Case Report

Overwhelmed by Heterologous Elements: The Hidden Identity of an Ovarian Sertoli–Leydig Cell Tumor with Extensive Heterologous Elements

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Abstract

Background: Sertoli–Leydig cell tumors (SLCTs) are rare ovarian sex cord–stromal tumors, often presenting diagnostic challenges due to their varied morphology and association with heterologous elements. **Case Presentation:** We report a case of 21-year-old female presenting with pelvic pain, secondary amenorrhea, and virilization. Radiology revealed a left ovarian mass. Patient underwent fertility sparing left partial oophorectomy. Histopathological examination demonstrated extensive calcification and ossification with scanty tumor cells, posing significant diagnostic difficulty. Based on morphology differential included were mesenchymal tumors of ovary, mature teratoma and sex cord stromal tumors. Immunohistochemistry played a crucial role in establishing the diagnosis of Sertoli–Leydig cell tumor with extensive heterologous elements. **Conclusion:** This case highlights the importance of correlating morphology, immunohistochemistry, and clinical features to arrive at an accurate diagnosis, especially in tumors with dominant heterologous components.

Keywords: sertoli–leydig cell tumor; ovary; heterologous elements; immunohistochemistry

Introduction

Sertoli–Leydig cell tumors (SLCTs) are rare ovarian neoplasms, accounting for less than 0.5% of all ovarian tumors and approximately 1–2% of ovarian malignancies in the pediatric and young adult population. These tumors originate from sex cord–stromal elements and exhibit a wide spectrum of histological differentiation. Approximately 22% of these tumors show heterologous elements, which may include cartilage, bone, skeletal muscle or mucinous epithelium.

The presence of extensive heterologous components can obscure the underlying sex cord–stromal tumor, leading to diagnostic confusion with teratomas or mesenchymal tumors. We present a diagnostically challenging case of SLCT with overwhelming calcification and ossification, where clinical correlation and immunohistochemistry were crucial for definitive diagnosis.

Case Report

A 21-year-old female presented with severe lower abdominal pain. Imaging by contrast-enhanced CT scan of the abdomen revealed a left ovarian mass measuring 40 × 38 × 35 mm. The patient subsequently underwent conservative fertility-sparing surgery, left partial oophorectomy and the specimen was submitted for histopathological evaluation.

On further clinical evaluation after pathological suspicion, the patient was noted to have secondary amenorrhea and signs of virilization, including excessive facial and body hair growth. Hormonal evaluation revealed elevated serum testosterone levels (300 ng/dl) and DHEA-S levels were within normal limits (180 ug/dl).

Gross examination revealed ovarian mass in multiple pieces with a smooth and congested capsule. No evidence of surface deposits. On cut section, the mass was grey-white, firm to gritty, with prominent calcified areas. Representative sections sampled from different areas and processed in 5 blocks initially and later more sections taken in additional 02 blocks to search for tumor components.

Histological examination showed an encapsulated ovarian tumor predominantly composed of extensive calcification, ossification, and areas of hyalinization. The cellular component was sparse. The tumor cells were arranged in lobules, cords, trabeculae, and sheets. Sertoli cells were spindle to oval in shape with moderate nuclear atypia. Leydig cells were very sparse and displayed epithelioid morphology with moderate to abundant eosinophilic and vacuolated cytoplasm. Mitotic activity was low (0–1/ 10 hpf) (Figure 1).

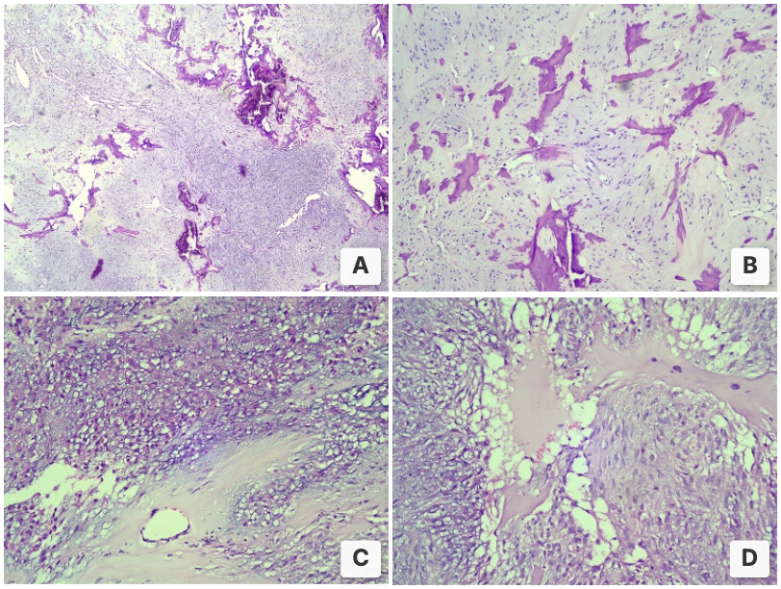

Figure 1: (A, B) Low power view showed predominantly calcifications admixed with tumor cells (H&E, 100x). (C) High power view showed few cellular areas composed of Leydig cells arranged in sheets and having moderate to abundant eosinophilic cytoplasm (H&E, 400x). (D) High power view showed vague cords and sheets of Sertoli cells with spindle and oval shaped nucleus (H&E, 400x).

