

## Case Report

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# Association of Pseudo-Meigs' Syndrome with Struma Ovarii and High CA125 Mimicking Ovarian Malignancy

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## ABSTRACT

Pseudo-Meigs' syndrome (PMS) is a rare condition in which a non-fibroma ovarian tumor, pleural effusion, and ascites coexist, and in which removal of the tumor resolves the condition. We present here a patient with struma ovarii-associated PMS, and with high serum CA-125 levels, bearing a resemblance to a malignant ovarian tumor. Arriving at an accurate diagnosis prior to surgery and before to receiving the final pathology report is very difficult to achieve. However, this association must be considered when pleural effusion is found, in addition to a heterogeneous pelvic mass with a rise in CA-125 is evident.

**KEYWORDS:** Pseudo-Meigs' syndrome; Struma ovarii; Elevated CA-125; Ovarian malignancy.

**ABBREVIATIONS:** PMS: Pseudo-Meigs' syndrome; CT: Computed Tomography; TTF1: Thyroid transcription factor; EMA: Epithelial Membrane Antigen; VEGF: Vascular Endothelial Growth Factor; FGF: Fibroblast Growth Factor.

## INTRODUCTION

Struma ovarii is a rare ovarian neoplasm composed predominantly of normal thyroid tissue and categorized as a variety of mature teratomas, representing only 2.7% of germ cell ovarian tumors.<sup>1,2</sup> It is generally benign, although it can present malignant transformation in 5-7% of cases, and is even more unusual as a metastatic disease.<sup>2</sup> The majority of cases are asymptomatic, but can be associated with a certain amount of ascitic fluid in up to 15-20% of the former, with reports of association with the hydrothorax, and development of the clinical features currently recognized as pseudo-Meigs' syndrome (PMS).<sup>3</sup> Among 20 cases reported as pseudo-Meigs' syndrome in a review of the literature from 1994-2014, only eight were related with struma ovarii (Table 1). The importance of this syndrome in benign pathology renders its recognition difficult.

Here, we present the case of a patient with struma ovarii associated with ascites, pleural effusion, and elevated CA125, simulating a malignant neoplasm of the ovary.

## CLINICAL CASE

This was a 48-year-old Mexican mestizo post-menopausal patient with no previous

Author	Year	Patient age (years)	Tumoral size (cm)	Ca125 (U/ml)	Ascitis (ml)	Type of surgery
Mui, et al. <sup>4</sup>	2008	56	6×5×4	5,218	5,000	Staging surgery
Mitrou, et al. <sup>5</sup>	2007	55	22×23×10	3,803	8,000	Staging surgery
Yücesoy, et al. <sup>6</sup>	2010	40	15×20	Not referred	Not referred	Hysterectomy + Right oophorectomy
Loizzi, et al. <sup>3</sup>	2005	65	7×7	161	Not referred	Right salpingo-oophorectomy
Paladini, et al. <sup>7</sup>	2008	42	11×7.3×8	2,548	8,000	Right salpingo-oophorectomy
Huh, et al. <sup>8</sup>	2002	66	5×4×4	402	20,000	Staging surgery
Rim, et al. <sup>2</sup>	2005	50	4×4	868.6	3,000	Staging surgery
Morán, et al. <sup>9</sup>	2006	46	25	1,808	500	Staging surgery
Present Report	2015	48	10×10	301	1,800	Staging surgery

Table 1: Cases reported of struma ovarii and Pseudo-Meigs' syndrome.

clinical history of importance, with complaint of abdominal distension. The patient reported her illness as having initiated 4 months previously, with an increase in abdominal perimeter, not painful, in addition to precordial pain as well as respiratory distress for 2 weeks. She presented at a community hospital for evaluation, where a chest x-ray was performed, revealing a right pleural effusion of more than 50%; cytology of the pleural effusion was performed with a report of reactive mesothelium without evidence of neoplastic cells. An abdominal Computed Tomography (CT) Scan (Figure 1) was performed, identifying a right ovarian tumor 10×13×7.67 cm above the median line of the hypogastrium, with mixed density and small calcifications. The patient was referred to our Institute for treatment. A Ca125 of 301 U/ml was reported. On physical examination, the patient presented without data of respiratory difficulty; her vital signs were normal, with soft abdomen, not painful, not under tension ascites, with a poorly defined palpable mass in the hypogastrium and approximately 7 cm in size. On gynecological examination: vulva and vagina without lesions; uterine cervix of normal appearance without lesions; on rectovaginal examination, uterus approximately 8 cm, and the aforementioned mass was palpated with inability for determining the origin. Rectovaginal septum and parametria were not involved.

