcinomatosis. While large ascites and pleural effusion resulting from advanced cancer require a carefully planned, patient-tailored, treatment strategy, myomectomy is usually sufficient for pseudo-Meigs syndrome with leiomyoma and fluid accumulation. In 2014, another case of uterine solid tumor associated with pleural effusion and ascites was reported. A clinical oncologist misdiagnosed the condition as malignant tumors with peritoneal carcinomatosis, on the basis of massive ascites and marked elevation of serum CA 125. This resulted in repeated tapping and immunotherapy administered to the patient²⁰. However, other case reports of pseudo-Meigs syndrome suggest an association

with uterine smooth muscle tumors of uncertain malignant potential, or leiomyosarcoma^{21,22}. Dong et al. reviewed available studies in the PubMed database and reported that pseudo-Meigs syndrome caused by benign leiomyoma with massive ascites and elevated CA125 was rare. Their case was the twelfth report of pseudo-Meigs syndrome, and degenerative changes were detected in fibroids in all reported cases²³. In 2019, Gibons reported a case of uterine leiomyoma presenting as pseudo-Meigs syndrome, with elevated CA125, and reviewed 21 cases identified in a PubMed/Medline search. The mean age of the 21 patients was 40 years (22-66), and tumor size was greater than 10 cm in 18 patients²⁴.

Table 1 summarizes 23 cases, including the present case. Ascites was observed in all cases, and pleural effusion was observed in 17 cases. Pleural effusion was present on the right side in 13 cases and was bilateral in 4 of these cases; pleural effusion was present on the left side in the other 4 cases. The mean CA125 level was 516 U/mL (83-1,854). Myomectomy or total abdominal hysterectomy was performed, and lymphadenectomy or lymph node sampling was done in 2 cases. No recurrence was noted.

Most uterine leiomyomas are easily distinguishable from other gynecologic or non-gynecologic pelvic tumors by ultrasonography. CT, MRI, and PET-CT scans are useful for differential diagnosis. However, conditions such as hemorrhage, degeneration, and focal necrosis may yield atypical imaging findings, thus complicating differential diagnosis²³. The distinction between a benign condition such as Meigs syndrome or pseudo-Meigs syndrome and a clinically similar but more severe condition such as carcinomatosis should be carefully considered when interpreting images and associated clinical parameters.

Conflict of Interest: The authors declare no conflicts of interest.

References

1. Meigs JV, Cass JW. Fibroma of the ovary with ascites and hydrothorax: With a Report of Seven Cases. *Am J Obstet Gynecol.* 1937;33:249-67.
2. Meigs JV. Fibroma of the ovary with ascites and hydrothorax; Meigs' syndrome. *Am J Obstet Gynecol.* 1954; 67:962-85.
3. Handler CE, Fray RE, Snashall PD. Atypical Meigs' syndrome. *Thorax.* 1982;37:396-7.
4. Jin C, Dong R, Bu H, Yuan M, Zhang Y, Kong B. Coexistence of benign struma ovarii, pseudo-Meigs' syndrome and elevated serum CA 125: Case report and review of the literature. *Oncol Lett.* 2015;9:1739-42.
5. Tajima Y, Kameyama H, Yamada S, et al. Long-term sur-

