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CASE REPORT

Struma Ovarii with Pseudo-Meigs' Syndrome and Raised Cancer Antigen-125 Levels Masquerading as an Ovarian Carcinoma

Case report and literature review

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ستروما أوفاري مع متلازمة شبيهة–ميغس المصحوبة بأرتفاع مستوى مستضد السرطان 125-في المشابه لسرطان المبيض

تقرير حالة ومراجعة الأدبيات

سوريخا ياداف، رينا تومار، نيدهي فيرما، نيتا خورانا، ريوا تريباثي

ABSTRACT: The monodermal teratoma *struma ovarii* is a rare ovarian tumour; however, *struma ovarii* presenting with pseudo-Meigs' syndrome and raised cancer antigen (CA)-125 levels is even rarer. In elderly patients, this presentation can potentially lead to a misdiagnosis of a malignant ovarian carcinoma, resulting in unnecessary extensive surgery. We report a 55-year-old female who presented to the Lok Nayak Jai Prakash Narayan Hospital, New Delhi, India, in 2016 with progressive abdominal discomfort, fatigue and abdominal distention. Clinical and radiological features were indicative of a malignant ovarian tumour and *ascites*. Serum CA-125 levels were elevated at 258 U/mL. A left-sided salpingo-oophorectomy was performed, after which the serum CA-125 levels normalised. There was no evidence of recurrence at a six-month follow-up. A frozen section procedure confirmed the diagnosis of a *struma ovarii*. This rare condition should be considered as a differential diagnosis in patients presenting with ovarian masses, *ascites* and raised CA-125 levels.

Keywords: Ovarian Cancers; Struma Ovarii; Meigs' Syndrome; Carcinoma; Ascites; Frozen Section; Case Report; India.

الملخص: يعتبر الورم المسخي أحادي الطبقة ستروما أوفاري من أورام المبيض النادرة ولكن وجوده مع متلازمة بسيودو-ميغس المصحوبة بأرتفاع مستوى مستضد السرطان 125-في المصل اكثر ندرة. في المرضى المسنين، من الممكن أن يؤدي هذا العرض إلى تشخيص خاطئ لسرطان المبيض الخبيث مما قد يؤدى إلى جراحة واسعة لا لزوم لها. هذا تقرير حالة عن أنثى تبلغ من العمر 55 عاما قدمت إلى مستشفى لوك نایاك جاي براكاش نارايان، نيودلهي، الهند، في عام 2016 بأعراض عدم الراحة والألم التدريجي في البطن، والأرهاق وانتفاخ البطن. وأظهرت الخصائص السريرية والإشعاعية دلائل على وجود ورم خبيث في المبيض مع الاستسقاء، وارتفاع مستويات المستضد كا 125-في المصل إلى 258 U/mL مل. تم إجراء عملية استئصال للمبيض وأنابيب فالوب على الجانب الأيسر، وبعد ذلك عادت مستويات كا 125-في المصل إلى قيمها الطبيعية. وبعد ستة أشهر من المتابعة لم يوجد هناك دليل على أرتداد أو عودة المرض. وأكد فحص العينة المجمدة تشخيص ستروما أوفاري. ينبغي أن تؤخذ هذه الحالة النادرة في الأعتبار في التشخيص التفريقي في المرضى الذين يعانون من أورام المبيض والاستسقاء وأرتفاع مستويات المستضد كا 125-في المصل.

الكلمات المفتاحية: سرطان المبيض؛ ستروما أوفاري؛ متلازمة ميغس؛ سرطان؛ استسقاء؛ العينة المجمدة؛ تقريرحالة؛ الهند.