The overwhelming presence of heterologous elements significantly masked the underlying neoplastic component, posing a major diagnostic challenge. Based on morphology alone, the differential diagnoses considered were Mature teratoma, Primary ovarian mesenchymal tumor and Sex cord–stromal tumor. Due to the limited cellularity and extensive calcification, definitive diagnosis could not be established without ancillary studies.

Immunohistochemical staining showed diffuse positivity for inhibin (clone R1, dilution 1:100), calretinin (clone DAK-Calret 1, dilution 1:200), and SF-1 (clone EP434, dilution 1:100), supporting sex cord–stromal differentiation. Pan cytokeratin (clone AE1/AE3, dilution 1:100) was focally positive, S-100 (clone EP32, 1:200) and SMA (clone 1A4, 1:100) were negative ruling out mesenchymal and epithelial origin of tumor. MIB-1 proliferation index (clone MIB-1, DAKO, 1:100) is 5% (Figure 2).

FIGO stage could not be allotted in this case as ovary is received in multiple pieces. Though sections did not show any surface capsular surface deposits, there was no clear intact capsule in this case and other organs were not received as the patient has undergone fertility preserving surgery.

Final impression was given as Poorly differentiated Sertoli-Leydig cell tumor with extensive heterologous elements. Further testing for germline *DICER1* was recommended.

Patient was lost to follow up and *DICER1* testing was not performed.

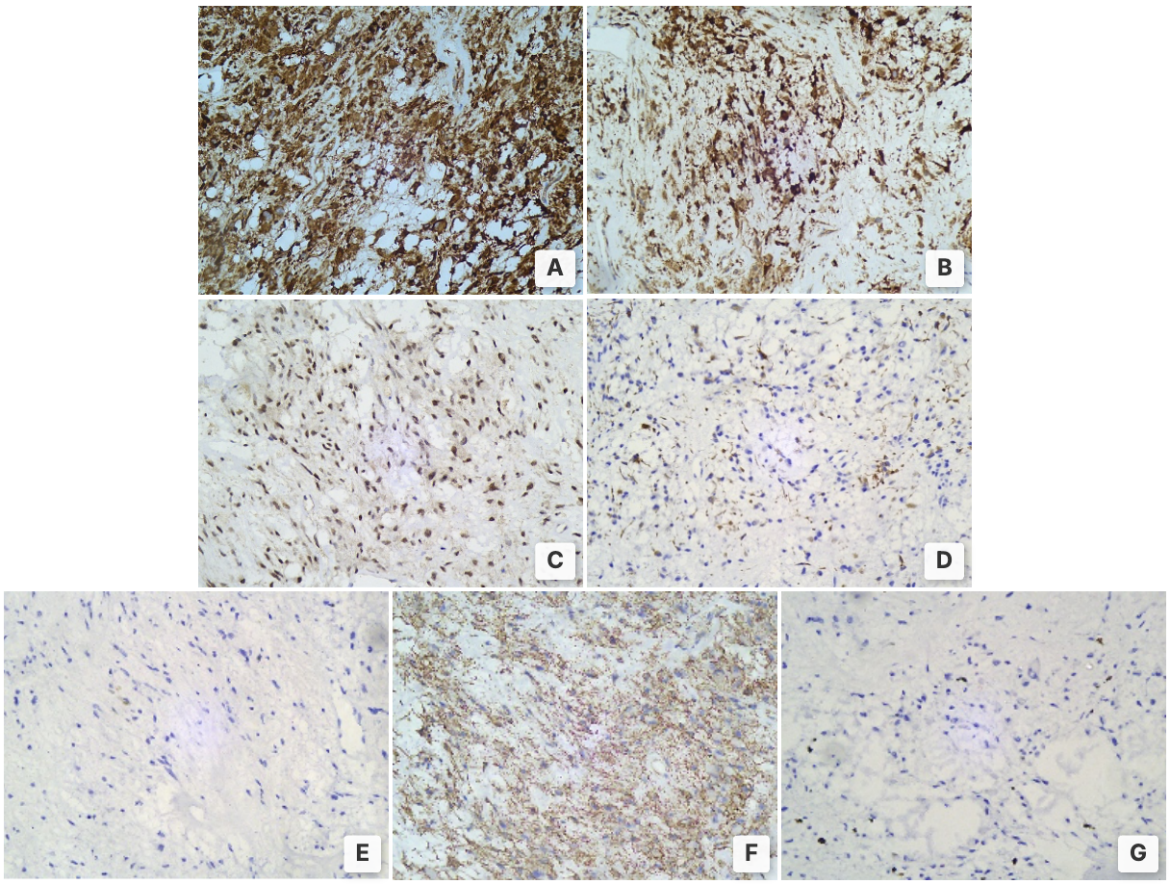

Figure 2: Immunohistochemistry: (A) Inhibin is positive. (B) Calretinin is positive. (C) SF-1 is positive. (D) Pan cytokeratin focal positive. (E) S-100 is negative. (F) SMA is negative. (G) MIB-1 is low, 5% (IHC, 400x).

