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AN ASYMPTOMATIC OVARIAN STEROID CELL TUMOR WITH COMPLETE CYSTIC MORPHOLOGY: A CASE REPORT

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Steroid cell tumors of the ovary are extremely rare, accounting for only 0.1% of all ovarian tumors. Of these, steroid cell tumors, not otherwise specified (NOS) constitute about 56% of all steroid cell tumors. Most steroid cell tumors secrete steroid hormones, and only about 10% to 15% of patients are asymptomatic. The morphology of steroid cell tumors, NOS is predominantly reported to be solid, and a review of case reports from 1979 until now revealed only 5 cases that were mainly cystic tumors. The present case, in a patient who had undergone a previous hysterectomy and surgery for a peritoneal inclusion cyst, is reported due to its rarity and its unusual presentation, together with a brief review of the literature. The tumor showed no clinical signs and symptoms typical of a steroid hormone secreting tumor and had an atypical morphology, being primarily multi-septate cystic with a minor solid portion.

Keywords: Steroid cell tumor; Ovary; Cystic

Introduction

Steroid cell tumors of the ovary are seldom identified and constitute only about 0.1% of ovarian tumors. These tumors have been divided into three subtypes according to their cells of origin: stromal luteoma, Leydig cell tumor, and steroid cell tumor, not otherwise specified (NOS) [1,2]. Of these subtypes, the steroid cell tumors, NOS are grouped by exclusion from the other two subtypes, and account for about 56% of steroid cell tumors [2]. An extensive review of the literature reveals the rarity of these tumors, with barely 100 cases of steroid cell tumors, NOS reported from 1979 to the present.

Most steroid cell tumors are associated with secretion of steroid hormones, which causes symptoms that lead to diagnosis. Generally, testosterone secretion causes virilization or hirsutism, and only 10% to 15% of patients have no clinical signs or symptoms associated with increased hormone levels [3]. Morphologically, steroid cell tumors, NOS are reported as well-circumscribed masses, yellow in color, and solid in about 89% of cases. Only rarely, in about 1.6% of cases, are the tumors completely cystic [2]. An overall incidence of 3.8% has been reported for ovarian pathologic findings requiring repeat operation after hysterectomy for benign conditions [4]. However, only 3 cases have been described of steroid cell tumor diagnosed after a previous hysterectomy. The present report focuses on a case of a rare steroid cell tumor, NOS,

diagnosed in a 52-year-old female. The case was significant due to its lack of clinical symptoms, the unusual tumor morphology that was primarily cystic, with septations, and a small inner solid portion, and the patient's surgical history of a previous hysterectomy and pelvic surgery for peritoneal inclusion cyst.

Case Report

A 52-year-old woman (2-0-1-2) was referred to the gynecology department of our hospital for a left adnexal mass incidentally found by liver computed tomography (CT). She was a hepatitis B

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carrier diagnosed with liver cirrhosis nine years previously, and the liver CT was part of her routine follow-up. Past surgeries included total abdominal hysterectomy for uterine myoma 14 years previously, and an exploratory laparotomy for abdominal adhesions and a peritoneal inclusion cyst 3 years ago. She had menarche at the age of 12 years, and her family history was unremarkable. She was taking hepatic protective medication.

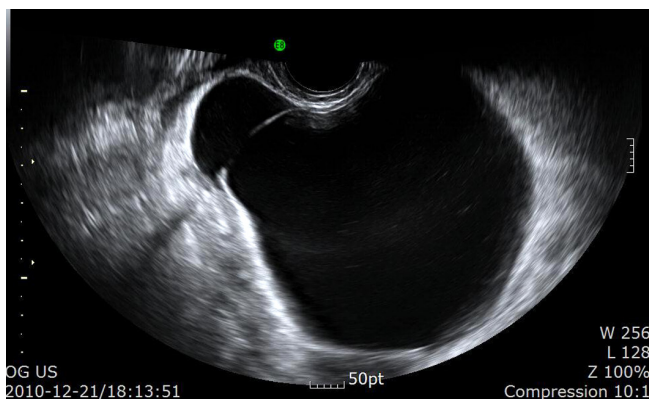Abdominal examination revealed a fist sized palpable mass,