- vival in pseudo-Meigs' syndrome caused by ovarian metastases from colon cancer. *World J Surg Oncol.* 2016;14: 286-90.
6. Maeda H, Okabayashi T, Hanazaki T, Kobayashi M. Clinical experience of Pseudo-Meigs' syndrome due to colon cancer. *World J Gastroenterol.* 2011;17:3265-6.
7. Saito H, Koide N, Miyagawa S. Pseudo-Meigs syndrome caused by sigmoid colon cancer metastasis to the ovary. *Am J Surg.* 2012;23:1-3.
8. Yip HK, Huang LW, Lin YH, Hwang JL. Massive ascites caused by a large pedunculated subserosal uterine leiomyoma that has feeding arteries from peripheral tissues and exhibits elevated CA125: a case report of atypical Pseudo-Meigs' syndrome. *J Obstet Gynecol.* 2014;34:107.
9. Samanth KK, Black WC 3rd. Benign ovarian stromal tumors associated with free peritoneal fluid. *Am J Obstet Gynecol.* 1970;107:538-45.
10. Krenke R, Maskey-Warzechowska M, Korczynski P, et al. Pleural effusion in Meigs' syndrome-transudate or exudate?: Systematic review of the literature. *Medicine (Baltimore).* 2015;94:1-9.
11. Rubin IC, Novak J, Squire JJ. Ovarian fibromas and theca-cell tumors: report of 78 cases with special reference to production of ascites and hydrothorax (Meigs' Syndrome). *Am J Obstet Gynecol.* 1944;48:601-61.
12. Ishiko O, Yoshida H, Sumi T, Hirai K, Ogita S. Vascular endothelial growth factor levels in pleural and peritoneal fluid in Meigs syndrome. *Eur J Obstet Gynecol Report Biol.* 2001;98:129-30.
13. Abramov Y, Anteby SO, Fasouliotis SJ, Barak V. Markedly elevated levels of vascular endothelial growth factor, fibroblast growth factor, and interleukin 6 in Meigs syndrome. *Am J Obstet Gynecol.* 2001;184:354-5.
14. Abramov Y, Anteby SO, Fasouliotis SJ, Barak V. The role of inflammatory cytokines in Meigs' syndrome. *Obstet Gynecol.* 2002;99:917-9.
15. Okuchi Y, Nagayama S, Mori Y, et al. VEGF hypersecretion as a plausible mechanism for pseudo-Meigs' syndrome in advanced colorectal cancer. *Jpn J Clin Oncol.* 2010;40:476-81.
16. Hahm TS, Ham JS, Kang JY. Unilateral massive hydrothorax in a gynecologic patient with pseudo-Meigs' syndrome: A case report. *Korean J Anesthesiol.* 2010;58:202-6.
17. Amant F, Gabriel C, Timmerman D, Vergote I. Pseudo-Meigs' syndrome caused by a hydropic degenerating uterine leiomyoma with elevated CA125. *Gynecol Oncol.* 2001;83:153-7.
18. Mitrou S, Manek S, Kehoe S. Cystic struma ovarii presenting as pseudo-Meigs' syndrome with elevated CA125 levels. A case report and review of the literature. *Int J Gynecol Cancer.* 2008;18:372-5.
19. Chhavi K, Akhila P, Yashvant S, Baruah BP. Case series: Cystic degeneration in uterine leiomyomas. *Indian J Radiol Imag.* 2008;18:69-72.
20. Felix Wong WS. A case of pseudo-Meigs syndrome mismanaged as peritoneal carcinomatosis. *Gynecol Minim Invasive Ther.* 2014;3:131-3.
21. Huang SE, Huang SC, Lee WY, Hsu KF. Pseudo-Meigs' syndrome caused by uterine smooth muscle tumor of uncertain malignant potential with low vascular endothelial growth factor expression. *Int J Gynecol Cancer.* 2008;18: 851-3.
22. Marci R, Giugliano E, Carboni S, Martinello R, Patella A. Pseudo-Meigs' syndrome caused by a uterine leiomyosarcoma: a new clinical condition. *Gynecol Obstet Invest.* 2011;72:68-72.

23. Dong R, Jin C, Zhang Q, Yang X, Kong B. Cellular leiomyoma with necrosis and mucinous degeneration presenting as pseudo-Meigs' syndrome with elevated CA125. *Oncol Rep.* 2015;33:3033-7.
24. Gibbons JA. Large uterine leiomyoma presenting as pseudo-Meigs' syndrome with an elevated CA 125: Case report and literature review. *J Case Rep Images Obstet Gynecol.* 2019;5:100046Z08JG2019.

(Received, June 23, 2019)

(Accepted, November 14, 2019)

(J-STAGE Advance Publication, December 27, 2019)

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