CASE REPORT

Hydropic leiomyoma presenting as a rare condition of pseudo-Meigs syndrome: literature review and a case of a pseudo-Meigs syndrome mimicking ovarian carcinoma with elevated CA125

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SUMMARY

The clinical scenario of a female patient with a pelvic mass, elevated CA125 tumour marker, pleural effusion and ascites is often associated with malignancy. However, not all cases are malignant. Non-malignant diseases, such as Meigs syndrome and pseudo-Meigs syndrome, must be part of your differential. We present a 56-year-old woman with dyspnoea secondary to a right pleural effusion. After further investigations, a serum cancer antigen-125 was found to be elevated at 437.3 U/mL. CT of her abdomen and pelvis showed a large heterogeneous mass in the pelvis measuring 13.2×9.7×15.1 cm with mild ascites. She was initially thought to have ovarian carcinoma and underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy with omental biopsy. Pathology from the surgical specimen revealed a hydropic leiomyoma and after removal of pelvic mass her pleural effusion and ascites completely resolved. She was ultimately diagnosed with the rare pseudo-Meigs syndrome.

BACKGROUND

Meigs syndrome is a rare condition and defined by an ovarian fibroma or fibroma-like tumour (thecoma, granulosa cell and/or Brenner tumour) presenting with ascites and/or pleural effusion.^{1–3} This extremely rare syndrome is associated with a low incidence rate. Only 1% of ovarian tumours present as Meigs syndrome.¹

Pseudo-Meigs syndrome has a similar clinical presentation as Meigs syndrome (pleural effusions and/or ascites, with an ovarian mass); however,

Figure 2 CT of the chest demonstrates large dependent right-sided pleural effusion.

the mass itself is not a fibroma or fibroma-like tumour.² Pathologies reported in pseudo-Meigs syndrome include tumours such as cystadenoma, mature teratoma, struma ovarii and leiomyoma.³ Currently, there is no clear incidence reported of pseudo-Meigs syndrome in the literature, making this presentation exceptionally rare.

Prior to the discovery of Meigs and pseudo-Meigs syndrome, patients with constellation of symptoms of abdominal mass, ascites and pleural effusion were initially thought to have a malignant tumour. However, on surgical removal of the tumour, some were found to be benign and in these cases, the prognosis was excellent. In this paper, we discuss a case of uterine hydropic leiomyoma mimicking ovarian malignancy and presenting as pseudo-Meigs syndrome with elevated cancer antigen-125 (CA125). In the literature to date, there are few cases of leiomyoma presenting with pseudo-Meigs syndrome and even fewer still presenting with elevated CA125 levels. We hope to add to the literature surrounding this syndrome and provide education about its diagnosis, treatment and prognosis.

CASE PRESENTATION

A 56-year-old woman was seen by the internal medicine consultation team in the emergency

Figure 1 Chest X-ray demonstrates large dependent right-sided pleural effusion (left image). Chest X-ray demonstrates complete resolution of pleural effusion after removal of pelvic mass (right image).

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Table 1 Pleural fluid analysis

Fluid analysis number	Serum LDH (U/L)	Pleural fluid LDH (U/L)	Serum protein (g/L)	Pleural fluid protein (g/L)	Cytology	Differential	Bacterial culture	Assessment by Light's criteria
1	223	<30	64	30.73	Reactive cells, mesothelial origin	908×10 ⁶ WBC	Negative	Transudate
2	276	294	68	33.58		2619×10 ⁶ WBC	Negative*	Exudate

*Bacterial, mycobacterial and acid-fast bacilli cultures were negative and fungal culture showed growth of a non-clinically significant *Penicillium* species. WBC, white blood cell.

department (ED) of a Canadian tertiary care hospital for evaluation and workup of 1 month of progressive dyspnoea. Her medical history included heart palpitations and pneumonia diagnosed and treated 3 months prior. She additionally noted increasing fatigue with weight gain. A review of systems for inflammatory or autoimmune aetiologies was negative. She was non-smoker and seldom consumed alcohol. Family history was unknown as the patient was adopted.

On arrival to the ED, she had Glasgow Coma Scale of 15, with mild respiratory distress at rest but no cyanosis. Her vital signs were normal other than baseline hypoxia with an oxygen saturation of 77% with mild excursion on room air. Respiratory examination showed diminished breath sounds, dullness to percussion and decreased tactile fremitus in the right lung base, with the remainder of the physical examination being unremarkable. Pertinent negatives included no additional signs of heart failure, chronic obstructive pulmonary disease, autoimmune and/or chronic disease on her examination to explain her dyspnoea.

