

## Case report

# Poorly differentiated Sertoli–Leydig tumor with heterologous, high-grade, sarcomatoid features: A case report



Rachel Brightwell<sup>a,\*</sup>, Kassondra Grzankowski<sup>a</sup>, John Kasznica<sup>b</sup>, Peter J. Frederick<sup>a</sup>

<sup>a</sup> Department of Gynecologic Oncology, Roswell Park Cancer Institute, Buffalo, NY, USA

<sup>b</sup> Department of Pathology, Roswell Park Cancer Institute, Buffalo, NY, USA

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## 1. Introduction

Sex-cord stromal tumors arise from the ovarian stroma that surrounds and supports the oocytes. They are relatively rare among ovarian neoplasms, accounting for only 1.2% of ovarian tumors (Quirk and Natarajan, 2005). These ovarian cancers are generally expected to be low-grade, diagnosed at an early stage, and lymph node metastases are exceedingly rare. Sertoli–Leydig tumors, in particular, account for less than 0.5% of ovarian neoplasms (Al-Agha et al., 2011). Sertoli–Leydig tumors are a subgroup of sex-cord stromal tumors, which tend more toward “male” differentiation, hence the term “androblastoma”. These tumors are comprised of cells normally found in the male gonads that produce androgens, often resulting in hirsutism and virilization in up to two-thirds of female patients (DiSaia and Creasman, 1997). Sertoli–Leydig tumors are typically firm and solid, composed of tubules surrounded by fibrous stroma. Most commonly, patients present during the second and third decades, with an average size of 16 cm in diameter. Heterologous elements such as cartilage, bone, or striated muscle are rare findings in sex-cord stromal tumors, particularly of Sertoli–Leydig differentiation. We present the first documented case that includes three rare findings within the same sex-cord stromal tumor: Sertoli–Leydig differentiation, heterology, and sarcomatoid overgrowth. Herein

we report the case of a 31-year-old female who developed a large pelvic mass with elevated tumor markers and an exceedingly rare histology.

## 2. Case history

A 31-year-old, gravida 4, para 2-0-2-2, Caucasian female presented complaining of sharp abdominopelvic pain radiating to her back. Furthermore, she noted increasing abdominal distension, early satiety, and bloating for the past 4–5 months. She had a 25 lb weight loss over that time without dieting. She denied nausea, vomiting, or diarrhea. She reported regular menses since the age of 11, until recently, when her menses began to consist of mostly spotting. She had regular visits with her gynecologist, the last approximately 8 months ago, at which time she had a normal exam. She took an oral contraceptive for birth control.

Her past medical history was only significant for exercise-induced asthma. Surgical history consisted of a myringotomy as a child and a suction D&C for termination of pregnancy. She had no known drug allergies. Her family history was significant for a paternal great-grandmother with ovarian cancer and paternal grandmother with breast cancer. The patient admitted to occasional marijuana use but denied alcohol and other illicit drug use. Though she no longer smoked cigarettes at the time of presentation, she reported a four pack-year history.

On physical exam, she was afebrile with normal vital signs. There was no cervical, supraclavicular, or inguinal lymphadenopathy. The abdomen was tense, with palpable mass effect extending approximately 5 cm above the umbilicus. Pelvic exam revealed grossly normal external genitalia. On bimanual examination, the mass was again appreciated filling the pelvis and extending into the abdomen. Due to the volume of the mass, the uterus was not well palpated, and the patient did not tolerate rectovaginal exam. Laboratory values were significant for a CA-125 of 271.2 U/mL and AFP of 87.9 ng/mL. All other relevant labs were normal. Computed tomography revealed a 25 × 22 × 15 cm mass, likely arising from the left adnexa, comprised of solid and cystic components. There was minimal ascites with no evidence of retroperitoneal lymphadenopathy or bowel obstruction.

We proceeded to surgery, noting that the patient preferred fertility preservation. A vertical midline incision extending from the symphysis pubis to midway between the umbilicus and xiphoid process was made. Upon entering the abdomen, the mass was noted to arise from the left ovary, with tumor involving the surface. Clear, straw-colored ascites

\* Corresponding author at: Department of Gynecologic Oncology, Roswell Park Cancer Institute, Elm & Carlton Streets, Buffalo, NY 14263, USA.

E-mail address: [Rachel.brightwell@roswellpark.org](mailto:Rachel.brightwell@roswellpark.org) (R. Brightwell).

