Pathologic Quiz Case

A 22-Year-Old Woman With a Large Right Adnexal Mass

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A 22-year-old African American woman, gravida 2, para 2, aborta 0, presented to the emergency department with lower abdominal pain, which intermittently radiated down her right leg. She noted an increase in her abdominal girth and a 10-lb weight gain during the past 4 months. She had nausea and early satiety without fever, chills, or vomiting. Her last normal menstrual cycle was 3 months ago. She has since experienced daily vaginal bleeding of 6 spotted pads per day. Physical examination revealed a large abdominal mass that extended from the pelvis up to the xiphoid process. A small amount of blood was noted in the vaginal vault. No hirsutism was noted. Urine β-human chorionic gonadotropin test results were negative. A contrast-enhanced computed tomogram of the abdomen and pelvis demonstrated a large, well-circumscribed, complex cystic mass extending from the right adnexa to the upper abdomen. The mass predominately consisted of fluid attenuation. There were multiple internal septations with variable degrees of thickness with some solid tissue component (Figure 1; arrow, solid area). No abdominal or pelvic lymphadenopathy was appreciated. The left adnexa were unremarkable.

Accepted for publication February 26, 2004.

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The authors have no relevant financial interest in the products or companies described in this article.

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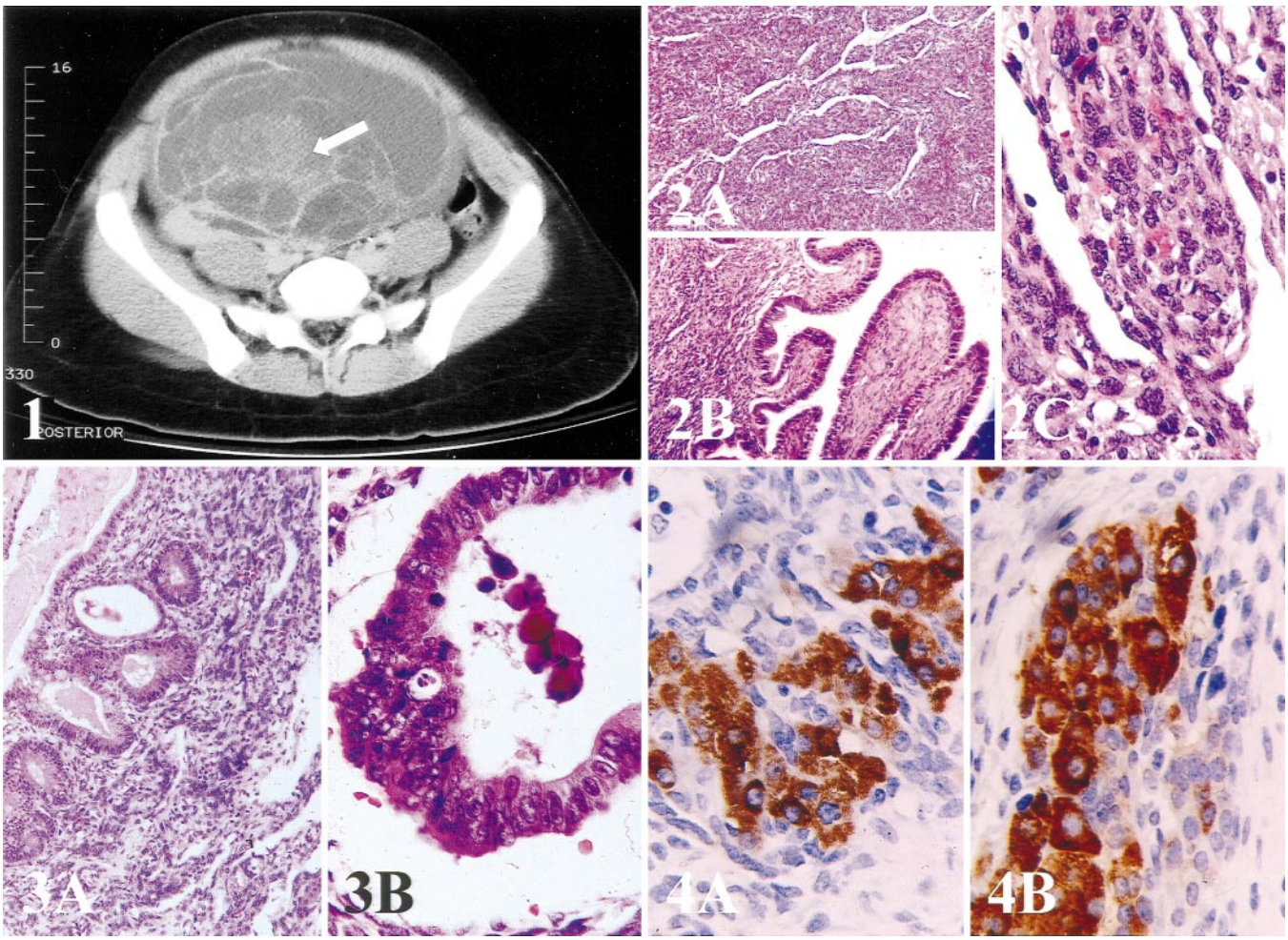
The patient underwent exploratory laparotomy, right oophorectomy, peritoneal fluid sampling, partial omentectomy, right periaortic lymph node sampling, wedge resection of the left ovary, and lysis of adhesions. A large pelvic mass that measured approximately 25 × 23 × 18 cm was noted arising from the right ovary. Grossly, it was a multiloculated cyst with abundant mucinous fluid. The cystic areas composed more than 60% of the entire tumor. The uterus and bilateral fallopian tubes were unremarkable. The left ovary was normal in size but hard in consistency. The frozen section was diagnosed as mucinous cystic tumor with borderline malignancy.

