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Ovarian Steroid Cell Tumor, NOS Presenting with Massive Ascites and Elevated CA-125

Layla S. Abdullah, MD, FRCPC
Department of Pathology
Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia
lsabdullah@hotmail.com

Abstract. Steroid cell tumors, not otherwise specified, are rare and usually benign. Ovarian sex cord stromal tumors of the ovary presenting with virulization in middle age women (average age: 43) are reported. Rarely, these tumors occur in postmenopausal women and, even more seldom, show a malignant clinical behavior. Although excess androgen secretion with virtualization is usually the primary presenting symptoms, rarely patients with this tumor present primarily with ascites. An unusual case was reported of a postmenopausal woman with a malignant steroid cell tumor, NOS, who was diagnosed with sudden onset of massive ascites as the primary clinical presentation. Aspects of clinical and pathologic findings as well as management pathways are introduced.

Keywords: Steroid cell tumor, NOS, Ovary, Malignant, Ascites.

Introduction

Sex cord stromal tumors account for 5% of all ovarian tumors and 2% account to be malignant[1]. Steroid cell tumors, not otherwise specified (NOS), are rare sex cord stromal tumors accounting for less than 0.1% of all ovarian tumors. It is also a subtype of ovarian steroid cell tumors with malignant potential. These steroid secreting tumors are usually presented with signs and symptoms of virulization in adults[1], and it may be incurred with pain or abdominal or pelvic mass[1,2]. Ascites is a very uncommon clinical presentation for these tumors and may cause diagnostic confusion.

Correspondence & reprint request to: Dr. Layla S. Abdullah
P.O. Box 80215, Jeddah 21589, Saudi Arabia
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This report describes a case of steroid cell tumor NOS with a malignant behavior in a postmenopausal woman who was presented with massive ascites and an elevated CA-125 levels as the primary clinical presentations. Aspects of clinical presentation, pathologic findings and management are presented.

Case Report

A 65-year-old married nulliparous woman was referred to King Abdulaziz University Hospital complaining of massive abdominal distention and pain. Her last menstrual period was over 10 years ago and had no post-menopausal bleeding. She had multiple medical problems including diabetes, hypertension, and ischemic heart disease with a mild degree of chronic renal failure with normochromic anemia.

On clinical examination, she was found to have massive ascites, major degree of bilateral lower limb edema and features of virulization (excessive facial hirsutism, male type beard, and frontal scalp baldness). No evidence of organomegaly or lymph nodes enlargement was found. Vaginal examination was normal. Relevant investigations included, elevated serum testosterone 37.3 mol/ml (normal value 0.7-2.8 mmol/ml) and elevated CA_{125} level 190 IU/ml (normal up to 35 IU/ml). Other tumor markers including carcinoembryonic antigen (CEA), CA 19-9 and alpha-fetoprotein were normal. Liver function tests were unremarkable and dehydroepiandrosterone sulfate (DHEAS) level was normal. Abdominal imaging studies, including magnetic resonance imaging (MRI) and ultrasound (US), revealed a 7 cm left ovarian mass and a 4.5 cm right ovarian mass with a small uterine fibroid. No pathological lymph nodes were seen, plus the kidneys and adrenal glands were normal. Exploratory laparotomy was performed and approximately six liters of clear amber ascitic fluid was drained. Cytological examination of the abdominal fluids was negative for malignant cells. The most striking feature was that the whole abdominal and pelvic cavities including surfaces of liver and diaphragm were studded with deposits of yellowish fatty material. The bilateral ovarian masses appeared firm solid and partially cystic with no clinical evidence of invasion to adjacent organs. A sub-serous uterine fibroid was identified. There were no palpable lymph nodes. The omentum was totally adherent to stomach and sigmoid colon. At the umbilicus, a round solid nodule within the substance of anterior abdominal wall at the umbilical region was seen,

which grossly resembled the morphology of ovarian masses. In view of the patient's medical condition, bilateral salpingoophorectomy was performed together with myomectomy; excision of the umbilical nodule and multiple peritoneal biopsies were sent for frozen section/histological examination. Frozen section of the left ovarian mass revealed a stromal tumor of unknown malignant potential. Frozen section of the umbilical nodule showed tumor cells identical to the ovarian primary.

Gross pathological examination of the left ovary revealed a 7 x 6 x 4 cm. diameter well-circumscribed yellowish-orange mass with focal area of cystic degeneration and a central area of scarring (Fig. 1). The external ovarian surface showed yellowish nodular deposits. On microscopic examination, the tumor cells were arranged in diffuse pattern and large nests separated by a thin reticular framework. The majority of the cells were large with either abundant vacuolated or eosinophilic cytoplasm or central nucleus. No significant nuclear atypia or necrosis was seen (Fig. 2). The mitotic count was 2/10 HPF. Multiple tumor surface deposits on ovaries, paratubal region, and the serosal surface of the uterine leiomyoma (fibroid) were present. The same tumor was also identified in the peritoneal and pelvic wall tissues as well as in the umbilical nodule. Immunohistochemical studies showed that the tumor cells were positive for inhibin and vimentin, while negative for keratin and epithelial membrane antigen (EMA). The findings were consistent with a malignant steroid cell tumor, NOS with multiple extra ovarian deposits (Stage IIIc).

