

CASE REPORT

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Pseudo-Meigs syndrome caused by a rapidly enlarging hydropic leiomyoma with elevated CA125 levels mimicking ovarian malignancy: a case report and literature review

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Abstract

Pseudo-Meigs syndrome is a rare syndrome characterized by hydrothorax and ascites associated with pelvic masses, and patients occasionally present with elevated serum cancer antigen-125 (CA125) levels. Hydropic leiomyoma (HLM) is an uncommon subtype of uterine leiomyoma characterized by hydropic degeneration and secondary cystic changes. Rapidly enlarging HLMs accompanied by hydrothorax, ascites, and elevated CA125 levels may be misdiagnosed as malignant tumors. Here, we report a case of HLM in a 45-year-old Chinese woman who presented with ascites and hydrothorax. Preoperative abdominopelvic CT revealed a giant solid mass in the fundus uteri measuring 20×15×12 cm. Her serum CA125 level was elevated to 247.7 U/ml, while her hydrothorax CA125 level was 304.60 U/ml. The patient was initially diagnosed with uterine malignancy and underwent total abdominal hysterectomy and adhesiolysis. Pathological examination confirmed the presence of a uterine hydropic leiomyoma with cystic changes. After tumor removal, the ascites and hydrothorax subsided quickly, with no evidence of recurrence. The patient's serum CA125 level decreased to 116.90 U/mL on Day 7 and 5.6 U/mL on Day 40 postsurgery. Follow-up data were obtained at 6 months, 1 year, and 2 years after surgery, and no recurrence of ascites or hydrothorax was observed. This case highlights the importance of accurate diagnosis and appropriate management of HLM to achieve successful outcomes.

Keywords Pseudo-Meigs syndrome, Hydropic leiomyoma, CA125

Introduction

Pseudo-Meigs syndrome is a rare condition characterized by ascites and hydrothorax, along with masses in the abdomen and pelvis, similar to Meigs syndrome, which is usually associated with ovarian fibromas or fibroid tumors. Surgical removal of the tumor leads to the rapid resolution of symptoms and a good outcome [1]. Tumors linked to pseudo-Meigs syndrome include uterine cancer [2], metastatic cancer [3], ovarian struma ovarii [4], and uterine leiomyoma [5]. Uterine leiomyoma is the most common benign tumor of the female reproductive system, and the diagnostic methods for these tumors

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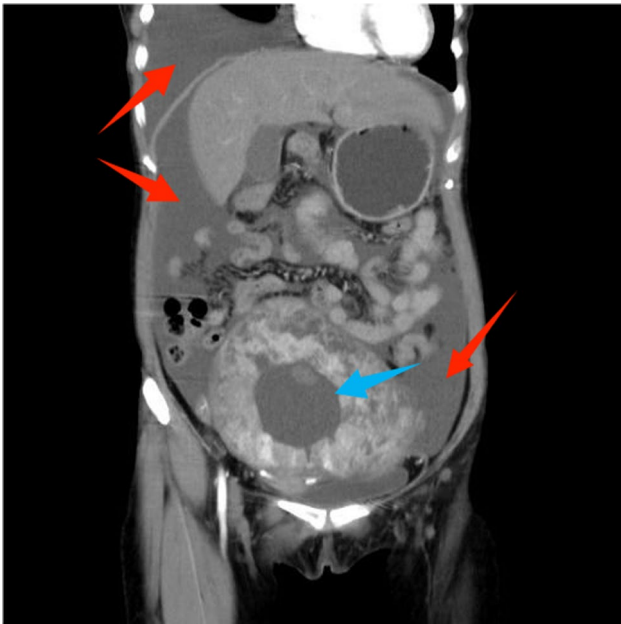


Fig. 1 Contrast-enhanced CT (coronal view) revealed a giant mass measuring $14 \times 12 \times 10$ cm in size in the pelvis, with heterogeneous and intense enhancement, a scattered low-density edema area, and a cyst in the center (blue arrow), and massive ascites and a right-sided hydrothorax were observed (red arrow)



