Struma Ovarii with Pseudo-Meigs Syndrome and Increased CA-125 Levels: Case Report

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Struma Ovarii com Síndrome Pseudo-Meigs e Aumento dos Níveis de CA-125: Relato de Caso

Struma Ovarii con Síndrome de Pseudo-Meigs y Niveles Elevados de CA-125: Informe de Caso

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ABSTRACT

Introduction: *Struma ovarii* is a rare type of ovarian tumor composed of more than 50% of thyroid tissue. It represents only 1% of solid ovarian tumors and 3% of dermoid subtypes, with the majority of cases following a benign course. It typically affects women between the third and fifth decades of life and often remains asymptomatic or presents with nonspecific signs. pseudo-Meigs syndrome, characterized by ascites and pleural effusion, may be present, complicating the diagnosis. **Case report:** A 43-year-old woman presented with abdominal discomfort, pelvic pain, and chronic dyspnea. A CT scan identified a solid-cystic pelvic mass, moderate ascites, and right-sided pleural effusion. Magnetic resonance imaging (MRI) confirmed the findings, raising suspicion of malignant ovarian tumor. The serum tumor marker CA-125 was elevated. The patient underwent exploratory laparotomy, resulting in bilateral salpingo-oophorectomy. Histopathological analysis of the specimen confirmed the diagnosis of *struma ovarii* in the left ovary and mature cystic teratoma in the right ovary. **Conclusion**: Elevated CA-125 levels can be found in cases of *struma ovarii*, posing a differential diagnosis challenge with malignant ovarian neoplasms, especially when associated with pseudo-Meigs syndrome. Therefore, although rare, it should be considered as a possibility during clinical investigation of ovarian masses with atypical presentations. Imaging studies can assist, but confirmation is established through microscopic analysis. Treatment involves simple surgical resection, and symptom disappearance follows, with favorable prognosis.

Key words: struma ovarii; ovarian neoplasms; pseudo-Meigs syndrome; CA-125 antigen.

RESUMO

Introdução: *Struma ovarii* é um tipo raro de tumor ovariano composto por mais de 50% de tecido tireoidiano. Representa apenas 1% dos tumores sólidos do ovário e 3% dos subtipos dermoides, com a maioria dos casos de curso benigno. Geralmente afeta mulheres entre a terceira e a quinta décadas de vida, sendo muitas vezes assintomático ou com sinais inespecíficos. A síndrome de pseudo-Meigs, caracterizada por ascite e derrame pleural, pode estar presente, dificultando o diagnóstico. **Relato do caso:** Mulher, 43 anos, com desconforto abdominal, dor pélvica e dispneia crônica. A tomografia identificou massa sólido-cística na pelve e ascite moderada, além de derrame pleural à direita. A ressonância magnética confirmou as alterações e, desse modo, suspeitou-se de tumor maligno ovariano. O marcador sérico tumoral CA-125 estava elevado. A paciente foi submetida a uma laparotomia exploradora que resultou em salpingo-oforectomia bilateral. A análise histopatológica do espécime confirmou o diagnóstico de *struma ovarii* em ovário esquerdo e teratoma cístico maduro à direita. **Conclusão:** Os níveis elevados de CA-125 podem ser encontrados em casos de *struma ovarii*, tornando-o diagnóstico diferencial nas neoplasias ovarianas malignas, especialmente quando associado à síndrome de pseudo-Meigs. Nesse sentido, embora raro, o tumor deve ser considerado uma possibilidade durante investigação clínica de massas ovarianas com apresentações atípicas. Os exames de imagem podem auxiliar, mas a confirmação é estabelecida pela análise microscópica. O tratamento consiste na ressecção cirúrgica simples, e o desaparecimento dos sintomas acontece em seguida, sendo de bom prognóstico.

Palavras-chave: estruma ovariano; neoplasias ovarianas; síndrome de pseudo-Meigs; antígeno CA-125.