INVESTIGATIONS

An initial chest X-ray identified the presence of a right pleural effusion (figure 1). CT of the chest further confirmed a right-sided pleural effusion without evidence of other intrathoracic pathology (figure 2). Considering this finding, diagnostic and therapeutic thoracentesis was performed in the ED. Thoracentesis fluid analysis was consistent with a transudative process by Light's criteria showing pleural fluid protein/serum protein ratio >0.5 and pleural fluid Lactate Dehydrogenase (LDH)/serum LDH ratio >0.6 (table 1). Workup for causes of transudative effusion such as congestive heart failure, constrictive pericarditis, cirrhosis, nephrotic syndrome and hypothyroidism was negative (table 2).

Abdominal ultrasound showed diffuse hepatic steatosis but no signs of cirrhosis, a 1.4×1×1.5 cm hypoechoic lesion in the left hepatic lobe, and unremarkable gall bladder and common bile duct. Spleen and kidneys were normal in size, and no free fluid was noted within the abdomen.

A pigtail catheter was placed for symptom management to drain the pleural effusion. Pleural fluid analysis was repeated

after the pigtail insertion and recalculated for Light's criteria. Repeat analysis was consistent with an exudate, showing pleural fluid LDH/serum LDH ratio >0.6 (table 1). This result led to workup for an exudative effusion, considering malignancy as a cause.

The patient underwent a CT scan of her abdomen and pelvis that showed a large heterogeneous mass in the pelvis measuring 13.2×9.7×15.1 cm (figure 3). Her CT scan also demonstrated a small amount of ascites in the paracolic gutters that was not noted on physical examination, and the absence of the hypoechoic liver lesion noted on ultrasound. Her serum CA125 was elevated at 437.3 U/mL. No gynaecological ultrasound was performed, as the CT scan of the abdomen was sufficient as per the gynaecological oncology service, who were consulted to discuss treatment decisions.

DIFFERENTIAL DIAGNOSIS

Despite the left ovary not being visualised on the CT scan of the abdomen, the mass was still suspected to be originating from this structure, with a favoured diagnosis of a left ovarian neoplasm given the elevated CA125 result. However, a benign mass and complex cysts also remained in the differential diagnosis.

TREATMENT

Gynaecological oncology was consulted to assist with the management of the pelvic mass. As there was no evidence of metastatic disease, the patient underwent a total abdominal hysterectomy and bilateral salpingo-oophorectomy with omental biopsy. In the operating room, the mass was noted to be oedematous with minimal vascularity. Subsequently, surgical pathology identified the mass as a perinodular hydropic leiomyoma characterised by cellular fluid uptake and oedema with a small focus of zonal adenomyoma (figure 4). There was no infiltration of the left ovary.

Table 2 Summary of investigations for workup of transudative effusion

Test/imaging	Result
N-terminal-Pro-B-type natriuretic Peptide	123 pg/mL
Echocardiogram	Normal cardiac structure and function
Albumin	31 g/L
Urinalysis	No protein
Thyroid Stimulating Hormone (TSH)	5.26 mIU/L
Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Alkaline Phosphatase (ALP), Gamma Glutamyl Transferase (GGT)	Normal

Figure 3 CT of abdomen, chest and pelvis preoperatively. There is a large heterogeneous mass arising from the pelvis. Coronal view and sagittal view.

Figure 4 H&E stain of surgical pathology demonstrating vessel smooth muscle in intersecting fascicles—leiomyoma (left image) and vessel with fibrin thrombi (right image).

OUTCOME AND FOLLOW-UP

On follow-up with gynaecological oncology, the patient was well and with no active intrathoracic disease. The pleural effusion completely resolved after removal of the pelvic mass (figure 1).

DISCUSSION

Leiomyomas rarely present as pseudo-Meigs syndrome with elevated CA125. In most cases, pelvic masses are thought to be malignant. What complicates the situation is pseudo-Meigs syndrome mimics the clinical picture of an ovarian malignancy, but instead of being malignant they are benign and thus have an excellent prognosis on removal of the mass. To date, only 13

cases of leiomyoma presenting as pseudo-Meigs syndrome with elevated CA125 have been reported in the literature (table 3).^{4–16} In this case report, we have described the 14th case since 1998 of leiomyoma presenting with pseudo-Meigs syndrome with elevated CA125.

Historically documented cases of the constellation of pelvic mass, pleural effusion and ascites were first identified in 1866.¹⁷ The first case by Demons in 1887 identified a pleural effusion in association with a benign ovarian cyst.¹⁷ However, this syndrome was not named until 1937 when Meigs and Cass documented a case series of patients with ascites and hydrothorax in association with an ovarian fibroma.¹⁸ This case series led to the current eponym and its general recognition as Meigs syndrome in the medical literature.¹⁸ In the early 1900s, Albert Demons contributed to the treatment of Meigs syndrome by recommending that the causative lesion should be surgically removed, instead of the previous treatment of multiple therapeutic thoracenteses.¹⁸ This change in practice led to the discovery that removal of the benign mass leads to complete resolution of ascites and/or pleural effusion.

