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Primary Retroperitoneal Granulosa Cell Tumor

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ABSTRACT

Granulosa cell tumors (GCT) of the ovary are rare tumors that represent 2% of all ovarian tumors. However, cases involving the retroperitoneum are exceedingly rare. We describe a case of primary retroperitoneal granulosa cell tumor, which, to our knowledge, has been previously reported in few cases.

A 64-year-old female presented with large intra-abdominal mass and vague abdominal pain. She had a history of hysterectomy and bilateral salpingo-oopherectomy 22 years ago for a large uterine leiomyoma. She underwent exploratory laparotomy that revealed a retroperitoneal mass measuring 11 cm x 13 cm in size, with multiple cyst formation and areas of necrosis and hemorrhage. The gross, histologic, and inhibin-positive immunostaining findings of the retroperitoneal mass were characteristic of adult-type GCT. Excluding any previous history of primary ovarian GCT with this patient, a de-novo retroperitoneal diagnosis was carried out.

INTRODUCTION

The name "granulosa cell tumor of the ovary" (GCT) was proposed by von Werdt in 1914 and has been widely adopted [1]. GCTs account for approximately 2% of all ovarian tumors belonging to the sex cord-stromal category and include tumors composed of granulosa cells, theca cells, and fibroblasts in varying degrees and combinations [2]. What's peculiar for this type of tumor is that it can recur or metastasize long after initial treatment [3]. However, to have primarily originated retroperitoneal GCT is extremely rare [4,7].

CASE REPORT

A 64-year-old postmenopausal female presented with intermittent, vague abdominal pain of a 1-year duration. She has known cases of hypertension, diabetes mellitus, left ectopic pelvic kidney, and hysterectomy with bilateral salpingo-oophorectomy that were performed 22 years prior to presentation, with a provisional diagnosis of uterine leiomyoma and normal ovaries which was confirmed by histopathology. Her physical examination revealed a large, left-sided, firm, irregular, 10 cm x 8 cm abdominal mass with ill-defined margins. On investigation, her hemoglobin, kidney function, and liver function tests were within normal limits, and she had negative urine cytology for malignancy. Tumor markers, including CEA, CA-125, AFP, B-HCG, and LDH, were normal. Her computerized tomography (CT) revealed a large, lobulated, heterogenous, faintly enhanced left retroperitoneal mass measuring 8 cm x 13 cm with cystic components, displacing the pancreas and the duodenojejunal flexure anteriorly, and it shifted great vessels slightly without significant mass effect (Figure 1 and Figure 2).

Ultrasound-guided Tru-Cut biopsy revealed a tumor characterized by proliferating small to medium sized cells with low mitotic rates and eosinophilic cytoplasm, arranged in trabecular pattern with rosette formations. The differential diagnosis was broad and included renal metanephric adenoma, primary renal malignant tumor, lymphoma, and others (Figure 3).

The patient underwent exploratory laparotomy, and the excision of a retroperitoneal mass was accomplished. It extended from the level of renal vessels to the level of bifurcation of great vessels. Grossly, the mass was encapsulated, grayish-yellow, and measured 13 cm x 11 cm x 7 cm. The cut section showed a white-to-yellow whorly cut surface with multiple foci of hemorrhages and necrosis.

Microscopically, the tumor was composed of islands of

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Figure 1. Axial CT section showing the retroperitoneal mass displacing great vessels, pancreas, and the duodenojejunal flexure (arrow).