Struma ovarii are mature ovarian teratomas derived from one type of germ cell; these monodermal variants account for >5% of mature teratomas and 0.3–1% of ovarian tumours.[1] These types of tumours predominantly consist of thyroid tissue (>50% of the overall ovarian mass) and the usual age of presentation is during the fifth and sixth decades of life.[1] The reported rate of malignant transformation is 5–37%, in which the *struma ovarii* transforms into a thyroid-type carcinoma.[2] The usual presentation of *struma ovarii* is as an abdomino-pelvic mass, although it may present with hyper-thyroidism in approximately 5% of cases.[3] Radio-logically, a benign ovarian mass presenting with *ascites* and raised cancer antigen (CA)-125 levels can be misdiagnosed as a malignant ovarian tumour.[2,4,5] In such cases, a correct intraoperative diagnosis can prevent extensive surgery.

Case Report

A 55-year-old female presented to the Lok Nayak Jai Prakash Narayan Hospital, New Delhi, India, in 2016 with progressively increasing abdominal discomfort,

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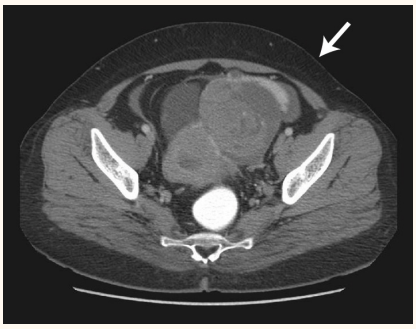

Figure 1: Abdominal computed tomography of a 55-year-old female with progressive abdominal discomfort and abdominal distention showing a left adnexal mass (arrow).

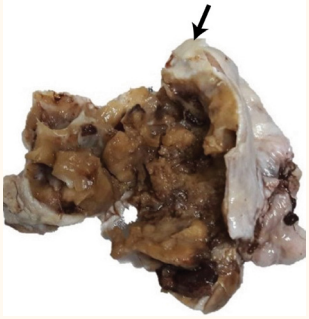

Figure 2: Photograph showing an encapsulated left ovarian solid-cystic mass (arrow), which had replaced the entire normal ovarian parenchyma.

fatigue and abdominal distention for the preceding five months. She had been postmenopausal for the last five years. She had three children, with her last childbirth having taken place 28 years previously. Her medical, surgical and family history was normal. A pelvic examination revealed a left-sided pelvic mass of 6 x 5 x 5 cm in which the uterus moved with the mass. Her CA-125 level was 258 U/mL (normal value: <35 U/mL). All haematological investigation results were within normal range. A chest X-ray was unremarkable, with no indications of pleural effusion.

Ultrasonography revealed a left-sided solid-cystic adnexal mass measuring 6 x 5 x 3.5 cm. The right-sided *adnexa*, uterus and cervix appeared normal. There was 680 mL of free fluid in the recto-uterine pouch. Computed tomography of the pelvis revealed a left-sided heterogeneously enhancing solid-cystic pelvic mass measuring 6.2 x 5 x 4 cm [Figure 1]. The left ovary was not visualised separately. There was no evidence of organomegaly or lymphadenopathy. Overall, the radiological findings were suggestive of a malignant mass. A total of 500 mL of peritoneal serous fluid was removed via abdominal paracentesis. Cytological examination of this fluid indicated only reactive mesothelial cells with a few leukocytes, with no malignant cells identified.

An exploratory laparotomy was performed. The left-sided adnexal mass measured 6 x 5 x 4.5 cm and was solid-cystic, with a smooth external surface. The uterus and cervix were normal and there was no evidence of intraperitoneal spread to the *omentum*, liver or appendix. The patient subsequently underwent a left-sided salpingo-oophorectomy and the excised specimen was sent for frozen analysis to rule out malignancy. During the postoperative period, the results of a thyroid function test were normal. The patient recovered well after surgery and there was no evidence of any re-accumulation of ascitic fluid. By the eighth postoperative day, her postoperative CA-125 levels had normalised. At a six-month follow-up, there were no signs of recurrence of the ovarian mass.

