Sertoli-Leydig cell tumor of the ovary masquerading as a mucinous adenocarcinoma: a frozen section pitfall

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Abstract

Sertoli-Leydig cells tumors are rare ovarian neoplasms that can be managed with conservative resection given their generally excellent prognosis. Here we report a case of Sertoli-Leydig cell tumor mistakenly diagnosed as an invasive mucinous adenocarcinoma at time of intraoperative consultation because of its blue-mucinous appearance in the frozen section material. The patient subsequently underwent an extensive staging procedure revealing unilateral, ovarian confined disease. The mucinous features seen on frozen section were lost on the slides prepared from formalin fixed tissues. Immunohistochemical work up confirmed the diagnosis of a pure Sertoli-Leydig cell tumor. No heterologous elements were identified in this tumor. This case illustrates a hitherto unrecognized frozen section pitfall in evaluation of ovarian neoplasms. To the best of our knowledge, this is the first well documented case of pure Sertoli-Leydig cells tumor which resembled a well differentiated mucinous adenocarcinoma during frozen section.

Introduction

Sertoli-Leydig cell tumors often present diagnostic dilemmas due to their relative infrequency and high degree of morphologic variability.[1,2] The potential for diagnostic uncertainty and misdiagnosis is amplified in the setting of intra-operative consultation where diagnosis must be made on frozen section material. Here we present a case of a pure Sertoli-Leydig cell tumor masquerading as a mucinous adenocarcinoma on frozen section.

Case Report

The patient was a 57-year-old woman who presented with worsening abdominal pain and increasing abdominal girth. Her past medical history was significant for a prior appendectomy and was otherwise unremarkable. Physical exam was notable for left lower quadrant tenderness and left side adnexal fullness. Further workup with magnetic resonance imaging (MRI) scan of the pelvis showed a multicystic and partially solid left ovarian mass measuring up to 20 cm in diameter. There was no obvious para-aortic, iliac or inguinal lymphadenopathy. Her CA-125 level was normal. The decision was made for the patient to undergo left salpingo-oophorectomy. Gross examination of the left salpingo-oophorectomy specimen consisted of one large, firm, pink-tan mass measuring 20.1×9.5×5.5 cm. The specimen had a smooth, glistening outer surface. Sectioning revealed a multilobulated solid tumor with focal areas of cystic degeneration. The underlying ovarian parenchyma was completely effaced. Areas of calcification were also seen. The specimen included an uninvolved and unremarkable attached fallopian tube. Frozen section examination (Figure 1) revealed a population of back-to-back, haphazardly arranged and infiltrative appearing epithelioid cells arranged in gland-like structures and set in a fibrous stroma. The gland-like structures appeared surrounded by a mild desmoplastic reaction. Minimal nuclear atypia was present as most nuclei were small, round and uniform in size with even chromatin and small nucleoli. The cells had abundant cytoplasm with a bluish hue suggestive of mucin. Some cells showed a vaguely signet ring-like morphology. Mitotic figures and necrosis were not conspicuous. A frozen section diagnosis was rendered as mucinous adenocarcinoma. The patient then was subjected to contralateral salpingo-oophorectomy, omentectomy, peritoneal biopsies and staging lymph node dissection (of note, the patient had a previous appendectomy). Permanent sections analysis demonstrated similar findings to the frozen section material (Figure 2). However, a more apparent overall sertoliform architecture was appreciated. Furthermore, the cellular cytoplasm no longer appeared mucinous, rather it was finely granular. Also, many of the gland-like structures appeared to be ciliated, a finding not appreciable on frozen sections. Scattered small polygonal Leydig cells could be seen coursing between gland-like structures. No lymphovascular invasion was identified. The bilateral fallopian tubes, the right ovary, lymph nodes, peritoneal biopsies, and omental specimens did not show any involvement by the tumor.

The tumor was stained with a panel of immunohistochemical markers including inhibin, calretinin, EMA, multiple cytokeratins (CK7, CK20, AE1/E3), CA125, CA19.9, estrogen receptor (ER), progesterone receptor (PR), synaptophysin and chromogranin. Inhibin highlighted all glandular elements as well as intercalating Leydig cells (Figure 3). Calretinin was similarly positive. ER and PR staining were weak to moderate. The tumor was otherwise negative for cytokeratins, CA125, CA19.9, EMA, synaptophysin and chromogranin. Based on the morphologic features and immunohistochemical profile a final diagnosis of well differentiated ovarian Sertoli-Leydig cell tumor was rendered.

Discussion

Here we present the first reported case of a pure Sertoli-Leydig cell tumor mimicking an invasive mucinous adenocarcinoma on frozen section evaluation. This particular case illustrates how the finely granular cytoplasm seen in some pure Sertoli-Leydig cell tumors may have a blue mucinous appearance in frozen section material and can be considered a diagnostic pitfall.