Microscopically, sections showed a multiloculated cystic lesion with complex glands separated by cellular stoma. Some areas revealed a network of irregularly branching, elongated, narrow, slitlike tubules (Figure 2, A and C) and papillary area (Figure 2, B). The glands and cysts were lined by moderately differentiated to well-differentiated intestinal-type mucinous epithelium, including goblet cells (Figure 3, A), and exhibited varying degrees of stratification and nuclear atypia (Figure 3, B). The cellular stroma was composed of solid, or less often, hollow tubules and polygonal cells, which were positive for inhibin immunohistochemical stain (Figure 4, A and B). Some cells of the tumor were spindle-shaped, resembling a sarcoma or cellular endometrial stroma with numerous mitotic figures (>10 per 10 high-power fields [HPF]) in some areas. The left ovary demonstrated peripheral fibrosis and a large number of atretic follicles. There was no metastatic tumor identified in the resected omentum and one lymph node (0/1) examined.

What is your diagnosis?



Pathologic Diagnosis: Poorly Differentiated Sertoli-Leydig Cell Tumor of the Right Ovary With Retiform Differentiation and Heterologous Elements (Mucinous Components)

Sertoli-Leydig cell tumors of the ovary are rare and account for less than 0.2% to 0.5% of all ovarian neoplasms.[1–3] Sertoli-Leydig cell tumors occur in all age groups but are more often seen in young women. According to the study by Young and Scully,[2] the average age was 25 years in more than 200 patients; 75% of the patients were younger than 30 years. This patient was even younger, only 22 years old. Clinically, one third of these tumors present with virilization. Under this circumstance, the patient typically begins to have oligomenorrhea, followed within a few months by amenorrhea, as was the case with our patient. However, no hirsutism, temporal balding, deepening of the voice, or enlargement of the clitoris was identified with this patient. These symptoms are usually of lower frequency in tumors that contain heterologous elements and lowest in tumors that have a prominent retiform component.[4]

Plasma levels of testosterone, androstenedione, and other androgens, alone or in combination, may be elevated in patients with Sertoli-Leydig cell tumors.[2] Our patient has never been tested for these hormones. Approximately 50% of the patients with Sertoli-Leydig cell tumors have no endocrine manifestations and usually complain of abdominal swelling and/or pain.[4] Some tumors have been associated with various estrogenic syndromes, including irregular menses, menorrhagia, or menometrorrhagia in women in the reproductive age group and postmenopausal bleeding in older women.[4]

Almost all Sertoli-Leydig cell tumors are unilateral anatomically. Only 1.5% were bilateral in the study by Young and Scully.[2] Most of the tumors are between 5 and 15 cm in diameter, with an average diameter of 13.5 cm. Poorly differentiated tumors, including those with mesenchymal heterologous elements, tend to be larger than those of better differentiation and to have worse prognosis. Tumors with heterologous or retiform components are cystic more often than tumors without these elements. The heterologous tumors occasionally simulate mucinous cystic tumor on gross examination,[2] especially those with a large heterologous mucinous component, such as in this case.

Histologically, Sertoli-Leydig cell tumors of the ovary are sex cord–stromal tumors. They are composed of Sertoli cells derived from the sex cords and stromal cells that include Leydig cells and fibroblasts, in variable proportions and degree of differentiation.[5] They are divided into well-differentiated, intermediate, or poorly differentiated with or without heterologous elements, retiform, and mixed subtypes. Well-differentiated Sertoli-Leydig cell tumors are characterized by a predominantly tubular pattern. The tubules can range from round to oval and small. They can also appear slightly irregular, cystic, and dilated or rarely even simulate endometrial glands. Intraluminal eosinophilic fluid may be present. The tubule cells are typically cuboidal or columnar with round or elongated nuclei without cytologic atypia and a prominent nucleolus. Mitotic figures are rare. The Leydig cells contain variable amounts of lipid. Occasionally, abundant lipochrome pigment is present. Rare crystals of Reinke can be identified in only approximately 20% of cases.