On gross examination, the excised ovarian mass measured 6 x 5 x 4 cm and there was no evidence of haemorrhage, bone, cartilage or hair. The external surface was smooth and glistening white. The cut surface revealed a solid-cystic mass which had replaced the entire ovarian parenchyma [Figure 2]. An omental biopsy and peritoneal washing was performed on the excised specimen, with benign results. The scrape smears showed cuboidal cells forming thyroid follicles and monolayered sheets in a thin colloid background [Figure 3A]. The frozen section revealed that the specimen was composed

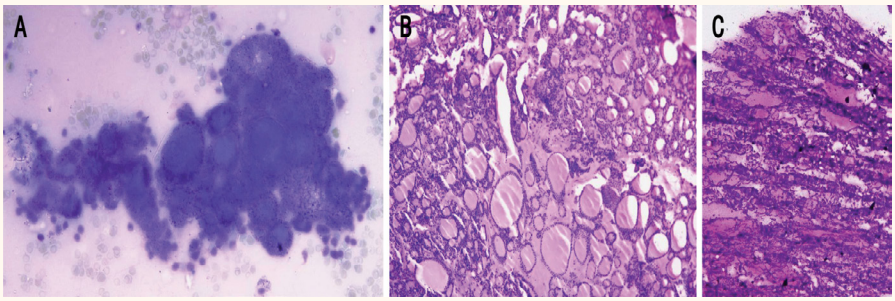

Figure 3: A: Toluidine blue scrape smear at x20 magnification showing thyroid follicles with colloid in the background. **B:** Haematoxylin and eosin (H&E) stained frozen section at x40 magnification showing variable-sized colloid-filled thyroid follicles. **C:** H&E stained frozen section at x20 magnification showing various thyroid follicles.

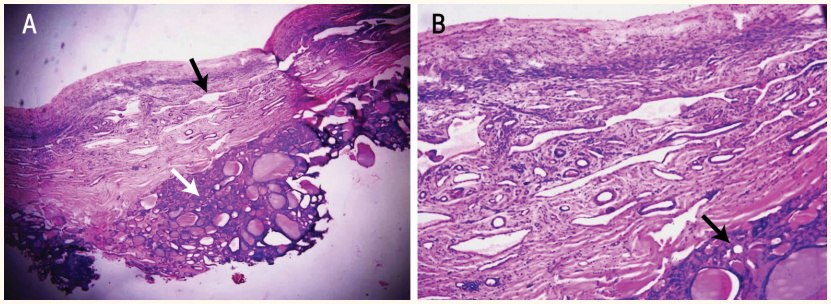

Figure 4: A: Haematoxylin and eosin (H&E) stained paraffin section at x10 magnification showing colloid-filled thyroid follicles (white arrow) and compressed normal thyroid parenchyma at the periphery (black arrow). **B:** H&E stained paraffin section at x40 magnification showing normal ovarian parenchyma at the periphery (arrow) with central thyroid parenchyma.

of colloid-filled follicles of various sizes, resembling thyroid follicles [Figures 3B and C]. Based on analysis of the scrape smears and frozen section, a provisional diagnosis of *struma ovarii* was made. The remaining specimen underwent routine histopathological examination. Microscopically, the tumour was lobular and composed of central normal thyroid parenchymal tissue with peripherally compressed normal ovarian tissue [Figure 4]. The tumour cells were cuboidal to the low columnar cells with eosinophilic cytoplasm and minimal cytological *atypia*. The intervening *stroma* was oedematous. There was no evidence of papillary carcinoma or mitotic figures. These histological features confirmed the diagnosis of a *struma ovarii*.

Discussion

Meigs' syndrome is a rare disorder involving the co-occurrence of a fibroma or fibroma-like tumour with *ascites* and hydrothorax, in which the *ascites* and hydrothorax resolve following removal of the tumour; in contrast, pseudo-Meigs' syndrome consists of *ascites*, pleural effusion with serous or serosanguinous fluid and tumours other than fibromas.[6,7] In their report of a case of pseudo-Meigs' syndrome due to a uterine leiomyoma, Amant *et al.* suggested various mechanisms which might cause *ascites* in such cases, including lymphatic obstruction by the tumour, irritation of the peritoneum by the tumour, the release of toxins and inflammatory products, hypoalbuminemia and decreased venous and lymphatic drainage.[7] In addition, the use of a dye test was advocated to determine the exact cause of pleural effusion. In their case, Amant *et al.* noted that the pleural effusion originated from the mechanical transfer of ascitic fluid through a diaphragmatic opening.[7] However, the aetiology of *ascites* and pleural effusion in patients with *struma ovarii* is still unclear.