Fig. 1. Transvaginal ultrasound indicating a large 10×8×7 cm³ sized cystic mass at the center of the pelvic cavity, with internal septation and no apparent solid portion.
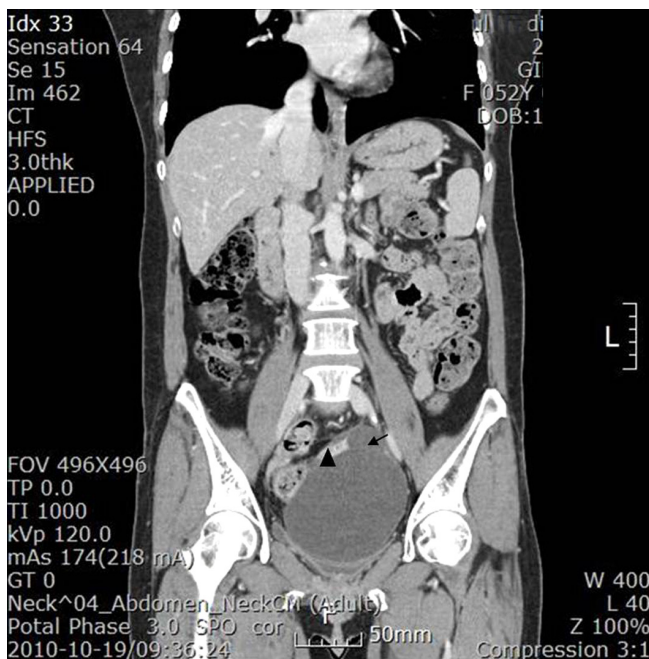

Fig. 2. An abdominopelvic computed tomographic scan after enhancement shows a 10×8 cm sized cystic mass in the left ovary, with internal septation (arrow) and a solid portion (arrowhead), which is enhanced by contrast media.

without tenderness or rebound tenderness. On pelvic examination, the uterus was absent due to previous hysterectomy and the right adnexa was not palpable due to the central location of the left adnexal mass. No signs of virilization or hirsutism were observed. Laboratory analysis revealed normal values of blood count, hepatic-renal function, coagulation, and electrolytes. Tumor marker studies showed a slightly increased CA-19-9 of 40.62 U/mL (normal range, 0 to 37 U/mL), a normal carcinoembryonic antigen (CEA) of 3.69 ng/mL, and a normal CA-125 of 8.04 U/mL. Transvaginal ultrasound examination revealed no uterus and a large 10×8×7 cm³ sized well defined cystic mass located at the center of the pelvic cavity, with internal septation and no apparent solid portion (Fig. 1). The right adnexa was not clearly observed and no ascites within the pelvic cavity was found, suggesting a recurrent peritoneal inclusion cyst formed after the previous two surgeries.

An additional CT scan of the abdomen and pelvis showed a 10×8 cm sized round mass at the left adnexa, with internal septations and an enhancing solid portion, indicative of a borderline or malignant epithelial ovarian tumor. There was no lymph node enlargement or ascites, but the liver showed signs of cirrhosis (Fig. 2).