Ultimately, these historical cases have taught us to keep a broader differential diagnosis as benign tumours can mimic malignancy even when the CA125 is elevated. It remains unclear why CA125 is elevated in pseudo-Meigs syndrome. CA125 is

Table 3 Summary of 14 cases of leiomyoma presenting as pseudo-Meigs syndrome with elevated cancer antigen-125 (CA125)

Year	Authors (ref)	Patient's age	Ascites	Hydrothorax	CA125 (U/mL)	Tumour size (cm)	Treatment	Outcome
1998	Domingo <i>et al</i> ⁴	46	Present (size not reported)	Bilateral pleural effusion	317	20 cm in diameter	TAH & BSO	Good health in 10 days
1998	Brown <i>et al</i> ⁵	31	Present (size not reported)	Right pleural effusion	83	17×11.5×8.5 cm	Laparotomy for surgical excision	8 months later no evidence of disease
1998	Dunn <i>et al</i> ⁶	46	Large	Right pleural effusion	254	15×30×18 cm	TAH & BSO	4 months later no evidence of disease
2000	Migishima <i>et al</i> ⁷	51	Large	Left pleural effusion	820	12.3×24.3×20.5 cm	TAH & BSO	4 month post surgery resolution of symptoms
2001	Amant <i>et al</i> ⁸	39	Large	Left pleural effusion	785	30×30×15 cm	Hysterectomy	7 week showed resolution of hydrothorax
2002	Weise <i>et al</i> ⁹	27	Clinically noticeable ascites (size not reported)	Small right pleural effusion	1854	Not reported	Organ preserving surgery	3 months post surgery resolution
2002	Kebapci <i>et al</i> ¹⁰	38	Large	Left pleural effusion	281	9×10×10.5 cm	Organ preserving surgery	6 months post surgery resolution
2004	Weinrach <i>et al</i> ¹¹	40	Ascites (size not reported)	Large right pleural effusion	734	19×11×10 cm	TAH & BSO	6 months post surgery resolution
2006	Munteanu <i>et al</i> ^{12*}	50	Ascites	Right pleural effusion	Ten times the normal value	Not reported	Not reported	Not reported
2008	Landrum <i>et al</i> ^{13*}	47	2 L ascites	Bilateral pleural effusion	Elevated (value not reported)	Not reported	Explorative laparotomy	8 weeks post surgery resolution
2009	Ricci <i>et al</i> ¹⁴	35	Large	None	231.4	15×10×8.5 cm	Explorative laparotomy (organ preserving surgery)	1 month post surgery resolution of symptoms
2014	Yip <i>et al</i> ¹⁵	41	Large	None	939.70	12×11×7.8 cm	Explorative laparotomy (organ preserving surgery)	Not reported
2015	Dong <i>et al</i> ¹⁶	37	Large	Bilateral pleural effusion	920.4	20×18×10 cm	Explorative laparotomy (organ preserving surgery)	1 month post surgery resolution of symptoms
Current case	Pauls <i>et al</i>	55	Minimal/none	Right pleural effusion	437.3	13.2×9.7×15.1 cm	TAH & BSO with omental biopsy	8 months post surgery resolution of hydrothorax and symptoms

*Full paper unavailable, abstract used to report values.

TAH & BSO, total abdominal hysterectomy and bilateral salpingo-oophorectomy.

a large mucinous membrane glycoprotein that is expressed by normal and abnormal tissue of Mullerian origin and epithelial ovarian tumours.⁴ It is widely used as a biomarker for ovarian cancer, with serum levels greater than 35 U/mL raising concern for malignancy.¹⁹ However, it remains a poor biomarker as it has a 60% positive predictive value for diagnosing ovarian malignancies due to its potential elevation in other conditions including endometriosis, peritoneal disease, other non-ovarian malignancies and benign tumours.^{20 21} In pseudo-Meigs syndrome, it is believed that CA125 elevation is due to inflammation and secretion from mesothelium cells.^{7 8}

This case report illustrates a leiomyoma which mimicked an ovarian malignancy with an elevated CA125 but was subsequently determined to be pseudo-Meigs syndrome. It is always important to keep a broad differential diagnosis when investigating similar cases. Diagnosis can only occur after surgery. If identified as pseudo-Meigs syndrome, the patient ultimately has an excellent prognosis post resection of the pelvic mass. Based on existing literature, most patients remain disease free without any evidence of pleural effusion and/or ascites on their follow-up assessments ranging from as early as 10 days to 8 months (table 3). In our case, follow-up after 8 months showed that our patient remained asymptomatic without any sign of pleural effusion or ascites postoperatively.

Learning points

- ▶ Although the clinical picture of a female patient with a pelvic mass, positive tumour markers and pleural effusion is often highly associated with malignancy, in clinical practice we need to keep non-malignant disease, such as Meigs syndrome and pseudo-Meigs syndrome on the differential.
- ▶ While this will not change the therapeutic course of a patient, it does affect the prognosis.
- ▶ This case is an illustration of the multidisciplinary cooperation of internal medicine and gynaecology in the workup, diagnosis and treatment of an interesting case.

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