1,800 ml of ascitic fluid, abdominal cavity and peritoneal surfaces without implants, as well as absence of tumor in contralateral adnexa and serosa of uterus, retroperitoneal lymph nodes were palpable and soft, considered to be inflammatory. The frozen section study of the tumor was reported as malignant but it could not be classified, and a complete cytoreduction and staging procedure was performed without complications. The patient evolved satisfactorily and was discharged from the hospital 3 days later.

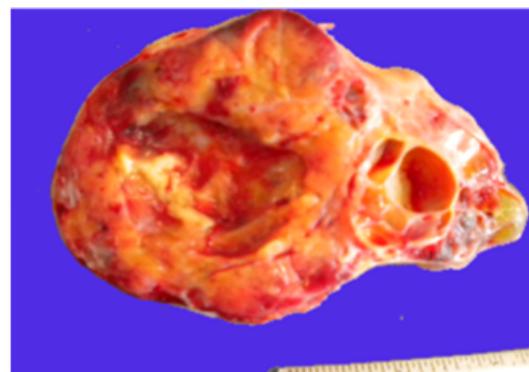


Figure 2: Macroscopic finding. Right adnexal mass of 10×10 cm, multilobular, with apparent capsular rupture.



Figure 1: Thoracic CT scan with pleural effusion. Abdominal CT scan identifying a right ovarian tumor 10×13×7.67 cm above the median line of the hypogastrium, with mixed density and small calcifications.

An exploratory laparotomy was performed with the following findings (Figure 2): right adnexal mass of 10×10 cm, multilobular, with apparent capsular rupture, the presence of

The final pathology report disclosed the following:

- Right ovary with monodermic pure teratoma (struma ovarii) with follicular hyperplasia.
- Tumor size, 10×7 cm without capsule involvement.
- Fifteen right pelvic lymph nodes, seven left pelvic lymph nodes, and seven para-aortic lymph nodes negative for metastatic disease.
- Biopsies of peritoneum and omentum negative for metastatic disease.

The following complementary immunohistochemical studies (Figure 3) were carried out: Thyroid transcription factor (TTF1): positive; Thyroglobulin: positive; Inhibin: negative; Epithelial Membrane Antigen (EMA): negative, and Calcitonin,

negative, supporting the previously mentioned diagnosis.

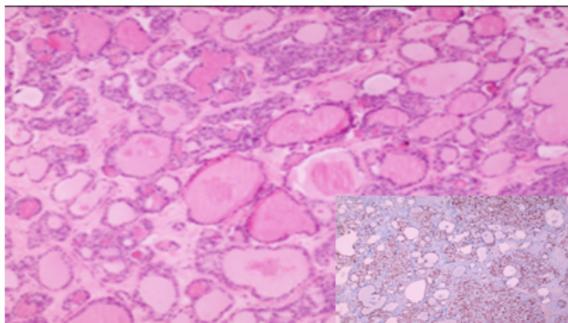


Figure 3: H&E and immunohistochemical stain. TTF1 positive.

The patient has remained under surveillance, and CA125 and thyroid profile studies have been conducted and reported as normal at her last clinical follow-up visit.

#### COMMENTARY

Struma ovarii is a rare variety of mature monodermal teratoma of the ovary that is composed entirely or primordially (>50%) of mature thyroid tissue.<sup>1,2,5,6</sup> It was originally described by Von Kalden in 1895.<sup>3</sup> At the beginning of the 20<sup>th</sup> Century, Pick identified struma ovarii as a germ cell neoplasm of the ovary comprising thyroid tissue.<sup>10</sup> In 1933, Plaut demonstrated that thyroid tissue of the struma ovarii is morphologically, biochemically, and pharmacologically identical to that of the thyroid gland.<sup>8,10</sup> Its frequency in ovarian neoplasms is less than 1%.<sup>2,7</sup> Peak incidence occurs between and 5<sup>th</sup> and 6<sup>th</sup> decades of life, and only 5% of these tumors comprise hyperthyroidism.<sup>3,5,6,8,10</sup> This is the most common type of monodermic teratoma, with a frequency of 3% among all ovarian teratomas.<sup>10</sup>

Macroscopically, struma is identified as a brown or brownish-green semi-solid mass that, on average, measures 10 cm.<sup>5,10</sup> Microscopically, the tumor is composed of thyroid tissue of normal appearance arranged in thyroid follicles of various sizes associated with mature cystic teratoma.<sup>10</sup>

Struma ovarii generally is a benign neoplasm; however, it has been reported that 5-37% can undergo a malignant transformation and is presents metastasis in less than 10% of cases.<sup>2-4</sup> It generally presents clinically as an asymptomatic mass that is diagnosed histologically after tumor resection; however, in 20% of instances, it can initially present with ascites.<sup>2-4</sup> The association of struma ovarii with ascites and pleural effusion is even rarer.<sup>3</sup>