Ovarian Sertoli-Leydig cell tumors are uncommon ovarian tumors that encompass less than 0.5% of ovarian neoplasms.[3] They tend to occur in young to middle age women (75% occur in women 30 years or younger) and fewer than 10% have been

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reported to occur in patients more than 50 years old.[4] The most common presenting complaints are androgen excess and abdominal pain.[4] At time of surgical resection the vast majority of tumors are stage 1 (~98%).[4] Most Sertoli-Leydig cell tumors are unilateral (2% are bilateral) and average 15 cm in size. Grossly they can be focally cystic with predominantly yellow-tan cut surfaces.[4]

Histologically, these tumors are divided into five morphologic patterns: well-differentiated (~ 10%), intermediately differentiated, poorly differentiated, retiform (~15%), and those with heterologous elements.[1] These tumors usually have a lobulated appearance with intervening broad fibrous bands. The tumor cells may be arranged in a variety of architectures including hollow tubules, solid tubules, nests, trabeculae, diffuse, pseudopapillary, follicles, alveolar, and pseudoendometrioid patterns.[2] Microcystic changes and retiform patterns also occur as noted above. Variable numbers of stromal Leydig cells are usually observed. The cytoplasm of Sertoli cells is known to be glycogen rich.[5] We believe that the blue cytoplasmic staining of glycogen on frozen section material resulted in a mucin-like appearance in the above case. Pure Sertoli-Leydig cell tumors do not show cytoplasmic mucin.[5]

Calcification, occasionally observed in testicular Sertoli-Leydig cells tumors, has been reported in the ovarian counterpart.[6] In the above case, the presence of grossly appreciable calcification could have been a helpful clue to at least point to an alternative diagnosis when mucinous adenocarcinoma was being considered on frozen section.

Clinical correlation with the hormonal status of the patient can be helpful during the time of surgery because 50% of patients with Sertoli-Leydig cell tumors present with endocrine manifestations including virilization.[3] However, in the above case no endocrine related symptoms or serologic abnormalities were noted.

Sertoli-Leydig cell tumors may display true areas of heterologous differentiation including mucinous elements.[7-10] This heterologous mucinous differentiated can also be a frozen section pitfall. The above case did not show true mucinous differentiation. Mucicarmine stain was negative as were all cytokeratin stains and epithelial membrane antigen (EMA) (Figure 3 C,D).

Well-differentiated Sertoli-Leydig cell tumors are considered benign and do not recur. Those of intermediate and poor differentiation behave in a malignant fashion in 11% and 59% of cases respectively.[4] Risk factors for aggressive behavior include large size (> 5 cm), necrosis, nuclear atypia, and increased mitoses (>5/10 HPF).[2]

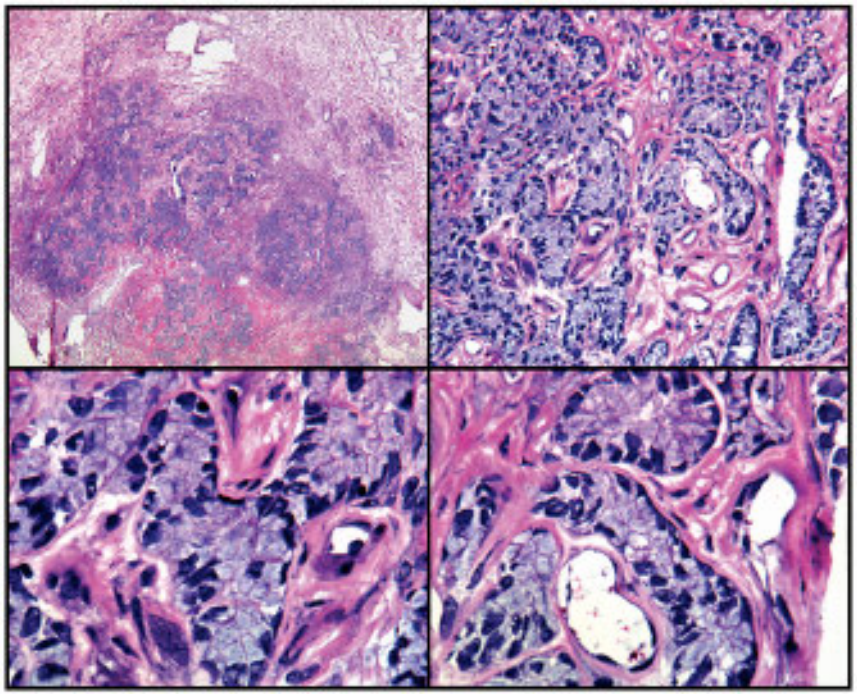

Figure 1. Light micrographs from Hematoxylin & Eosin stained frozen tissue sections of the ovarian tumor demonstrated infiltrative appearing gland-like structures with intracytoplasmic blue mucinous hue.