The patient underwent a laparoscopy under general anesthesia. The peritoneum and ileum displayed extensive adhesion from the umbilical trocar site to the previous laparotomy site, and although there was no ascites, the mass was not readily observed due to substantial adhesion. Adhesiolysis was performed on the adhesions to the surrounding peritoneum, small bowel, descending colon and sigmoid colon, revealing several septations of the mass and about 100 mL of dark brown serous fluid. As the adhesions were removed, no uterus was revealed, due to the previous hysterectomy, and adhesiolysis of the bladder revealed a 5×4 cm sized bluish left adnexal mass with a thin wall and serous contents. No abnormal signs were noted in the right adnexa, peritoneum, or omentum. After the left salpingo-oophorectomy, the ileum and sigmoid colon were injured from adhesiolysis by a tendency to tear easily, so laparotomy was performed with the general surgery department. The ileum had a 5 cm linear tear at 80 cm superior to the ileocecal valve and segmentectomy with anastomosis was performed. The sigmoid colon had a 3 cm linear tear, which was sutured. During surgery, gross examination and palpation of the internal abdominal organs yielded no notable abnormalities. The abdominal CT suggested a borderline or malignant epithelial ovarian tumor, but because of the patient's history of surgery 3 years before for abdominal adhesion and peritoneal inclusion cyst, and because extensive adhesion was noted during surgery, a recurrent peritoneal inclusion cyst was suspected and the surgery was con-
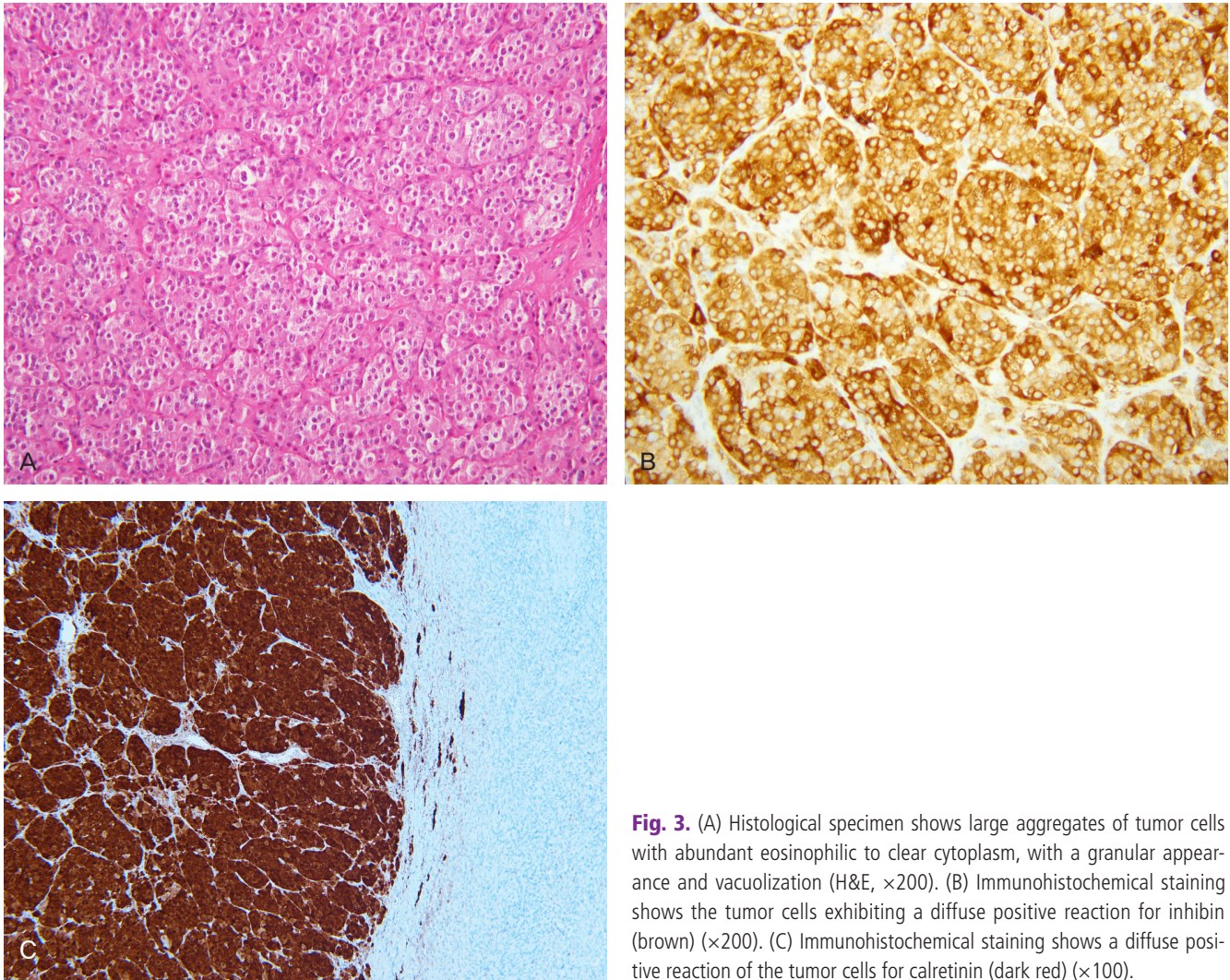
Fig. 3. (A) Histological specimen shows large aggregates of tumor cells with abundant eosinophilic to clear cytoplasm, with a granular appearance and vacuolization (H&E, ×200). (B) Immunohistochemical staining shows the tumor cells exhibiting a diffuse positive reaction for inhibin (brown) (×200). (C) Immunohistochemical staining shows a diffuse positive reaction of the tumor cells for calretinin (dark red) (×100).

cluded without any additional procedures.