Although it is usually a serum tumour marker of great diagnostic importance, CA-125 has poor specificity in the diagnosis of epithelial ovarian cancers since it is also raised in other malignancies, a few benign conditions and certain physiological states.[8] The mechanism behind raised CA-125 levels in cases of Meigs' and pseudo-Meigs' syndromes is still not understood, although Mui *et al.* have postulated that it is the result of free fluid irritation leading to inflammation of the pleural and peritoneal surfaces.[9] In the current case, features of a complex solid-cystic pelvic mass with *ascites* and raised serum CA-125 levels in a middle-aged woman were initially suggestive of a pelvic malignancy. However, the CA-125 levels normalised on the eighth postoperative day without any adjuvant therapy. Postoperatively, a thyroid hormone profile was also normal. Unfortunately, a preoperative thyroid hormone profile was not performed as the patient was asymptomatic and a *struma ovarii* was not considered during the differential diagnosis.

In an extensive search of the literature, Obeidat *et al.* presented 26 *struma ovarii* cases associated with *ascites* and raised CA-125 levels.[10] All of these patients were initially thought to have malignant tumours; in addition, in all cases, the *ascites* disappeared completely and CA-125 levels returned to normal after the removal of the tumour. Most of the diagnosed patients were in their fifth decade or older, with the exception of one patient who was 31 years old.[11] The tumour sizes ranged between 4–23 cm in the greatest dimension, with an average size of 12 cm.[10] In all cases, the volume of ascitic fluid was over 1 L, except for five cases.[5,12–15] The most common presenting symptom was abdominal distension.[2–4,9,10,12,13,15–22] Pleural effusion was noted in 15 cases.[10] In one case, the *struma ovarii* was an incidental finding.[14] No relationship was reported between pleural effusion and the volume of *ascites*.[10] The mean follow-up period was approximately 8 months, ranging from 1–36 months.[4,5,9–11,15,17,18,20,22–25] Most cases were treated via total abdominal hysterectomy and bilateral

salpingo-oophorectomy.[2–5,9,11,12,15,17–22,24,25] Only three patients underwent conservative surgery.[13,14,23] In the present case, the patient underwent conservative surgery in the form of a salpingo-oophorectomy, as there was no evidence of malignancy according to the frozen section analysis. All other organs were healthy-looking with no adhesions or evidence of organomegaly or lymphadenopathy.

Scrape smears and frozen sections are of great importance in accurately diagnosing ovarian neoplasms and planning surgical management. According to various studies, the accuracy of an intraoperative frozen section varies from 80% to >90%.[26] A scrape smear of a *struma ovarii* shows benign follicular epithelial cells forming follicles of various sizes and a monolayered sheet in a colloid-filled background.[27] A frozen section also shows the classical pattern of variable-sized follicles filled with colloid. Malignant transformation in *struma ovarii* usually results in a thyroid-type carcinoma (i.e. a papillary and follicular carcinoma), which is ruled out via histological examination.[15] The criteria for malignancy in *struma ovarii* are the same as those of a thyroid carcinoma.[27] Nuclear features such as nuclear grooves are more clearly visible on scrape smears and their absence rules out a papillary carcinoma. In addition, follicular carcinomas have capsular breaches and vascular invasion.[27]

Conclusion

Intraoperative frozen section and scrape cytology analyses are of critical importance in cases of ovarian masses wherein the clinical, biochemical and radiological features indicate a malignant aetiology. In the present case, a correct diagnosis due to an intraoperative frozen section analysis prevented radical surgery in a patient with *struma ovarii*, pseudo-Meigs' syndrome and raised CA-125 levels. This rare presentation of a *struma ovarii* should therefore be considered during the differential diagnosis of a patient with a suspected ovarian carcinoma.

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