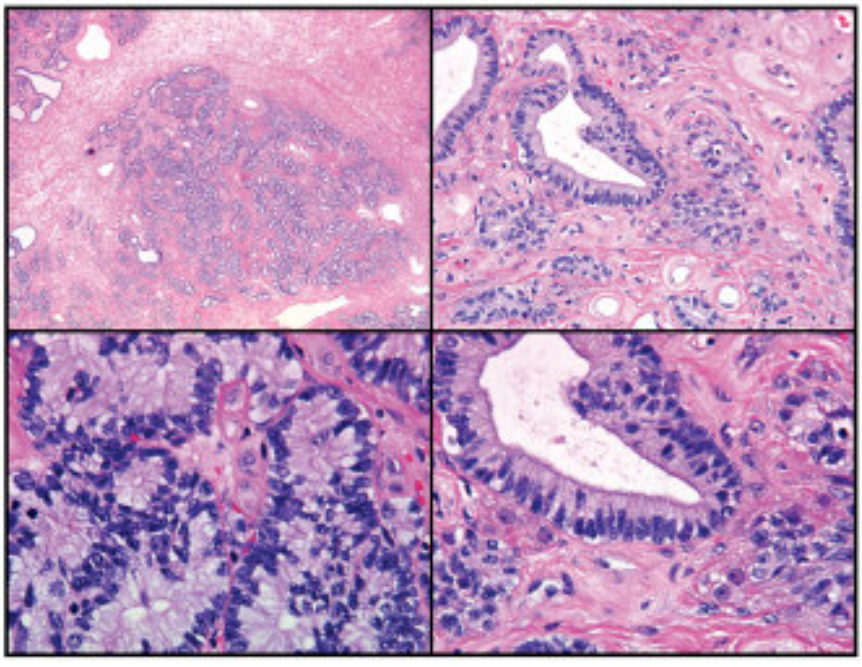

Figure 2. Light micrographs from Hematoxylin & Eosin stained formalin-fixed tissue sections of the ovarian tumor demonstrated more apparent sertoliform architecture with loss of blue-mucinous hue. Ciliated tubules were also present.

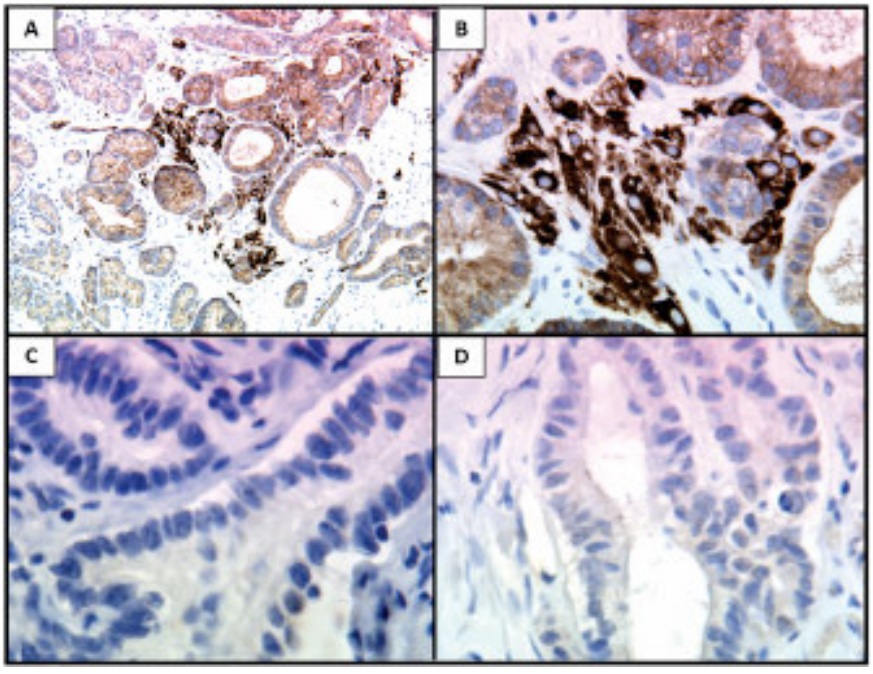

Figure 3. Immunohistochemical characterization of the ovarian tumor demonstrate (A-B) Inhibin expression and lack of (C) Pan cytokeratin and (D) EMA.

Conclusions

The above case highlights an important diagnostic pitfall in frozen section evaluation of ovarian lesions. The intraoperative management consequences of this mistake are not inconsequential. Given that the majority of Sertoli-Leydig cell tumors are unilateral and benign, fertility-sparing surgery can be used as the primary treatment modality.[3] In the above case, a more extensive surgical resection was performed due to the incorrect frozen section diagnosis. Therefore, knowledge of the potential pitfall is important especially in younger patient where preservation of fertility is desired.

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