Fig. 2 Contrast-enhanced CT (sagittal view) revealed a giant mass measuring $14 \times 12 \times 10$ cm in size in the pelvis, with a noted cyst in the center (blue arrow)

include ultrasound examination, transvaginal ultrasound examination, computed tomography (CT), and magnetic resonance imaging (MRI). The clinical behavior and imaging features of leiomyomas can vary, especially in those with degenerative changes, which make it difficult to distinguish them from malignant tumors in the uterus or ovaries. Pseudo-Meigs syndrome caused by uterine leiomyoma in patients with elevated CA125 levels is extremely rare, with only a few cases reported in the literature, and this syndrome be mistaken for ovarian cancer or uterine sarcoma. Accurate diagnosis is crucial for appropriate treatment. We present the case of a 45-year-old Chinese woman with a rapidly growing pelvic mass, ascites, hydrothorax, and elevated CA125 levels who was initially misdiagnosed with a malignancy. Pathological examination revealed a large uterine leiomyoma with hydropic degeneration and cystic changes. This case highlights the importance of recognizing pseudo-Meigs syndrome in patients with elevated CA125 levels caused by uterine leiomyoma and emphasizes the need for accurate diagnosis, appropriate treatment, and an improved understanding of patient prognosis.

Case report

A 45-year-old Chinese woman presented with complaints of abdominal distension and intermittent abdominal pain. She was admitted to the gynecology department of our hospital. Her medical and family history was unremarkable. Menarche occurred at the age of 13 years, and

her menstrual cycles were regular. An abdominopelvic MRI revealed a solid mass measuring $7.3 \times 6.1 \times 6.9$ cm in the fundus uteri. The patient was discharged without intervention. Eight months later, the patient returned to the gynecology department with complaints of abdominal pain, discomfort in the lower-abdominal region, and vaginal bleeding.

Physical examination revealed the presence of a large, solid mass on the right side of the lower abdomen, with no other abnormalities detected. Palpation revealed tenderness in the area of the mass, which filled the pelvic cavity. An abdominopelvic CT scan revealed a cystic solid mass located in the posterior wall of the uterus. The mass measured $14.7 \times 11.3 \times 12.7$ cm in size and was accompanied by a significant amount of ascites (Figs. 1 and 2). The solid component demonstrated clear and uniform enhancement on enhanced scanning, in contrast to the low-density area. A chest CT scan revealed the presence of a right hydrothorax. The initial diagnosis favored an ovarian tumor or leiomyoma with degeneration. Prior to surgery, 6 L of hydrothorax fluid and 6 L of ascites fluid were collected for laboratory examination and cytology. The results revealed elevated levels of CA125 in both the serum and hydrothorax, with values of 304.60 U/mL and 247.7 U/mL, respectively (normal values < 35 U/mL). The levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol, progesterone, prolactin, testosterone II, total protein, albumin, lactate dehydrogenase (LDH), and carcinoembryonic antigen (CEA) were within the normal ranges in all the samples.

Cytology was negative for malignant cells or *Mycobacterium tuberculosis*.

According to imaging tests and laboratory analyses, the patient was diagnosed with either ovarian cancer or leiomyosarcoma before surgery. Total abdominal hysterectomy was performed, along with excision of the mass and adhesiolysis. Intraoperative observations revealed a distinct subserosal solid tumor arising from the uterine fundus and extending into the pelvic cavity, accompanied by a moderate quantity of light-red ascites.

The tumor measured 20×15×12 cm on gross examination. The cut surface of the tumor exhibited a pale and fleshy appearance, with evidence of hydropic and cystic degeneration. No evidence of hemorrhage or necrosis was observed (Fig. 3). Microscopic examination revealed that the tumor demonstrated the typical characteristics of a leiomyoma, with no evidence of myometrial or vascular invasion. The tumor cells demonstrated mild cytologic atypia, with no mitoses or necrosis present, and were surrounded by edema or a watery matrix (Figs. 4 and 5). Immunohistochemical staining revealed diffuse positivity for h-Caldesmon (Fig. 6) and desmin but negativity for HMB45, Melan-A, CD10, P16, and P53. The Ki67 index was less than 1%. A pathological diagnosis of hydropic leiomyoma was established on the basis of these findings.