RESUMEN

Introducción: El *struma ovarii* es un tipo raro de tumor ovárico compuesto por más del 50% de tejido tiroideo. Representa solo el 1% de los tumores ováricos sólidos y el 3% de los subtipos dermoides, siendo en su mayoría benigno. Típicamente afecta a mujeres entre la tercera y quinta década de vida y a menudo permanece asintomático o presenta signos inespecíficos. El síndrome de pseudo-Meigs, caracterizado por ascitis y derrame pleural, puede estar presente, complicando el diagnóstico. **Informe del caso:** Una mujer de 43 años consultó por malestar abdominal, dolor pélvico y disnea crónica. La tomografía identificó una masa pélvica sólido-quística, ascitis moderada y derrame pleural en el lado derecho. La resonancia magnética confirmó los hallazgos, levantando sospechas de un tumor ovárico maligno. El marcador tumoral sérico CA-125 estaba elevado. La paciente fue sometida a una laparotomía exploratoria, resultando en salpingo-ooforectomía bilateral. El análisis histopatológico de la muestra confirmó el diagnóstico de *struma ovarii* en el ovario izquierdo y teratoma quístico maduro en el ovario derecho. **Conclusión**: Los niveles elevados de CA-125 pueden encontrarse en casos de *struma ovarii*, lo que lo convierte en diagnóstico diferencial con neoplasias ováricas malignas, especialmente cuando se asocia con el síndrome de pseudo-Meigs. Por lo tanto, aunque sea raro, se debe considerar como una posibilidad durante la investigación clínica de masas ováricas con presentaciones atípicas. Los estudios por imágenes pueden ayudar, pero la confirmación se establece mediante análisis microscópico. El tratamiento implica la resección quirúrgica simple y los síntomas desaparecen después, con un pronóstico favorable.

Palabras clave: estruma ovárico; neoplasias ováricas; síndrome de pseudo-Meigs; antígeno CA-125

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INTRODUCTION

Struma ovarii is a highly specialized variety of mature ovarian teratoma, it is composed predominantly of thyroid tissue (>50%)[1], the most common type of ovarian monodermal teratoma[2], accounting for 1% of solid tumors and 3% of ovarian dermoid tumors[3]. This neoplasm is either malignant or benign and both are rare entities. Its age of incidence is similar to cystic mature teratoma peaking between the third and fifth decade of life[4,5].

Most patients are asymptomatic[5]. A pelvic painful mass with local pressure, abdominal distention and menstrual disorders are signs and symptoms if present[3]. Ascites occur in one third of the cases and occasionally courses with pseudo-Meigs syndrome – presence of ascites and hydrothorax but not related to ovarian fibroma or tecoma[1,5,6], and symptoms disappear following surgical resection[7]. Most of the *struma ovarii* is functionally inactive and incidence of hyperthyroidism is rare, accounting for nearly 5% to 8% of the cases[8,9]. The physical examination may reveal a palpable mass depending on size and location[1].

The first case of *struma ovarii* dates back to more than 100 years but several aspects remain as an enigma needing macro and microscopic multidisciplinary evaluation, but excluding the possibility of malignancy[3,5]. Given this scenario, the main objective of this article is to contribute to the literature with an atypical case with few global epidemiologic data.

The Institutional Review Board of "*Faculdade Evangélica Mackenzie do Paraná*", report number 4991187 (CAAE (submission for ethical review): 51395921.3.0000.0103) according to the last update of the Surgical Case Report – SCARE guidelines[10], following every ethical request for studies with human beings and ensuring the anonymity of the information in compliance with Resolution number 466/12[11] of the National Health Council.

CASE REPORT

Woman, 43 years of age, sought medical consultation in July 2020 complaining of abdominal pains, moderate pelvic pain and chronic dyspnea. Her medical history revealed cirrhosis of the liver in treatment, pleural effusion up to the left apex and family history of malignant neoplasm.