Gross pathological findings showed a 6×6 cm sized mass, mostly cystic. The outer surface had heavy adhesions, and the mass was untidy internally, with a small inner solid portion, but no signs of hemorrhage or necrosis. Microscopic findings exhibited diffuse tumor cells with abundant eosinophilic granular cytoplasm and vacuolization, with no signs of nuclear atypicality and a mitotic count of 5 per 10 HPF (Fig. 3A). Immunohistochemistry revealed a positive reaction to inhibin, calretinin, and vimentin, a moderately positive reaction to CD99, and a negative reaction to pan-CK, S-100, placenta-like alkaline phosphatase, and chromogranin (Fig. 3B, C). The Ki-67 labeling index was low, under 5%. The histopathologic features supported a diagnosis of an ovarian steroid cell tumor, NOS.

Postoperatively, the patient's testosterone level was normal, at 0.32 ng/mL (normal range, 0.14 to 0.76 ng/mL). No hormonal assays were done before surgery as there were no clinical manifestations of any hormone secretion. She is on regular follow-up at our outpatient clinic, with no evidence of recurrent disease for 21 months.

Discussion

Ovarian tumors are rarely diagnosed as steroid cell tumors; these account for less than 0.1% of all ovarian tumors. Steroid cell tumors of the ovary have a diverse cellular origin; they are a group of ovarian neoplasms with morphologic similarities that, in the past, were termed as lipid or lipoid cell tumors. These tumors are made of cells that resemble steroid hormone secreting cells, but

some cases show scarce or no lipid components and some tumors have a tendency to secrete various steroid hormones with specific clinical presentations. For these reasons, Hayes and Scully [2] proposed the term steroid cell tumor, which was accepted by World Health Organization in 1999.

Steroid cell tumors, NOS are found in almost any age group, from premenarchal girls to postmenopausal women, with an average age at diagnosis of 43 years [2]. The clinical presentation may take many forms, including abdominal pain, distention, and bloating. However, the more noticeable presentations are those associated with hormonal activity. Steroid cell tumors secreting steroid hormones are prevalent, mostly secreting testosterone in 50% of steroid cell tumors, NOS [3]. About 8% to 23% of steroid cell tumors, NOS, show signs of estrogen secretions, and cortisol secretion may be diagnosed in 6% to 10% of cases [2,5]. A minority of 10% to 15% of patients with steroid cell tumor, NOS have no symptoms of increased steroid hormone production [3]. In this case, the apparent absence of androgenic manifestations is an unusual finding.

The size of steroid cell tumors, NOS range from under 1 cm to over 45 cm, and the average size at diagnosis is known as 8.4 cm [2]. These tumors are mostly unilateral, with 6% bilateral, and are typically well circumscribed solid tumors in 89% of cases, generally yellow in color, and in some cases lobulated [2,5]. Necrosis and hemorrhage may be found, and only one tumor of the 61 cases studied by Hayes and Scully was described as almost completely cystic [2,5]. An extensive review of case reports in the PubMed database from 1979 until the present revealed only 5 cases that were mainly cystic tumors. No cases have been illustrated, to our knowledge, with inner septa and extensive adhesion to surrounding structures. In our patient, the tumor was a 9 cm sized overall cystic mass with septations and a small solid portion, with tight adhesions to the bladder and bowels (so much so that reparative procedures were necessary after extraction of the mass).

The majority of steroid cell tumors have benign or low-grade behavior. These tumors are found comparatively early due to endocrine activity, and show low rates of recurrence and metastasis [2,5]. About 25% to 43% are reported clinically malignant [2,5], and in such cases 44% to 83% show symptoms of hormone impairment such as virilization, and 17% are associated with Cushing's syndrome due to cortisol increase [2]. Hayes and Scully [2] detailed five microscopic findings that are highly associated with malignancy: 1) the presence of two or more mitotic figures per 10 HPF in 92%, 2) necrosis in 86%, 3) a diameter of 7 cm or greater in 78%, 4) hemorrhage in 77%, and 5) grade 2 or 3

nuclear atypia in 64% of cases [2]. In our case, as the size of the mass was large (9 cm) and 5 mitotic figures per 10 HPF were observed, malignancy was a possibility, but as no foci of necrosis or hemorrhage, no nuclear atypia, and no signs of invasion or metastasis were evident, we considered the tumor to be benign, and the patient has shown no signs of recurrence during 21 months of follow-up.