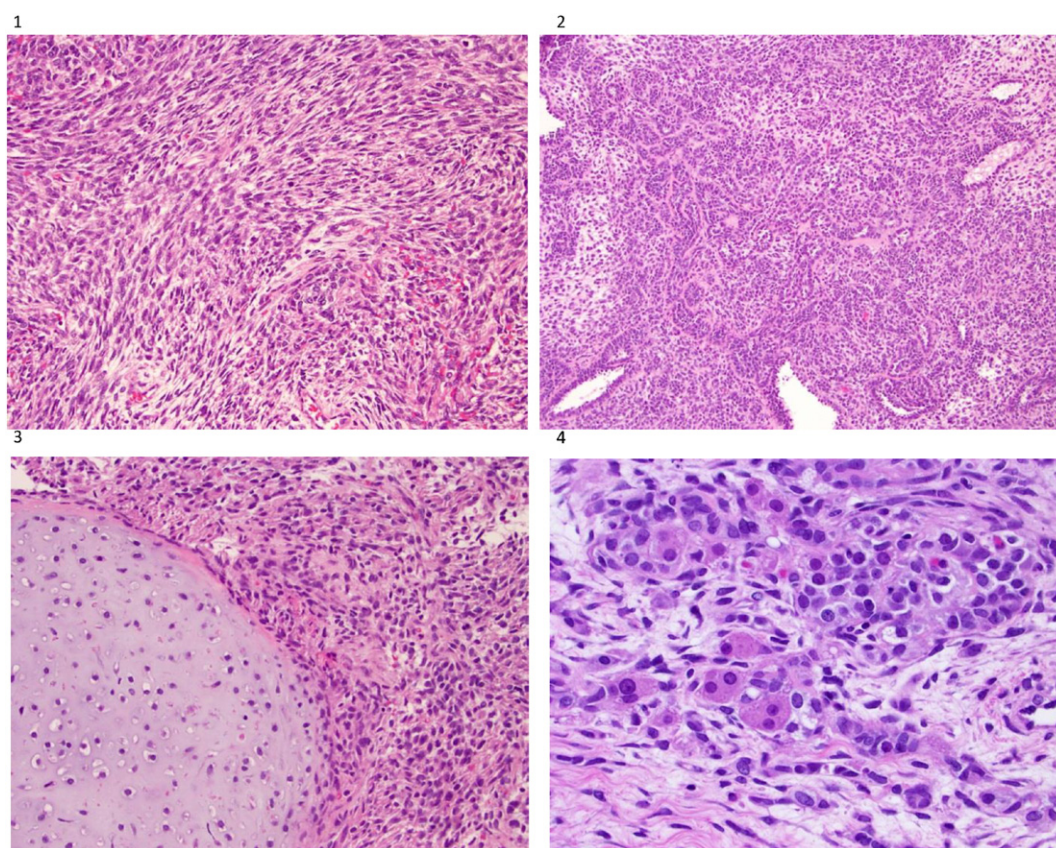
was removed. The uterus, fallopian tubes, and right ovary were free of tumor. There were no other metastatic implants visualized in the abdomen or pelvis. A small cystic pouch on the external surface of the mass was incidentally ruptured during the extraction, making her a clinical stage IC1. The patient's postoperative course was uneventful. The final pathologic report reflected Sertoli–Leydig tumor with heterologous elements and a high-grade component with sarcomatoid features. Omental tissue showed a benign finding of leiomyomatosis peritonealis disseminata-like changes. The measured size of the ovary was  $34 \times 31 \times 19$  cm with 75% solid and 25% cystic components. Immunohistochemistry showed positive staining for desmin, MYO D1, and focal myogenin, cytokeratin AE 1/3 and inhibin- $\alpha$  (Fig. 1). Desmin is typically positive in striated and smooth muscle, MYO D1 and myogenin are striated muscle markers, cytokeratin AE 1/3 is positive in epithelial cell elements, and inhibin- $\alpha$  is a good marker for some sex-cord stromal tumors and positive in Leydig cells. After discussion of her case at our multidisciplinary tumor board conference and given the fact that she had high-grade, sarcomatoid features, it was decided to give the patient carboplatin and taxol for six cycles, however the patient suffered a taxol reaction during her second cycle and was switched to carboplatin and taxotere for the remaining four cycles. She is currently eighteen months postoperative without evidence of disease with normal AFP and CA-125.