Sertoli-Leydig cell tumors of intermediate differentiation show patterns between well-differentiated and poorly differentiated tumors. The tumor cells are small and round. Oval and angulated nuclei are arranged in ill-defined masses with a lobulated appearance on low-power examination.[4] Within the ill-defined masses, the Sertoli cells may be arranged in a diffuse manner or in an aggregated form. The Sertoli and Leydig cells may contain variable and sometimes large amounts of lipid. The lipid may form small or large droplets. The tumors of intermediate differentiation have an average of 5 mitotic figures per 10 HPF.[4]

Poorly differentiated Sertoli-Leydig cell tumors are sarcomatoid in appearance. They are composed of poorly differentiated Sertoli cells growing in a diffuse pattern. Most poorly differentiated tumors do not demonstrate lobulations or orderly arrangement of Sertoli and stromal elements. This is in contrast to most tumors of intermediate differentiation, which exhibit these features to a minor extent. In addition, poorly differentiated Sertoli-Leydig cell tumors typically have high mitotic figures (10 per 10 HPF), which were seen in this case.

Heterologous components are noted in approximately 20% to 25% of intermediate or poorly differentiated Sertoli-Leydig cell tumors.[6] Among the heterologous elements, gastrointestinal-type intestinal mucinous epithelium, including goblet cells, is most frequently revealed. However, other tissues, including carcinoid, skeletal muscle, and cartilage, also occur.[6] The mucinous epithelium may appear benign or have features of borderline malignancy or even low-grade adenocarcinoma. In this case, the heterologous component is intestinal-type mucinous epithelium with features of borderline malignancy. It was reported as mucinous cystic tumor with borderline malignancy during frozen section diagnosis.

Ovarian stromal tumors with minor sex cord elements have been also reported.[7,8] One case of ovarian mucinous cystadenoma coexisting with stromal tumor with minor sex cord elements has been reported in the literature to date.[9] Mucinous neoplasms rarely occur in association with cystic teratoma, Sertoli-Leydig cell tumor, granulosa cell tumor, and carcinoid tumor.[10]

It is important to differentiate a poorly differentiated Sertoli-Leydig cell tumor with retiform differentiation and heterologous elements (mucinous components) from a mucinous cystadenoma with borderline malignancy. The ages of the patients with the former are younger (mean age, 25 years) than the latter (mean age, 53–54 years). The former has a worse prognosis than the latter, although both respond well to complete surgical excision. Chemotherapy of the former is used to elicit response but not cure.

References

1. Jung SE, Lee JM, Rha SE, Byun JY, Jung JI, Hahn ST. CT and MR imaging of ovarian tumors with emphasis on differential diagnosis. *Radiographics.* 2002;22:1305–1325.
2. Young RH, Scully RE. Sex cord-stromal, steroid cell, and other ovarian tumors. In: Kurman RJ. *Blaustein's Pathology of Female Genital Tract.* 5th ed. New York, NY: Springer-Verlag; 2002:929.
3. Outwater EK, Wagner BJ, Mannion C, McLarney JK, Kim B. Sex cord-stromal and steroid cell tumors of the ovary. *Radiographics.* 1998;18:1523–1546.
4. Young RH, Scully RE. Ovarian Sertoli-Leydig cell tumors: a clinicopathological analysis of 207 cases. *Am J Surg Pathol.* 1985;9:543–569.
5. Scully RE, Young RH, Clement PB. Tumors of the ovary and maldeveloped gonads: fallopian tube and broad ligament. Washington, DC: Armed Forces Institute of Pathology; 1996. *Atlas of Tumor Pathology*; 3rd series, fascicle 23.
6. Young RH, Clement PB, Scully RE. The ovary. In: Sternberg SS, ed. *Diagnostic Surgical Pathology.* Vol 2. 2nd ed. New York, NY: Raven Press; 1994:2236–2239.
7. Zaloudek C. The ovary. In: Gompel C, Silverberg SG, eds. *Pathology in Gynecology and Obstetrics.* 4th ed. Philadelphia, Pa: JB Lippincott Co; 1994:368–371.
8. Young RH, Scully RE. Ovarian stromal tumors with minor sex cord elements: a report of seven cases. *Int J Gynecol Pathol.* 1983;2:227–234.
9. Seok WY, Mee-Yon C, Soon-Hee J, Kwang GL, Dong SC, Kyu RK. Mucinous cystadenoma coexisting with stromal tumor with minor sex-cord elements of the ovary. *J Korean Med Sci.* 2001;16:237–240.
10. Yoon YJ, Suh KY, Le JY, Kim JY, Lee SA. A case of ovarian stromal tumor with minor sex cord element. *Korean J Obstet Gynecol.* 1993;36:2756–2761.