After tumor removal, the hydrothorax and ascites subsided rapidly. A follow-up was conducted at 6 months, 1 year, and 2 years postsurgery. The patient recovered uneventfully. A final diagnosis of pseudo-Meigs syndrome was made.

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

Discussion

In 1937, ovarian fibroma accompanied by ascites and hydrothorax was first described by Meigs and Cass. In 1954, Meigs reviewed the cases of 84 patients who presented with rapid resolution of ascites and/or hydrothorax following the removal of ovarian fibromas or fibroma-like tumors. These patients were subsequently diagnosed with Meigs syndrome [6]. Pseudo-Meigs syndrome, similar to Meigs syndrome, is frequently associated with ovarian cancer, metastatic tumors, mature teratoma, struma ovarii, borderline tumors, and uterine leiomyoma [7, 8]. The clinical features of pseudo-Meigs syndrome include the presence of a large pelvic mass, recurrent ascites and hydrothorax. The presence of elevated CA125 levels in patient with pseudo-Meigs syndrome can result in the misdiagnosis of malignancy with pelvic and pleural metastases, resulting in unnecessary treatment. Patients with pseudo-Meigs syndrome who have elevated CA125 levels caused by uterine leiomyoma are exceedingly rare and are likely to be misdiagnosed [1].

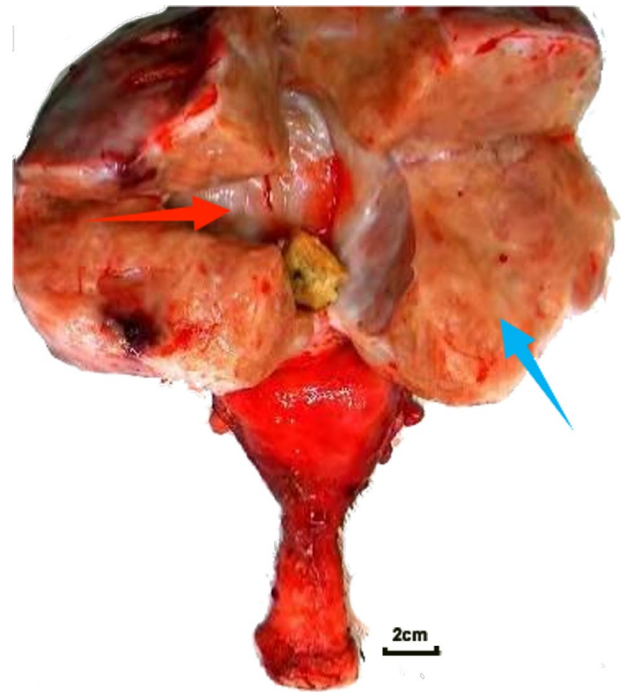


Fig. 3 Gross examination revealed a solid grayish-white tumor located at the uterine fundus that protruded into the pelvic cavity (blue arrow). The cut surface was grayish-white and fleshy with water degeneration and cystic changes (red arrow)

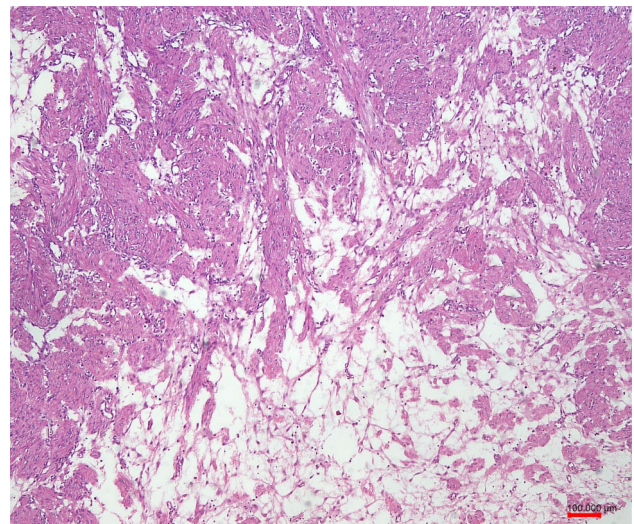


Fig. 4 The tumor was composed of spindle cells arranged in intersecting fascicles. The cells had eosinophilic cytoplasm and cigar-shaped nuclei with small nucleoli, absent mitoses, and hemorrhagic necrosis (HE, 40X)

This report describes a case of pseudo-Meigs syndrome caused by a rapidly enlarging uterine hydropic leiomyoma in a patient with elevated CA125 levels, and a review of the relevant literature is provided.