The physical examination showed mobile infra-abdominal palpable lesion without alterations of the cervix at vaginal touch. Complementary abdominal ultrasound revealed 10 cm diameter solid, heterogeneous mass, accentuated vascularization, located at the projection of the umbilical scar. Total abdominal and thoracic tomography was requested for best visualization showing expansive lesion – multilobulated, irregular and heterogeneous, measuring 120 x 86 mm at the pelvis – and moderate ascites associated with the presence of 11 mm osteolytic lesion with regular margins and sclerotic at the right iliac wing and right pleural effusion.

Complementing the diagnosis, magnetic resonance of total abdomen showed pelvic solid-cystic lesions with partially defined boundaries and lobulated contours, with contrast heterogeneous enhancement, with no restriction to spread, hypersignal in T2 and hyposignal in T1. The lesions were located above and posterior to the uterus and anterior to rectum well above the bladder (Figure 1). The radiologist did not present characterization of the ovary, suggestive of malignant ovarian tumor.

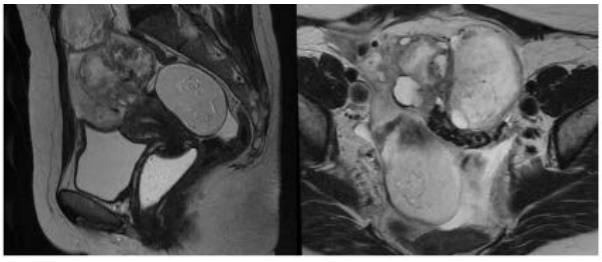

Figure 1. Abdominal magnetic resonance showing pelvic cystic lesions, measuring 97 x 104 x 114 mm (T x AP x L)

Laboratory parameters complete blood count and thyroid hormone dosage (TSH, T4) were normal. Diagnostic thoracocentesis and paracenteses were performed to obtain additional information on pleural and peritoneal liquids. Given the clinical and radiologic possibility of a malignant ovarian neoplasm, tumor markers were requested showing elevation of CA-125 (302 U/ml), while BHCG (< 2.39 mlU/ml) and CEA (0.80 ng/ml) were within the reference values.

The results corroborated the suspicion of ovarian cancer; in August 2020, the patient was submitted to exploratory laparotomy to evaluate the tumor extension and intraoperatory analysis of the characteristics of the lesion together with pathologic anatomy.

During surgical evaluation, large left ovarian mass with approximately 12 cm in its longest diameter and cystic-solid lesions with 6 cm in its longest extension in the right ovary were noticed, with no additional findings. Intraoperatory anatomopathological analysis of the sample collected by salpingo-oophorectomy revealed benignancy. As the tumor was bilateral, a right salpingo-oophorectomy was also performed for further histological post-surgery evaluation.

Cytological exams of peritoneal and pleural liquids collected revealed non-malignancy like the neoplastic-free infiltrated omentum and peritoneal biopsies samples.

The ovary weighted 310 g and measured 12.3 cm in its longest axis according to the macroscopic analysis of the left surgical piece. The ovarian capsule was not affected. The cuts section revealed irregular, solid-cystic, yellow citrine, sebaceous serous mass with well-defined contours, variegated, brownish and deep-purple color, soft and elastic lesion. The findings of the histopathology confirmed the presence of *struma ovarii* (Figure 2) associated with mature teratoma.

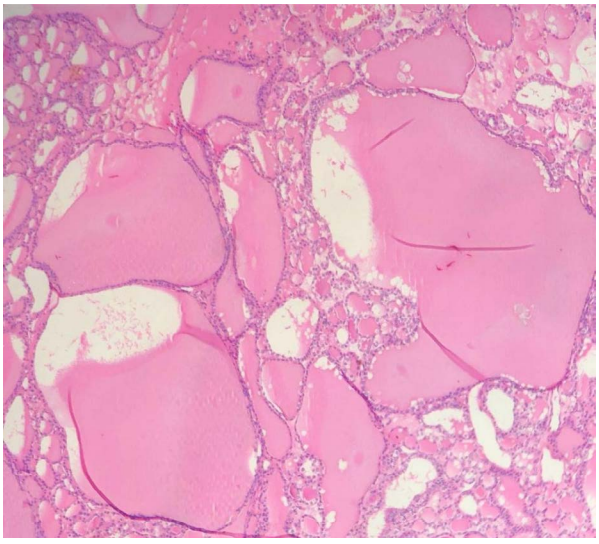

Figure 2. Details of thyroid follicles with colloid of *struma ovarii* at the left ovary (optical microscopy, hematoxylin-eosin, 100x)