Immunohistochemistry may be utilized in diagnosis, and generally inhibin is used. Inhibin is present in ovarian granulosa and lutein cells, where it suppresses the production of pituitary gonadotropins [6]. Steroid cell tumors, NOS are positive for inhibin and vimentin in 75%, 7% are positive for S-100 protein, and they are negative for chromogranin A [7]. Calretinin, a calcium-binding protein discovered in mesothelial cells, is also present in the ovary and testis, and is expressed by sex-cord stromal tumors [6]. Deavers et al. [6] found that the extent of staining for inhibin ranged from under 5% to over 90%, and 60% to over 90% for calretinin, in 6 cases of steroid cell tumor, NOS; all cases were positive for inhibin and calretinin. CD99 is another marker expressed by sex-cord stromal tumors and it reacts with normal granulosa and Sertoli cells, and it showed membranous staining in one of the previous 6 cases [6]. Our case was positive for inhibin, calretinin, and vimentin, moderately positive for CD99, and negative for S-100 protein and chromogranin A, with a diagnosis of steroid cell tumor, NOS.

No specific tumor markers or imaging techniques are known for preoperative diagnosis of steroid cell tumors. Tumor markers such as CA-125 and α-fetoprotein, etc., are generally normal and the literature does not indicate if elevated levels signify malignant potential. This case demonstrated a normal level of CA-125, and although CA-19-9 was temporarily mildly elevated, this is considered to result from the patient's underlying liver cirrhosis. Imaging before surgery may be checked for ovarian or adrenal masses, and vaginal or abdominal ultrasound may help to identify ovarian mass characteristics. Wang et al. [8] found preoperative magnetic resonance imaging to be an effective means for staging and gadolinium-diethylene-triamine-pentaacetic acid enhancement to be helpful for locating metastasis within the pelvic cavity. In another study, Wang et al. [9] reported whole-body positron emission tomography with [11C]acetate to aid in the diagnosis of steroid cell tumors that were secreting testosterone. Most recently, Sakamoto et al. [10] proposed chemical shift magnetic resonance imaging as a technique for diagnosis by observing the cytoplasmic lipid content of steroid cell tumors.

No definitive treatment is established for steroid cell tumors,

NOS, due to their rarity, but the tumors are considered to be sex cord-stromal tumors and the primary treatment is surgery. Only 6% are bilateral, so a young woman desiring future childbearing with a low stage tumor may undergo unilateral salpingo-oophorectomy, with regular monitoring of any preoperatively increased hormones. An older woman with a low stage tumor and no desire for parity may have a total hysterectomy with bilateral salpingo-oophorectomy. A high stage tumor should undergo size reduction and adjuvant chemotherapy or radiation therapy should be considered [2]. However, as symptoms lead to early diagnosis and as recurrence or metastasis is rare, the research on adjuvant therapy is insufficient and many are skeptical. If preoperatively increased testosterone does not change after surgery, gonadotropin releasing hormone agonists may be utilized [11]. As steroid cell tumors, NOS are rare, their staging and prognosis is unclear, but Hayes and Scully [2] analyzed 63 cases as 88% stage 1, 6.8% stage 2, 12% stage 3, and 1.7% stage 4 [2]. Cases with a higher stage, larger size, gross necrosis, or hemorrhage were found to have higher malignant potential with worse prognosis [2]. Recurrence or metastasis were also associated with worse prognosis due to insufficient research on additional treatment options.

Some observations indicate that the incidence of ovarian tumors rises after hysterectomy. The overall incidence of ovarian pathologic findings requiring repeat operation after hysterectomy for benign conditions has been reported as 3.8% [4]. Only 3 cases of steroid cell tumor diagnosed after a previous hysterectomy have been described, and our case is the fourth [12-14].

The almost completely cystic characteristic of our case was unusual for a steroid cell tumor, NOS, which are usually solid tumors, and this case shows that even in an apparently benign, mostly cystic, ovarian tumor, a rare steroid cell tumor with undetermined behavior may be diagnosed. Careful clinical assessment should be carried out when evaluating ovarian tumors. In our case, the patient showed no signs of recurrence or metastasis, which are considered to be malignant behavior. The most important factor to be determined in steroid cell tumors of the ovary is whether the tumor has malignant features. Steroid cell tumors, NOS are clinically malignant in 25% to 43% of cases, and pathologically benign steroid cell tumors are known to behave in a clinically malignant fashion. Therefore, careful follow-up after surgery is imperative even in those cases that do not have clinical or pathological evidence of malignancy.

We report a patient with a history of hysterectomy, with an incidentally found, asymptomatic, predominantly cystic tumor with internal septa and an inner solid portion, which was diagnosed as steroid cell tumor, NOS. The patient has had no signs of recurrence for 21 months after surgery. We also provide a brief review of the existing literature.

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