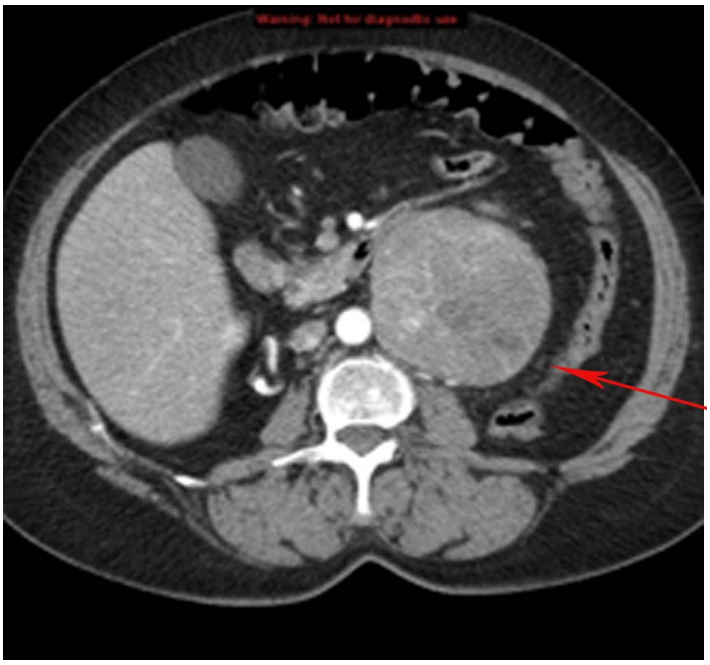
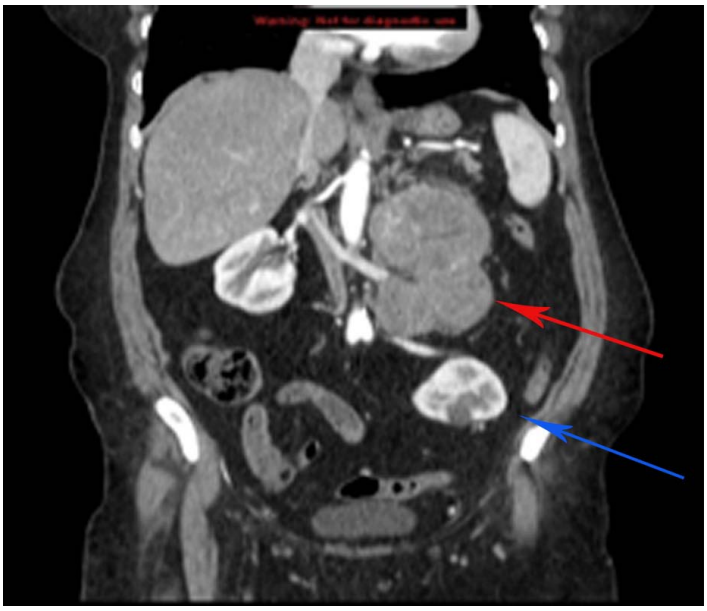


Figure 2. Coronal CT section showing the retroperitoneal mass displacing great vessels and taking direct blood supply from them (red arrow). See also the congenital, malrotated, left ectopic pelvic kidney (blue arrow).



proliferating uniform cells with hyperchromatic nuclei, and ill-defined cell borders with ill-defined and abundant eosinophilic cytoplasm. Longitudinal nuclear grooves were present. Mitotic activity was low; microfollicular patterns with Call-Exner bodies were also evident (Figure 4).

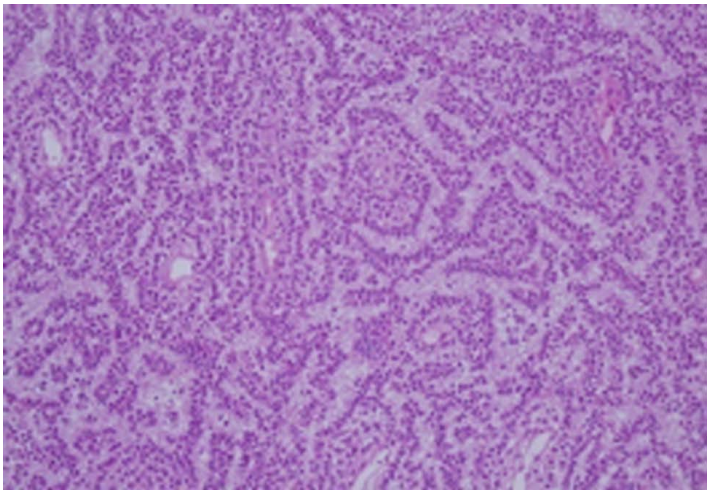
The morphology showed granulosa cell tumors, which were confirmed by strong, diffuse, cytoplasmic positive reactions of the tumor cells for alpha-inhibin antibodies upon immunohistochemical (IHC) staining, and then a diagnosis of primary retroperitoneal granulose cell tumor was rendered (Figure 5).

After surgery, the patient recovered well; no adjuvant chemotherapy or radiotherapy was given, and the patient was sent home for regular follow-up with history, clinical examination, imaging, and tumor markers.

DISCUSSION

GCTs are uncommon ovarian tumors that compromise 2% of all ovarian cancers. There are 2 subtypes: adult and juvenile, based on different clinical and histological features [3]. Adult granulosa cell tumors of the ovary are oftentimes hormonally active stromal cell neoplasms that are distinguished by their ability to express aromatase and secrete sex steroids such as estrogen [5].

Figure 3. Trabecular (gyriform) growth pattern of the tumor presented in the core biopsy.