The right ovary was cystic-like, weighing 25 g and 6.3 cm in its longest axis. The capsule was ruptured with brownish surface, irregular and opaque. Cuts sections revealed unilocular sebaceous and brownish cystic lesion. The anatomopathological diagnosis after microscopic evaluation was mature cystic teratoma (Figure 3).

Uterine tubes measured approximately 6.0 cm in length and 1.3 to 1.5 cm in its longest diameters. Both were serous, purple-like, smooth and shiny without significant histopathological alterations and neoplastic-free infiltration.

The patient was hospital-discharged after 24 hours of surgery, in good general condition and due to the benign nature of the lesion, the month outpatient follow-up was discontinued after the 10th day visit post hospitalization. The imaging and lab parameters including CA-125 levels were within normal range at the annual follow-up and with no signs of relapse even after two years and five months.

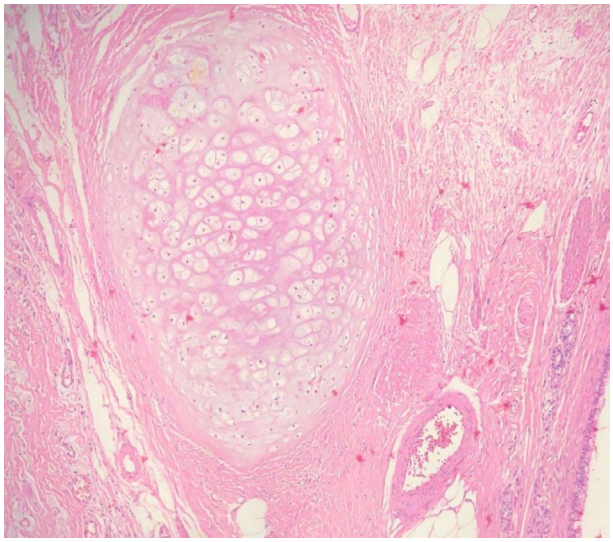

Figure 3. Right, mature cystic teratoma (optical macroscopy, hematoxylin-eosin, 200x)

DISCUSSION

Struma ovarii is a rare variety of mature ovarian teratoma, it is composed predominantly of thyroid tissue. Most of the times has a benign and asymptomatic course, adding complexity to the diagnosis[12]. Additionally, the difference from ovarian malignant neoplasms is challenging, especially when the clinical status is associated with pseudo-Meigs syndrome with elevated CA-125 and patient's age[6,12].

Echography can be an interesting ally to help the differential diagnosis of adnexal masses. Typically, *struma ovarii* presents as a node or complex mass, generally multi-cystic with lobulated surface, septa or thickened cyst walls and occasionally well vascularized cyst walls and evidences of mature teratoma of difficult distinction between benign and malignant lesion as mentioned earlier[3]. CA-125 is an important tumor marker during the investigation, at the diagnosis, treatment and prognosis of ovarian carcinoma. However, due to its low specificity, it is possible that it presents exceptional elevation in cases of *struma ovarii* based in scarce literature reports[6,9].

Overall, *struma ovarii* does not cause alterations of the thyroid hormone levels[13], however, Morrissey et al.[13] described a condition where *struma ovarii* might potentially provoke the formation of antithyroid hormones which could lead to a secondary thyroiditis to ovarian neoplasm with clinical signs of hyperthyroidism. Furthermore, the decline of T4 levels and thyrotoxicotic symptoms post tumor removal – combined with anatomopathological findings – could suggest an extraglandular cause of hyperthyroidism[13]. If suspicion exists, the profile of these hormones can be incorporated in the clinical investigation[7].