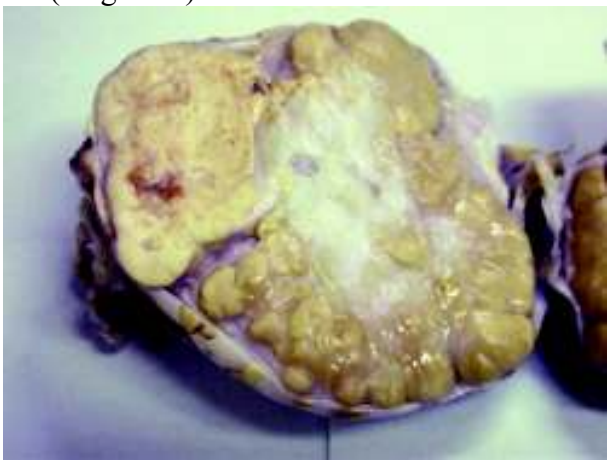

Fig. 1. Steroid cell tumor, NOS; the section surface of the ovarian tumor is yellowish orange and solid with central area of scarring.

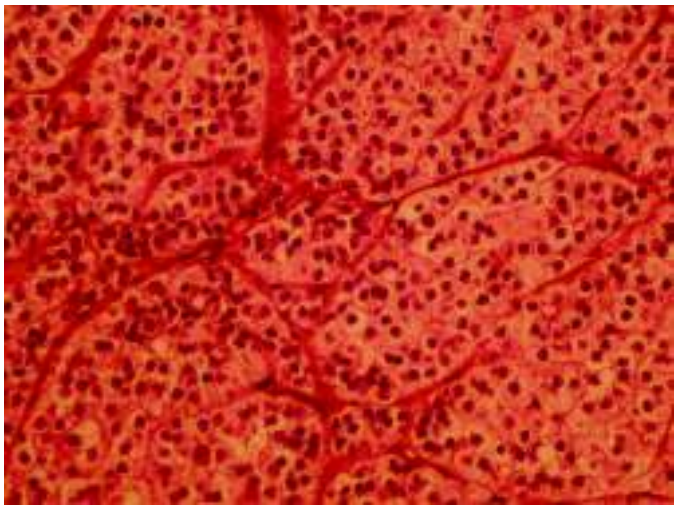

Fig. 2. Steroid cell tumor, NOS; Microscopic examination shows large nests of cells separated by a reticular framework. The cells are uniform with vacuolated cytoplasm and mitotic count of 2/10 HPF. H&E stain (40 objectives).

The patient received her first cycle of chemotherapy with Cisplastin, Bleomycin and Etopside followed by five (5) more cycles. The initial response to chemotherapy was present, however, on the follow up, ascites failed to resolve, serum CA-125 remained high, and signs of virulization persisted; 18 months following the primary surgery. No further follow up was possible since the patient left the region.

Discussion

Steroid cell tumor of the ovary is a term initiated by Scully in 1979[1] to describe neoplasm that are entirely composed of cells resembling typical steroid hormone-secreting cells. The term reflects both, the morphologic features as well as their ability to secrete steroid hormones, and is preferred over the old nomenclature lipid cell tumors, especially since more than 25% of these tumors do not contain lipid[1]. These rare tumors are classified into stromal luteoma, Leydig cell tumor and steroid cell tumor, and NOS. The latter differs from Leydig cell tumor by the absence of crystalloids of Reinke both, on light and microscopic examination. The origin of steroid cell tumor, NOS is not determined in the majority; however, theories suggest that its origin from ovarian stromal cells or Leydig cells. Rarely, they may arise from ovarian adrenocortical nests, especially in cases presented with Cushing's syndrome[1,2].

Steroid cell tumor, NOS occur at any age, but typically in a younger age group, rather than other subtypes, with an average age of 43 years. Patients with malignant steroid cell tumors NOS are, on an average, 16 years older than patients with benign ones[2,3]. The patient presented in this study was 65 years of age at the time of diagnosis. These tumors rarely occur in the prepubertal years[2]. Hormonal activity, commonly androgenic, is the most common clinical presentation as well as hirsutism and virulization are the most common clinical presentation seen in 56% to 77% of patients[1,2]. Hormone secretion other than androgen, such as estrogen (in 6-23% of cases), cortisol (6-10%) and rarely prorenin have been reported[4]. Twenty-five percent (25%) of steroid cell tumors, NOS do not secrete hormones[2]. Steroid cell tumors NOS may also be presented with abdominal distention and bloating, however, massive ascites and elevated CA-125 levels are infrequent[5]. Kim *et al.*[5] reported a case of steroid cell tumor NOS similar to our case. Concur with them, that the elevated CA-125 levels can be explained by the irritation of mesothelium by ascites and tumor deposits. The diagnosis of steroid cell tumor NOS can be difficult, especially in the absence of a palpable ovarian mass. A complete patient medical history including possible use of androgenic steroids can adequately eliminate medications as a cause of hirsutism[6]. Our patient reported no history of the use of androgenic medications. Transvaginal and abdominal imaging studies such as MRI and ultrasound are also useful modalities in evaluating ovarian size and morphology[6]. The case presented here revealed bilateral ovarian masses with liver and peritoneal deposits on the ultrasound examination.