### 3. Discussion

Approximately 10% of Sertoli–Leydig tumors of the ovary are well-differentiated with a large majority of the histological component consisting of Leydig cells in the stroma (Lenhard et al., 2007). Heterologous tumors, accounting for 20% of Sertoli–Leydig neoplasms, differ in that they are more predominantly cystic than their homologous

counterparts. Mesenchymal heterology is typically seen with poorly differentiated tumors and is associated with worse clinical prognoses. Most commonly, surgery alone is the gold standard for patients with localized disease. However, given that this patient presented with a stage IC1 heterologous Sertoli–Leydig tumor with sarcomatoid features, the patient's prognosis is poorer than the majority of other patients in her demographic that have well-differentiated, homologous tumors. In one clinicopathologic study of 207 patients with Sertoli–Leydig tumors by Young et al., the prognosis correlated most meaningfully with the stage and degree of differentiation of the tumor. Also, radiation therapy, chemotherapy, or a combination of the two, in addition to surgical excision, was of benefit in the management of the malignant tumors (Young, 2005). Therefore surgery without adjuvant therapy is ill-advised in this patient.

The National Comprehensive Cancer Network (NCCN) guidelines recommend adjuvant chemotherapy with a platinum-based regimen such as BEP (bleomycin, etoposide, cisplatin), even in an early stage disease when considering poorly differentiated, high-grade, heterologous tumors (Homesley et al., 1999). These recommendations are not based on any large randomized studies in gynecologic malignancy secondary to the rarity of these tumors, but were borrowed from the landmark trials of Einhorn et al. in the treatment of testicular and other germ cell tumors (Einhorn et al., 1989). One report of 207 patients with ovarian Sertoli–Leydig tumors showed that 18% of patients had tumor that metastasized or recurred. 59% of patients with high-grade tumors and 19% of those with heterologous elements exhibited these malignant features (Young, 2005). These tumors are exquisitely sensitive to chemotherapy, though recurrence rates are high for high-grade histologies. As this patient has both heterologous morphology with sarcomatoid features and high-grade histology, she is likely at high risk for



**Fig. 1.** 1) Sheets of spindle cells representing the frankly sarcomatous areas of this malignant Sertoli–Leydig tumor. Scattered mitoses are readily seen in this photomicrograph. Hematoxylin and eosin stain. Original magnification:  $200\times$ . 2) Area of tumor showing Sertoli-form tubules. Hematoxylin and eosin stain. Original magnification:  $100\times$ . 3) Heterologous element (cartilage) in this malignant Sertoli–Leydig tumor. Hematoxylin and eosin stain. Original magnification:  $200\times$ . 4) Higher power view of Leydig cells and adjacent Sertoli cells. The Leydig cells show abundant cytoplasm and an occasional Reinke crystal. Hematoxylin and eosin stain. Original magnification:  $400\times$ .

recurrence based on what we know about correlation between histology, heterology, and recurrence rates. According to the EXPeRT trial, spillage, stage, and histopathologic differentiation are cornerstones of outcome prediction (Young and Scully, 1985). This case was also unique in that AFP was significantly elevated. Typically, the most common marker in Sertoli–Leydig tumors is CA-125 (DiSaia and Creasman, 1997). As AFP and CA125 were markers elevated at diagnosis, they are ideally suited to aid in monitoring of recurrence after treatment. Additionally, the usual BEP regimen was substituted with intravenous carboplatin (AUC 6) and paclitaxel (175 mg/m<sup>2</sup>) every three weeks secondary to an improved toxicity profile and presumed activity against higher grade tumors. Due to the presumed higher malignant potential of the tumor based on having both heterologous elements and sarcomatoid features, even in the setting of early stage disease, we will continue to monitor this patient's clinical course closely for progression-free and overall survival. Ovarian Sertoli–Leydig tumors are infrequently diagnosed, but this particular neoplasm was exceptional in that it displayed heterologous elements and sarcomatoid overgrowth. We will need many more case reports and retrospective studies such as these, due to the rarity of the tumor, to determine optimal treatment regimens; however we believe carboplatin and taxane-based therapy for such a unique, high-grade histology may afford the best outcome for our patient. She is currently without evidence of disease more than 18 months from her surgery and pregnant with her third child. Of course we will continue to closely monitor her for recurrence with tumor markers and imaging as warranted.

## Conflict of interest

The authors have no conflicts to declare.

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