Granulosa cell tumors can arise in locations other than the ovary and may be derived from the mesenchyme of the genital

ridge. Women who have undergone oophorectomy may have the potential to develop granulose cell tumors [8]. An 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 [4,7].

The cytogenetic abnormalities of GCT of the ovary are only partially known. Up to now, mainly numerical chromosomal aberrations have been described; for example, trisomy 12 and 14 are frequent aberrations. However, monosomy 22 is even more prevalent [6].

It has recently been reported that 95 to 97% of adult granulosa cell tumors carry a unique somatic mutation in the FOXL2 gene. This mutation is a potential driver in the pathogenesis and appears to play a major role in the cell-cycle regulation of adult-type GCTs [9]. Patients with GCT require long-term follow-up with history, physical examination, and tumor marker studies because 17% of relapses occur more than 10 years after diagnosis [3]. The most common site of recurrence is in the pelvis [3].

Extraovarian GCT should be differentiated from other metastatic carcinomas of the ovary as it has similar morphology. It also has to be differentiated from other tumors such as small-cell carcinoma, undifferentiated carcinoma, endometrial stromal sarcoma, carcinoids, and lymphoma. Inhibin, calretinin, and epithelial membrane antigen (EMA) immunostains can help in differentiating these tumors. GCT is positive for inhibin and calretinin and negative for EMA. Other tumors do not show positivity for inhibin and calretinin [10].

Figure 4. Microfollicular pattern with Call-Exner bodies. Eosinophilic material and debris are in the center. Longitudinal grooves are seen in the right lower corner.

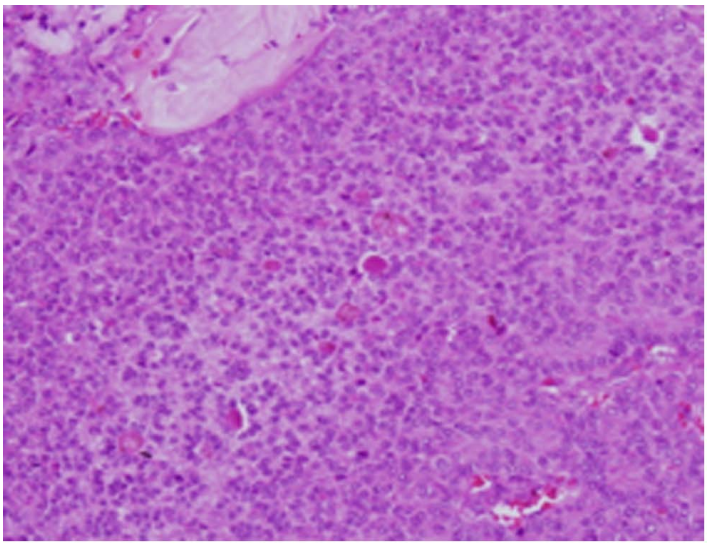
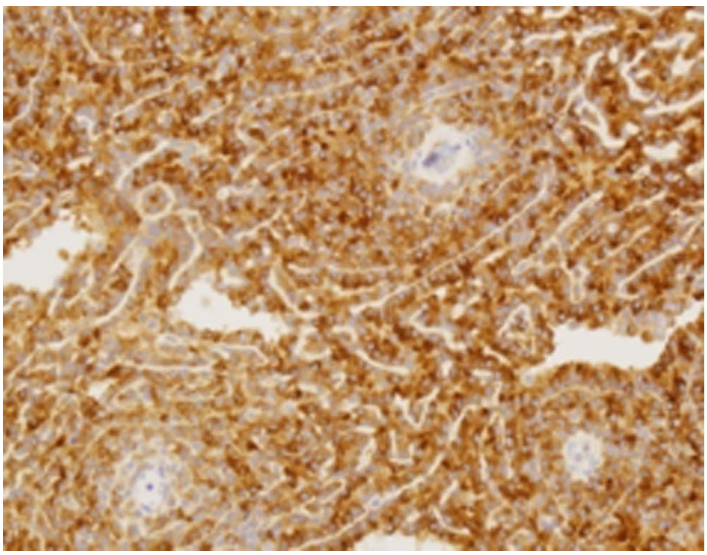


Figure 5. Alpha-inhibin positive cytoplasmic staining.



CONCLUSION

The case of primary retroperitoneal granulosa cell tumor is reported for its rarity after excluding previous ovarian origins. We have noticed during our thorough literature review that all those rare cases, including ours, occurred in patients with a history of previous oophorectomy. Surgery is the primary treatment for these tumors; however, long-term follow-up with history, clinical exams, and tumor markers is crucial for GCTs, since later relapse is a behavior for these unique tumors.

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