Meigs' syndrome is the association of fibromas, ascites, and pleural effusion that resolve after surgical resection of the ovarian tumor.<sup>3,4,11,12</sup> Spiegelberg was the first to present the description of the syndrome in 1866; two decades later, Trait reported that the presence of an ovarian tumor with ascites and pleural effusion is not always associated with malignancy.<sup>12</sup>

In 1903, Demons described resolution of symptoms with ovarian tumor resection, and in 1937, Meigs and Cass described, in seven patients, the classical triad of pleural effusion, ascites, and ovarian tumor; in 1954, these authors described the syndrome, which consists of fibromas (fibromas, thecomas, or granulosa cell tumors) with ascites and hydrothorax, characterizing later resolution on removing the benign tumor.<sup>3,8,12-14</sup> Later, Rhoads and Terrell assigned the term Meigs' syndrome to this association.<sup>13</sup>

Meigs' syndrome is rare, presenting fibromas with pleural effusion in 10-15% of cases and with ascites and pleural effusion in 1%.<sup>2,15</sup> Other tumor types distinct from the fibroma, such as teratomas or uterine leiomyomas, are associated with Meigs' criteria, the preferred term being Pseudo-Meigs' syndrome (PMS).<sup>1,3,16</sup> The distinction between Meigs' syndrome and PMS is mainly academic, because the therapeutic strategy is identical in the two scenarios.<sup>17</sup>

Patients can present respiratory difficulty caused by massive ascites and by pleural effusion and, in extreme cases, may experience hypoxia, hypercapnia, and respiratory acidosis.<sup>15</sup> The pressure of lymphatic tissue by the tumor can result in the escape of fluid through the lymphatic vessels that are localized together within the epithelial layer covering the tumor, in combination with filtration of intratumor fluid, mechanical irritation of the tumor, and peritoneal inflammation as a result of ascites.<sup>8,15</sup> Other proposed mechanisms comprise active secretion of fluid by the tumor or the peritoneum, venous or lymphatic obstruction, decrease in serum proteins, or the presence of toxins or inflammatory products.<sup>3</sup>

The formation of pleural effusion in Meigs' syndrome and in PMS can be the result of the mechanical transference of ascites fluid through diaphragmatic openings or lymphatic vessels.<sup>2,8,15</sup> This theory is supported by the rapid occurrence of pleural effusion after thoracentesis and its identical biochemical composition in peritoneal as well as in pleural fluid.<sup>13</sup> It has recently been suggested that Vascular Endothelial Growth Factor (VEGF), Fibroblast Growth Factor (FGF), and Interleukin 6 (IL-6) are related with the production of ascites and hydrothorax, in that these possess properties of vascular permeability.<sup>15</sup> The elevation of Ca125 in the serum of postmenopausal women suggests that, in 80% of cases, the presence of ovarian cancer.<sup>1,5,7,12,18,19</sup>

PMS associated with struma ovarii and accompanied by a rise in Ca125 is very rare: only eight cases have been reported in the medical literature to date (Table 1).<sup>2-4,7,8,11,12,18,19</sup> The possible causes of the increase of Ca125 in Meigs' syndrome include irritation of the mesothelial cells by the ovarian tumor, ascites, or pleural effusion, which leads to the antigen being released onto the surface of the serous membranes or the peritoneum.<sup>7,16,18,19</sup>

To date, no correlation has been found among volume

of ascites fluid volume, tumor size, or the value of Ca125 in Meigs' syndrome.<sup>5</sup> What has been observed is that in Meigs' syndrome, Ca125 values are much lower than those typically found in ascites originating from malignant tumors.<sup>3</sup>

Authors have previously reported that if an ovarian solid mass is similar to thyroid tissue, in terms of its being both hyperechoic on Ultrasound (US) and hyperdense on unenhanced CT scan, struma ovarii should be considered in the differential diagnosis. The latter was confirmed in this patient, whose abdominal CT revealed a right ovarian tumor comprising mixed density and small calcifications.<sup>20</sup>

The surgeon should always consider atypical mature teratomas, cystadenofibromas, and even a malignant epithelial tumor as part of the differential diagnosis when pondering this entity.<sup>21</sup>

#### CONCLUSION

This case is uncommon due to the presentation of pleural effusion, ascites, high Ca125, and a complex pelvic mass, suggesting a malignant ovarian neoplasm and subsequently revealing struma ovarii in the histological report; thus, it is very difficult to perform an accurate diagnosis prior to surgery and before receiving the final pathology report. However, it is necessary to bear this possibility in mind in order to perform the appropriate tumor cytoreduction procedure.

#### CONFLICTS OF INTEREST

The author(s) declare that there is no conflict of interests regarding the publication of this paper.

#### CONSENT

The patient described in the case report has given their informed consent for the case report to be published.

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