The etiology of ascites and hydrothorax remains unclear, with several hypotheses proposed for the

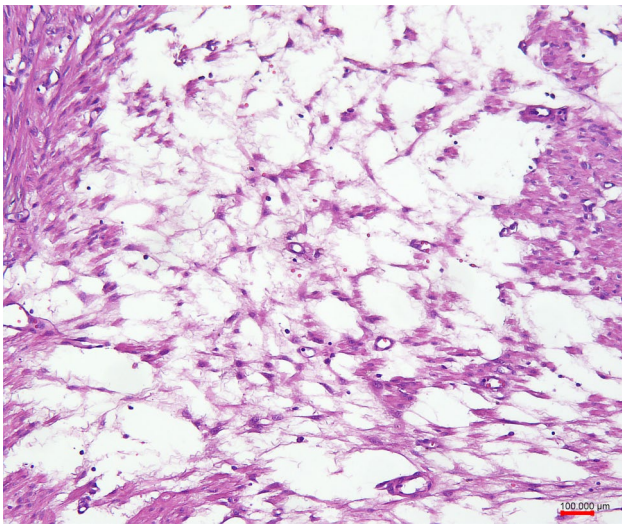


Fig. 5 Noted edema areas or an extracellular watery matrix were observed in the tumor (HE, 100X)

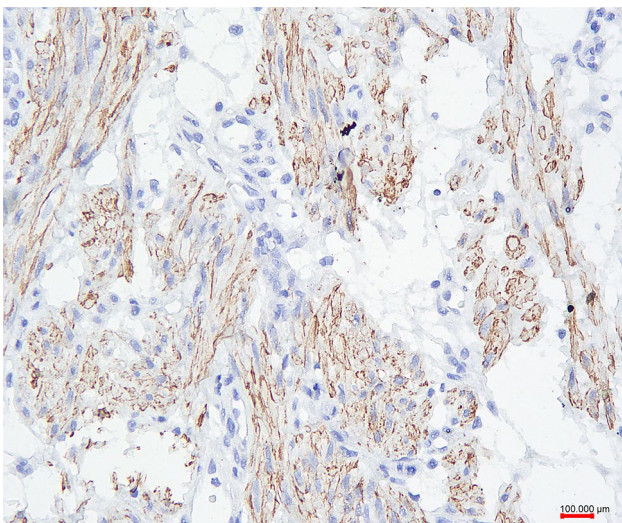


Fig. 6 Immunohistochemical staining revealed that the tumor cells were positive for h-Caldesmon (EnVision, 200X)

development of ascites: (1) Mechanical irritation of the peritoneum by a large tumor may lead to pelvic inflammation and fluid accumulation [6, 9, 10]; (2) fluid secretion due to lymphatic obstruction, increased permeability of the neovasculature from tumor pedicle torsion, and low serum protein levels may occur [11–13]; and (3) cytokines and inflammatory mediators may promote the production of ascites, with studies demonstrating that elevated serum vascular endothelial growth factor (VEGF) is associated with ascites and hydrothorax [14]. Furthermore, cytokines such as VEGF, fibroblast growth factor (FGF), and interleukin (IL)-6 have been demonstrated to stimulate mesothelial cells and promote ascites and hydrothorax in patients with Meigs' syndrome or pseudo-Meigs syndrome, with levels returning to

normal following tumor removal [15]. Further research has revealed the pivotal role of VEGF, FGF, IL-1 β , IL-6, and IL-8 in the development of ascites and hydrothorax [16]. In patients with pseudo-Meigs syndrome, right-sided hydrothorax is more common due to developmental defects in the right hemidiaphragm, typically occurring approximately 3 h after ascites formation and potentially originating from pelvic effusions [11].