Histopathological, steroid cell tumor NOS shows a diffuse pattern of cell growth. The neoplastic cells are usually of two cell types. The predominant cell type is polygonal with eosinophilic cytoplasm and central nucleus. The second cell type is larger and has a vacuolated cytoplasm. The mitotic activity is variable and foci of hemorrhage and necrosis may be seen[1,2]. Although the histological appearance of these tumors is usually diagnostic, steroid cell tumors must be distinguished from other sex cord stromal tumors, primary ovarian clear cell carcinoma and metastatic renal cell carcinoma[5,6]. Immunohistochemical studies help in the distinction of steroid cell tumor NOS from other primary and metastatic tumors. Inhibin is considered one of the most important stains as most steroid cell tumors express this marker[6]. The tumor presented

here showed a diffuse positivity for inhibin. Recent reports have suggested calretinin as a sensitive marker for steroid cell tumors NOS and EMA to distinguish ovarian clear cell carcinoma and metastatic renal carcinoma from steroid cell tumors NOS[6].

The majority (94%) of steroid cell tumors are benign. It is known, however, that pathologically benign steroid cell tumors can behave in a clinically malignant fashion and the presence of metastasis may be the only concise evidence of a malignant behavior[7]. Liver metastasis from malignant ovarian steroid cell tumor NOS have been reported in the literature[8]. The patient in this report presented with ascites and ovarian mass, hence, laparotomy showed evidence of extra ovarian spread.

Hayes and Scully[2] published the largest series of these tumors (63 cases) in which only 18 cases had a malignant behavior. In their study, they determined the pathologic criteria, which may indicate a malignant behavior. These include mitotic figures of > 2/10 HPF, size of > 7 cm, Grade 2-3 nuclear atypia and necrosis. The ovarian mass in this patient was 7 cm. in size and the mitotic count was 2/10 HPF, however, no significant atypia or necrosis was identified. Management of ovarian steroid cell tumor, NOS include surgery with staging, hormone assays on follow up, and adjuvant chemotherapy when indicated[1,2]. Full staging procedure, *i.e.* total abdomibal hysterectomy and bilateral salpingo-oopherectomy TAH and BSO, plus lymph node dissection was considered to be hazardous for our patient in view of her general medical condition, and the lack of obvious invasion property seen in classic ovarian tumor. The patient presented above had three cycles of Bleomycin, Etoposide & Cisplatin (BEP) chemotherapy regimen with relapse and malignant ascites. In the series published by Hayes and Scully[2], 12 patients had pelvic recurrences despite chemotherapy regime. Patients with large ovarian tumors and advanced stage of disease have poorer prognosis than those with early stage. Persistence of ascites and hyperandrogenism with persistent elevated CA-125 in our case was most likely due to wide persistent peritoneal tumor deposits producing high serum androgen, after the removal of the primaries.

Conclusion

Steroid cell tumors, NOS are very rare sex cord stromal tumors with a malignant potential. These tumors, usually present with sudden onset of

virulization, and may rarely present with ascites as the primary symptom. In these situations, these tumors may be difficult to diagnose and proper radiological. Histopathological and immunohistochemical investigations should be carried out to reach the correct diagnosis. Malignant steroid cell tumor, NOS should be managed by surgery followed by a combination of chemotherapy, which, in this particular case had extensive peritoneal implants which failed to control symptoms 18 months after the surgery.

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أورام الخلايا الستررودية المبيضية غير المعرفة مع استسقاء شديد وارتفاع في نسبة سي ايه ١٢٥

ليلى صالح عبد الله

استشاري وأستاذ مشارك

قسم علم الأمراض، كلية الطب، جامعة الملك عبد العزيز

جدة – المملكة العربية السعودية

المستخلص. أورام الخلية الستيرويدية، غير المعرفة نادرة وعادة ما تكون حميدة. وأفادت التقارير أن أورام أنسجة المبيض الجنسية الحبلية مع التغيرات الذكورية تحدث في المرأة في منتصف العمر (٤٣ متوسط عمر). ولكن نادرا ما تحدث هذه الأورام عند النساء بعد سن اليأس، وحتى أكثر ندرة تكون من النوع الخبيث. على الرغم من أن زيادة إفراز الهرمون الذكري هي عادة الأعراض الأولية في مثل هذه الحالات. نادرا ما يشتكي المرضى الذين يعانون من هذا الورم في المقام الأول من استسقاء. نقدم هنا حالة غير عادية للمرأة بعد سن اليأس مع وجود ورم خبيث للخلايا الستيرويدية، كانت قد شخصت مع ظهور مفاجئ لاستسقاء ضخم، كما نعرض الجوانب الإكلينيكية السريرية الأولية والمخبرية، وكذلك مسارات الخطة العلاجية.