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Primary Retroperitoneal Extraovarian Granulosa Cell Tumor: A Case Report

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ABSTRACT

A primary extragonadal granulosa cell tumor (GCT) is very rare. It is believed to arise from the ectopic gonadal tissue along the embryonal route of the genital ridge. We encountered one such tumor in a 45-year-old female who presented with a large intraabdominal mass. She had an abdominal hysterectomy with unilateral salpingo-oophorectomy 10 years previously for dysfunctional uterine bleeding. She underwent exploratory laparotomy and excision of the mass. The histologic features failed to differentiate between a carcinoid and granulosa cell tumor. Immunohistochemistry showed that the neoplastic cells expressed calretinin, smooth muscle actin, melan-A, inhibin-alpha, and progesterone receptors and were negative for desmin, CD10, cytokeratin, epithelial membrane antigen, synaptophysin, or chromogranin-A. An English literature search revealed only 4 similar cases, primarily arising from the retroperitoneum. Immunohistochemistry helps to differentiate GCTs from other tumors.

INTRODUCTION

Granulosa cell tumors (GTCs) comprise 2%-5% of all ovarian tumors [1]. These tumors are composed almost entirely of granulosa cells or a mixture of granulosa and theca cells. Few cases of extraovarian GCTs have been reported. These tumors arise primarily in the retroperitoneum and are exceedingly rare. To date, only 4 such retroperitoneal tumors have been reported in the literature.

CASE REPORT

A 45-year-old female presented with continuous dull-aching pain of 1 month duration in the right lumbar and umbilical regions. The physical examination revealed a large, hard intraabdominal mass with indistinct margins that extended from the costal margin to the infraumbilical region. She had undergone an abdominal hysterectomy with unilateral salpingo-oophorectomy 10 years previously for dysfunctional uterine bleeding. There were no endocrine symptoms. There was no vaginal secretion or breast tenderness, which may occur in estrogenic tumors. There were no virilizing signs, which may occur in androgenic tumors. We did not perform a hormonal assay because the nature of the tumor was not suspected until it was removed.

Preoperative Evaluation. The patient's computed tomography scan showed a large heterogenous retroperitoneal mass measuring 20 cm x 15 cm. It extended from the right renal hilum to the bifurcation of the great vessels compressing the inferior vena cava (Figure 1). Tumor markers (CEA, CA125, CA19-9, betaHCG) were within normal limits. Ultrasound-guided fine-needle aspiration cytology was inconclusive.

Surgery. An exploratory laparotomy was performed. The bowel

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Abbreviations and Acronyms
EMA = epithelial membrane antigen
GCT = granulosa cell tumor
PgR = progesterone receptors
SMA = smooth muscle actin

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Figure 1. Computed Tomography Scan of the Abdomen Showing a Large Retroperitoneal Mass Compressing the Inferior Vena Cava.

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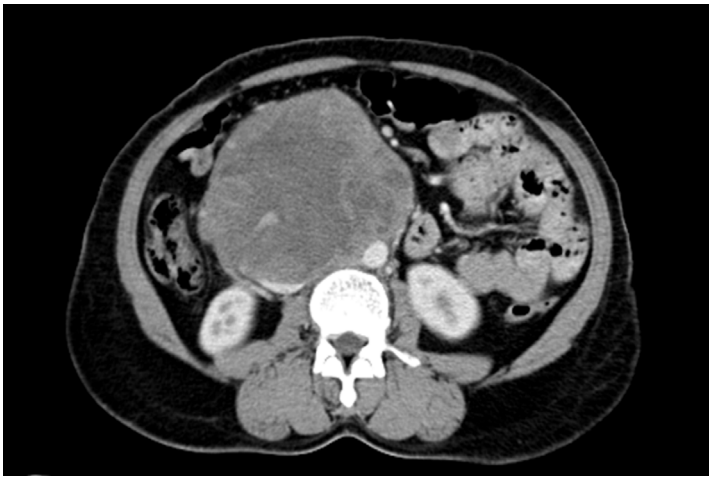

was reflected as in retroperitoneal lymph node dissection. There were few rents in the mesentery because it was stretched over the large retroperitoneal mass extending from the level of the right renal vessels to the bifurcation of the inferior vena cava and aorta. The mass pushed the right ureter anterolaterally. It was densely adherent to the underlying great vessels. The left ovary and fallopian tube were normal. The right ureter was then dissected from the mass. Next, the mass was dissected all around and separated from the vena cava, aorta, iliac vessels, and the inferior mesenteric artery. A few branches supplying the mass were ligated. All of the vessels looked bare after excision of the mass (Figure 2). The bowel was replaced and the peritoneal reflections were sutured. The midline incision was closed in a single layer. The operative time was 4.5 hours.