The occurrence of Meigs syndrome or pseudo-Meigs syndrome in conjunction with elevated CA125 levels is relatively uncommon, and the underlying mechanism remains unclear [8, 17]. CA125, also known as MUC16, is a glycoprotein that was first identified in 1981 [18]. CA125 is not considered a reliable marker for the diagnosis of malignancy because of its low sensitivity and specificity. Elevated CA125 levels can be observed in individuals with various benign and malignant conditions, such as pregnancy, pelvic inflammatory disease, endometriosis, tuberculosis, cirrhosis, and autoimmune diseases [18, 19]. The CA125 present in ascites may be produced by activated mesothelial cells, whose expression is potentially upregulated by proinflammatory cytokines [20].

Pseudo-Meigs syndrome, caused by leiomyomas in patients with elevated CA125, is a rarer condition. A total of 24 cases have been documented in the English literature (Table 1). Uterine leiomyomas are the most common benign tumors of the female reproductive system, with an incidence rate of approximately 70% [21]. Approximately 50% of uterine leiomyomas undergo degenerative changes, including myxoid degeneration, hyalinosis, calcification, steatosis, red degeneration, watery degeneration, and cystic degeneration. These changes can be precipitated by pregnancy or hormonal therapy. Although degeneration of uterine leiomyomas can lead to rapid tumor enlargement, infiltration or metastasis is not observed [22]. Edema leiomyoma or hydropic leiomyoma (HLM) is a rare subtype characterized by diffuse watery degeneration and secondary cystic changes [23]. Such lesions may undergo rapid enlargement and may be misdiagnosed as leiomyosarcomas or ovarian malignancies. HLMs display characteristics distinct from those of typical leiomyomas, including differences in tumor size, edema area, extracellular matrix composition, vascular proliferation, and molecular genetic changes. Studies have demonstrated that t(4;8)(p16;q22) is a unique abnormality found in individuals with HLMs [24]. Additionally, overexpression of the HMGA2 gene, HMGA2 gene rearrangement, and increased pAKT activity have been identified in HLM patients, which strongly suggests a distinct association with HMGA2 overexpression [25].

As previously stated, uterine leiomyoma is a rare cause of pseudo-Meigs syndrome. Accurate diagnosis prior to surgical intervention can be challenging, particularly

Table 1 Articles of leiomyoma presenting as pseudo-meigs' syndrome with elevated CA-125

No.	Article	Age (y)	Symptoms	Ascites (volume)	Hydrothorax (side, volume)	CA125 level	Tumor size / weight	Treatments	Follow-up
1	Lee, 1992 [26]	29	Uterine myomata treated with GNRH agonist.	7 L	Left side, small amount.	768 U/mL	19.6×13.1×13.8 cm	Total abdominal hysterectomy, right salpingo-oophorectomy, left ovarian cystectomy, and appendectomy.	Uneventful and no reaccumulation of ascites.
2	Ollendorff, 1997 [27]	31	Acute respiratory distress with massive ascites, pleural effusion.	19 L	Right, Not reported.	301 U/mL	27×18×15 cm	Myomectomy.	4 weeks, fully recovered.
3	Brown, 1998 [28]	31	Pelvic mass, dyspnoea, abdominal swelling, intermittent difficulty in passing urine, and a 6 kg weight loss.	Not Reported	Right, Not reported.	83 iu/ml	17×11.5×8.5 cm	Complete removal of the tumor.	18 months, no recurrent.
4	Dunn, 1998 [1]	46	Nausea, vomiting, and diarrhea.	1.6 L	Right, Not reported.	254 U/mL	15×30×18 cm	total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and lymph node sampling	4 months, the effusion was resolved completely.
5	Migishima, 2000 [29]	51	Gradual abdominal distension, progressive dyspnea.	7.6 L	Left, Not reported.	820 U/ml	12.3×24.3×20.5 cm	Total hysterectomy and a bilateral salpingo-oophorectomy	4 months, no evidence of recurrent effusion. CA125 level dropped to normal.
6	Amant, 2001 [11]	39	Abdominal swelling.	12 L	Left, Not reported.	785 kU/L	20 cm and 16 cm in Diameters	hysterectomy	7 weeks, uneventful, the hydrothorax was nearly complete resolution.
7	Kebapci, 2002 [30]	38	Low back pain, distension, weakness, and loss of appetite.	Massive	Left, massive.	281 U/mL	9.0×10.0×10.5 cm	Exploratory laparotomy and excise the mass	6 months, uneventful, ascites and pleural effusion disappeared and serum CA125 level declined to normal.
8	Weise, 2002 [31]	27	Increasing abdominal volume.	3.5 L	Right, 0.1 L	1854 U/ml	7×8×6 cm	myomectomy	3 months, excellent general condition. CA125 level was normal.