As imaging and clinical signs are uncharacteristic, the definitive diagnosis is reached through anatomopathological analysis postsurgical resection[1], the perioperative cyto-histological evaluation can also contribute to the definition of the therapeutic approach[7]. The macroscopic evaluation usually reveals generally unilateral solid or cystic-solid mass, of various dimensions, typically smaller than 10 cm with brownish surface of lobulated contours[2]. At microscopy, the regular thyroid tissue is characterized by follicles of various sizes filled with colloid, exhibiting a single layer of eosinophilic cuboid cells with rounded nuclei, frequently associated with wide cystic areas containing foci of classic cystic mature teratoma[2].

Occasionally, the thyroid tissue may appear as an adenomatous node or nodular goiter. In cases of clinical hyperthyroidism (8%), characteristics indicative of toxic goiter can be observed microscopically as follicles lined by hyperplastic epithelium with pseudopapillary form and peripherical vacuolated areas to colloid. Focal lymphocytes infiltrates can be present. The accurate distinction of these alterations is very important to avoid possible wrong interpretations as thyroid papilliferous carcinoma, an entity already documented in the literature in association with malignant transformation of *struma ovarii*[8].

In cases where neoplasms exhibit solid or microfollicular pattern, tumor cells usually present with clear eosinophilic cytoplasm, possibly with oncocytic appearance and be confounded with oncocytic cells, primary or metastatic tumors. They can also mimic ovarian tumors of the sexual chord, adopting pseudo tubular arrangement similar to Sertoli cells tumor[2], or configuration of small follicles suggestive of granulosa cells tumor. Recognize typical forms of *struma ovarii* or utilize immunohistochemical markers for thyroglobulin or thyroid transcription factor 1 (TTF-1) can help the differential diagnosis[5,9].

Malignant transformation described in one fifth of the cases[5] fails to present well established diagnosis even with variation of nomenclature as "malignant *struma ovarii*" and "*struma ovarii*-derived thyroid carcinoma", the latter is the most appropriate to describe this condition. Several types of thyroid carcinoma deriving from *struma ovarii* have been reported, among them, papilliferous, including the follicular variant and follicular carcinoma with the oncocytic variant[2]. Papilliferous carcinoma is the most common and its histological components are: cell overlap, ground glass opacity with intranuclear inclusions, irregular contours nuclei amidst vascularized papillary formations and fine granular chromatin, positive for thyroglobulin and TTF-1[9]. The identification of psammoma bodies is highly suggestive of malignancy[14].

The aforementioned histological alterations rarely signify a clinical malignant behavior and will hardly evolve with extra-ovarian spread[5]. Tumors larger than 10 cm and with more than 80% of stromal component are associated with great risk of progression[14]. Mutations of the gene BRAF and rearrangements of the gene RET/PTC, in the molecular perspective were identified in the *struma ovarii*[2] derived thyroid papillary carcinoma. Therapeutic approach is simple surgical resection, and most of the cases of *struma ovarii* is benign[5]. Even for malignant cases, the prognosis is good with low possibility of relapse and the treatment should be patient-centered[2]. Elevated CA-125 levels at the diagnosis usually return to post-surgery regular standards.

CONCLUSION

Struma ovarii, although barely frequent, should be considered a differential for ovary malignant neoplasms, specially concomitant with elevated CA-125 and manifestations indicative of pseudo-Meigs syndrome. The anatomopathological study of the lesion is essential for a definitive diagnosis. After surgical resection of the tumor, the levels of CA-125 and clinical signs normalize evolving with good prognosis and low possibility of relapse.

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CONTRIBUTIONS

All the authors contributed substantially to the study design, acquisition, analysis and interpretation of the data, wording and critical review. They approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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