Assessment of the tumor. Grossly, the tumor was well capsulated and the cut surface showed a pale yellowish-grey soft surface with areas of necrosis and hemorrhage. Microscopic examination revealed neoplastic cells that had a moderate amount of eosinophilic granular cytoplasm; round-to-oval vesicular nuclei were arranged in nests and cords, and trabecular, insular, and diffuse patterns (Figure 3). A moderate degree of pleomorphism and mitotic figures were present. Vascular emboli were noted beneath the capsule. A differential diagnosis of GCT and carcinoid was suggested. Immunohistochemistry showed that the neoplastic cells expressed calretinin (Figure 4), smooth muscle actin (SMA), melan-A (Figure 5), inhibin-alpha, and progesterone receptors (PgR). Tumor cells were negative for desmin, CD10, cytokeratin, epithelial membrane antigen (EMA), synaptophysin, or chromogranin-A. The MIB-1 labeling index

Figure 2. Bare Great Vessels and Ureters After Excision of the Mass.

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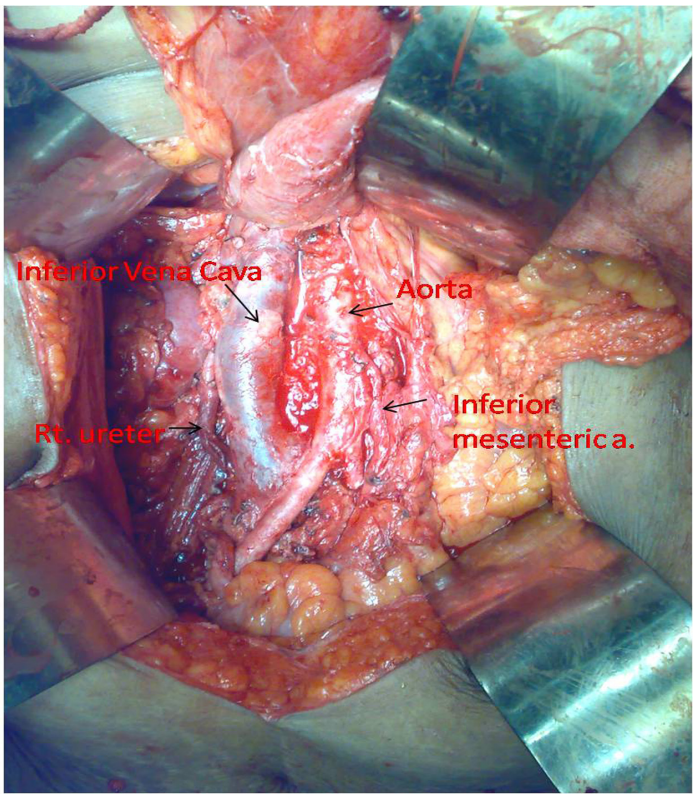

Figure 3. Microphotograph Showing Round-to-Polygonal Cells With Vesicular Nucleus and Scant Eosinophilic Cytoplasm (40x).

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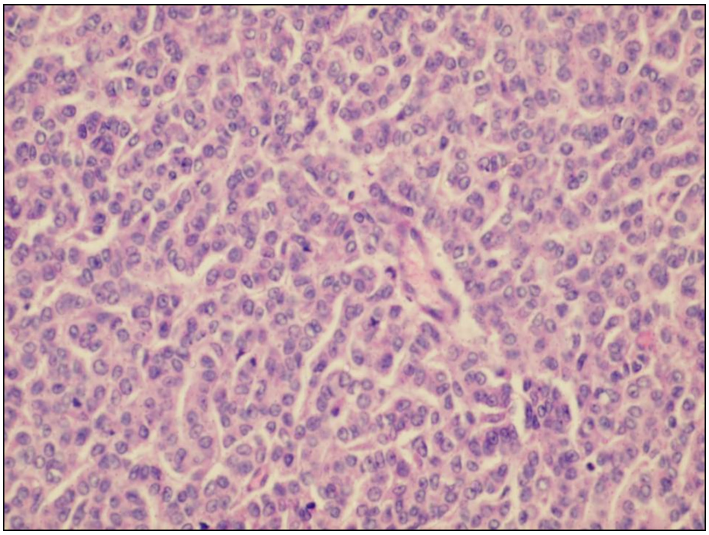

Figure 4. Microphotograph Showing Positive Reaction to Calretinin Immunostain.
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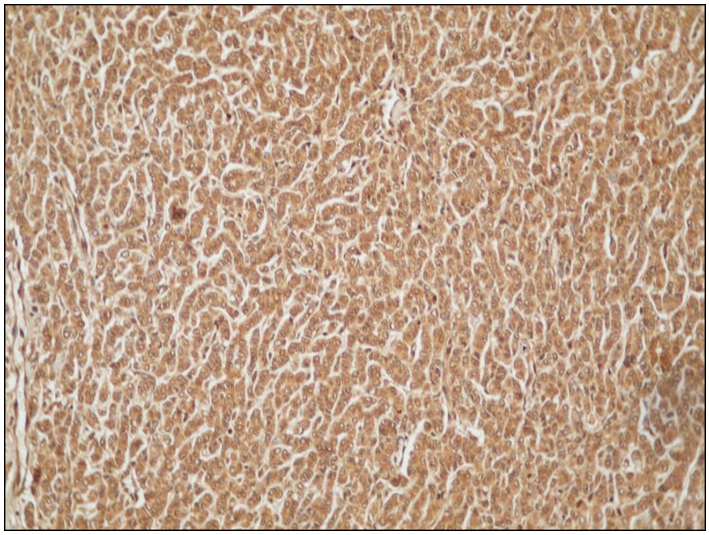