Table 1 (continued)

No.	Article	Age (y)	Symptoms	Ascites (volume)	Hydrothorax (side, volume)	CA125 level	Tumor size / weight	Treatments	Follow-up
9	Weinrach, 2004 [32]	40	Increasing abdominal distention and progressive shortness of breath.	Massive	Right, massive.	734 U/mL	19×11×10 cm	total abdominal hysterectomy and bilateral salpingo-oophorectomy.	6 months, no evidence of recurrent ascites or hydrothorax, and serum CA125 level returned to normal.
10	Kurai, 2005 [33]	79	chest pain and dyspnea. A solid mass of the ovary, ascites, pleural effusion, and elevated serum CA125.	Slight	Right, 600–800 ml daily.	163 U/mL	9×7×7 cm	total hysterectomy and bilateral salpingo-oophorectomy	The post-operative course was uneventful. Pleural effusion disappeared and thoracic drainage was removed 3 days after the operation. Serum CA-125 became normal 7 days after surgery
11	Munteanu, 2006 [34]	50	severe respiratory insufficiency, arterial high blood pressure, tachycardia.	Massive	Right, massive.	ten times the normal value	Not reported.	Not reported	Not reported
12	Landrum, 2008 [35]	47	Pelvic mass, ascites, bilateral pleural effusions, and an elevated CA 125.	2 L	Bilateral, Not reported.	Elevated	20,120 g	Exploratory laparotomy and excise the mass.	Patient had return to full activity with 50 pound weight loss at 8 weeks after surgery.
13	Ricci, 2009 [36]	35	Abdominal distension 2 days after a spontaneous vaginal delivery.	5 L	Negative.	231.4 U/mL	15×10×8.5 cm	Exploratory laparotomy and excise the mass.	3 years, no any medical problem, the transvaginal ultrasound is negative and the CA125 value is 67 U/mL.
14	Chourmouzi, 2010 [37]	41	Abdominal swelling, discomfort, urinary frequency and incontinence.	Abundant	Not reported.	436.7 U/mL	13×16 cm	Exploratory laparotomy and excise the mass.	Had an uneventful post-operative course.

Table 1 (continued)