Discussion

SLCTs account for less than 0.5% of ovarian neoplasms. Patients presenting age can be 1–84 years, with mean age being 25 years. Around 40–60% cases present with symptoms related to androgen excess. Rarely they present with estrogenic manifestations. Certain patients may present with ascites and abdominal pain. These tumors are predominantly sporadic, but can be associated with DICER1 syndrome.[1, 2]

Molecular subtypes of Sertoli Leydig tumors include *DICER1*-mutant, *FOXL2* c.402C>G (p.Cys134Trp)-mutant, *DICER1*/*FOXL2*-wildtype. Recent molecular studies have shown an association between *DICER1* mutations and SLCTs occurring at a younger age, particularly those exhibiting heterologous elements and retiform patterns. In contrast, *FOXL2* mutations are more commonly associated with postmenopausal patients and tumors lacking heterologous differentiation.[1]

Morphologically SLCTs are classified as well-differentiated, moderately differentiated, and poorly differentiated forms according to degree of tubular differentiation of the Sertoli cell component and the quantity of primitive gonadal stroma. Leydig cells decrease with increasing grade. Sertoli cells are noted in tubules without significant nuclear atypia. Leydig cells are seen in clusters and cords, the cells are vacuolated.[3]

Moderately differentiated tumors have a lobular pattern. Sertoli cells are seen as nests, solid tubules and cords. Leydig cells present as small nests at the periphery of the tumor.

Poorly differentiated SLCTs consist of sarcomatoid stroma, which resembles primitive gonadal stroma with minor component of moderately differentiated SLCT. Leydig cells are very scanty. Retiform SLCTs consists of anastomosing cords or papillae lined by Sertoli cells.[1, 4]

Heterologous elements are usually seen in moderately and poorly differentiated tumors. They may also be present in some retiform tumors. Heterologous elements include epithelial or mesenchymal components, among them epithelial are most common. Mucinous epithelium, hepatocyte differentiation, cartilage, skeletal muscle and ossification are seen. Rarely carcinoids and carcinomas develop from heterologous elements.[4]

The presence of heterologous elements, particularly when extensive, is associated with higher-grade tumors and poorer prognosis.[4, 5] In this case, the dominant calcified and ossified components overshadowed the sparse Sertoli–Leydig cell population, mimicking other ovarian tumors and significantly complicating diagnosis.

The primary treatment for Sertoli-Leydig cell tumors (SLCTs) is surgery which will be decided based on patient age, tumor stage, and grade. Fertility preservation is very crucial in reproductive age women and this can be achieved with ovarian cystectomy or unilateral adnexectomy. For patients who have completed childbearing, total hysterectomy with bilateral salpingo-oophorectomy and staging procedures are recommended.[3, 6, 7]

Lymph node metastasis is rare and hence dissection of lymphnodes is not routinely recommended. Adjuvant chemotherapy is recommended for moderately or poorly differentiated tumors, though its benefit is limited and particularly reserved for recurrent disease.[7]

Currently, chemotherapy options including BEP (bleomycin/etoposide/cisplatin), paclitaxel/carboplatin, EP (etoposide/cisplatin), CAP (cyclophosphamide/doxorubicin/cisplatin), but the chemotherapy duration is still controversial. For chemotherapy-resistant patients, hormonal therapies are available such as progesterone and aromatase inhibitors. Radiotherapy can be recommended patients who are contraindicated for surgery, have residual lesions after surgery and resistant to chemotherapy.[7]

Fertility-sparing surgery is the treatment of choice in young patients, while platinum-based chemotherapy may be beneficial in selected high-risk cases. Genetic counseling and consideration of germline *DICER1* testing are recommended.[5, 6]

Conclusion

This case highlights the diagnostic difficulty posed by Sertoli–Leydig cell tumors with extensive heterologous elements. The overwhelming calcification masked the true nature of the tumor, making morphology alone insufficient for diagnosis. Clinical correlation and targeted immunohistochemistry were pivotal in uncovering the hidden identity of this neoplasm. A high index of suspicion and a multimodal diagnostic approach are essential to ensure accurate diagnosis, guide appropriate management, and improve long-term outcomes. Early and accurate diagnosis is essential, as management differs significantly from other ovarian tumors.

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Consent: Written informed consent could not be obtained despite reasonable efforts. The patient's identity has been fully anonymized and her identity was not revealed anywhere. The report complies with ethical standards.

Ethical Approval: The patient's identity has been fully anonymized and her identity was not revealed anywhere. The report complies with ethical standards.

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