Figure 5. Microphotograph Showing Positive Reaction to Melan-A Immunostain.
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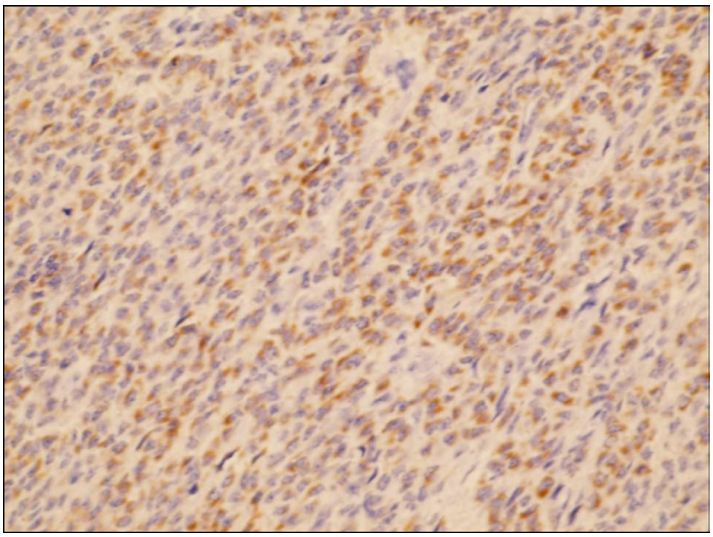

was approximately 10%. Based on these factors, the tumor was determined to be a sex-cord tumor of granulosa-cell type.

Patient follow-up. The intraoperative and postoperative courses were uneventful. Postoperatively, the patient was started on oral feeds on the first postoperative day. She was discharged on the 5th postoperative day. Sutures were removed on the 10th postoperative day. She did not receive any adjunctive treatment and has remained disease free at 3-years follow-up.

DISCUSSION

Although GCTs usually arise from the ovary, several extraovarian sex-cord stromal tumors have been reported. A Medline (U.S. National Library of Medicine) English literature search to 2009 revealed 16 such primary extraovarian sex-cord stromal tumors: 7 arose in the broad ligament, 4 in the retroperitoneum, 1 in the fallopian tube, 1 in an umbilical hernia sac, 1 in the adrenal gland, 1 in the pelvic side wall, and 1 in the mesentery of the ileum [2-4]. Although approximately 70% of the ovarian GCTs are hormonally active, no endocrine symptoms have been reported in the earlier published cases of the extraovarian GCTs (similar to the present patient).

Because the sex cord originates from the mesonephros, the ectopic gonadal stromal tissue is believed to be responsible for the histogenesis of extraovarian sex-cord stromal tumors [5]. Motta and Makabe [6] proposed a dualistic theory in which both celomic epithelium and mesonephros may contribute to the origin of pregranulosa cells. The influence of mesonephros in the origin of the sex cord explains why the sites of extraovarian sex-cord stromal tumors are limited to the broad ligament, retroperitoneum, and adrenals; all of these differentiate close to the mesonephros or the mesonephric duct [6].

Several histologically similar tumors need to be distinguished from GCTs (eg, undifferentiated carcinoma, small-cell or neuroendocrine carcinoma, endometrial stromal sarcoma, carcinoid, malignant melanoma, intraabdominal desmoplastic small-cell tumor) [7]. The use of a panel of immunoantibodies to SMA, melan-A, inhibin-alpha, PgR, desmin, CD10, cytokeratin, EMA, synaptophysin, and chromogranin-A helps to confirm the diagnosis [2]. GCTs are characterized by immunopositivity for calretinin, melan-A, inhibin-alpha, and progesterone receptors and by negativity for EMA. The prognosis for extraovarian sex-cord stromal tumors seems favorable; however, long-term follow-up of these patients needs to be done.

In the present case, the preoperative workup did not lead to a definitive diagnosis. Gross and microscopic features failed to differentiate between carcinoid tumor and sex-cord stromal tumor of granulosa cell type. The immunopositivity for calretinin, melan-A, inhibin, and PgR and negativity for EMA and chromogranin clinched the diagnosis in favor of extraovarian GCT.

In conclusion, GCTs can arise in locations other than the ovary. Immunoreactivity is useful in diagnosing this type of tumor.

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