No.	Article	Age (y)	Symptoms	Ascites (volume)	Hydrothorax (side, volume)	CA125 level	Tumor size / weight	Treatments	Follow-up
15	Yip, 2014 [38]	41	Abdominal fullness and prolonged menstrual periods.	4 L	Negative.	939.70 U/ml	12×11×7.8 cm	Exploratory laparotomy and excise the mass.	The post-operative course was uneventful.
16	Seo, 2014 [39]	22	Painless abdominal distension.	Abundant	Negative.	450 kU/l	8.9×5.2 cm	Exploratory laparotomy and excise the mass.	Serum CA125 was reduced to normal at the post-operative three-month and had no relapse of ascites in the subsequent five years follow-up.
17	Dong, 2015 [40]	37	Right lower abdominal dull pain and abdominal distension.	8.1 L	Bilateral, 3.35 L.	920.4 U/ml	20×18×10 cm	Total abdominal hysterectomy and omentum sampling	> 82 months, remained disease-free.
18	Musleh, 2017 [41]	44	3 months' history of painless progressive abdominal distension and weight loss of more than 15 kg.	2.0 L	Negative.	546 kU/L	15×20 cm	Exploratory laparotomy and myomectomy.	4 weeks, no more complaints and regained the lost weight.
19	Kim, 2019 [42]	52	Increasing abdominal distension and progressive shortness of breath.	Massive.	Bilateral, massive.	392 U/mL	Not reported.	Partially resect the tumor	9 months, had no recurrent ascites or pleural effusion.
20	Pauls, 2019 [43]	56	Progressive dyspnoea.	Minimal/none	Right, Not reported.	437.3 U/mL	13.2×9.7×15.1 cm	total abdominal hysterectomy and bilateral salpingo-oophorectomy with omental biopsy.	8 months, pleural effusion completely resolved.
21	Yaguchi, 2020 [5]	37	Progressive abdominal distension and anorexia.	8.05 L	Not reported.	331.8 U/mL	27×15×13 cm	myomectomy and ovarian cystectomy.	Symptoms and ascites disappeared and serum CA125 returned to normal.
22	Wang, 2021 [44]	22	Abdominal pain.	5.0 L	Not reported.	569.5 U/mL	20 cm in diameter	Resection of the mass and appendix	Recovery in a stable condition.
23	Abdelgawad, 2022 [45]	35	Progressive abdominal pain, swelling and weight gain.	2.0 L	Negative.	272.9 ng/ml	29×19 cm	Mass excision, hysterectomy and bilateral salpingo-oophorectomy	Resolution of the ascites.

Table 1 (continued)

No.	Article	Age (y)	Symptoms	Ascites (volume)	Hydrothorax (side, volume)	CA125 level	Tumor size / weight	Treatments	Follow-up
25	Present case	45	abdominal distension and occasional abdominal pain	6.0 L	Right, 6.0 L	247.7 U/mL	20 × 15 × 12 cm	Total abdominal hysterectomy with mass excision and adhesiolysis.	12 months, no recurrence.

when the tumor exhibits rapid enlargement with water degeneration and elevated levels of CA125. A review of reported cases in the English literature revealed that the majority of patients present with symptoms such as abdominal swelling or distension and dyspnea. Imaging modalities such as CT, MRI, and ultrasound lack the capacity to differentiate between benign and malignant tumors, particularly in cases of degeneration. Consequently, there is a high likelihood of misdiagnosis as an ovarian or uterine malignancy, despite the tumor having a favorable prognosis. In patients with pseudo-Meigs syndrome and elevated CA125 levels, an accurate diagnosis is crucial for determining appropriate treatment. To achieve an accurate diagnosis, it is essential to perform a preoperative cytological analysis of ascites or hydrothorax, as well as a pathological examination via frozen section during surgery, particularly in patients with rapidly enlarging tumors and elevated CA125 levels.

Conclusion

In this case report, we describe a rare case of pseudo-Meigs syndrome in a patient with elevated CA125 levels caused by a rapidly enlarging hydropic leiomyoma. This condition is frequently misdiagnosed as ovarian cancer or uterine malignancy, and a comprehensive differential diagnosis encompassing both benign and malignant tumors is essential. A definitive diagnosis may be made intraoperatively through pathological frozen section analysis. In cases of pseudo-Meigs syndrome, patients generally have a favorable prognosis following resection of the pelvic mass. The available literature indicates that the majority of patients do not exhibit any signs of hydrothorax or ascites during follow-up assessments, which range from 10 days to 8 months postoperatively. At the two-year follow-up, the patient in our case remained free of hydrothorax and ascites.

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Author contributions

LQ.Z. Provided and analyzed the cases. JLL. and HR.H. organized the Literature database. LQ.Z. wrote the first draft of the manuscript. LX. analyzed the cases and revised the manuscript. All authors reviewed the manuscript and approved the submitted version.

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Data availability

The authors confirm that the data supporting the findings of this study are available within the article.

Declarations

Ethics approval and consent to participate

The studies involving human participants were reviewed and approved by the Ethics Committee of Zigong Fourth People's Hospital.

Consent for publication

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

Competing interests

The authors declare no competing interests.

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