Pathologic Quiz Case

Cystic and Solid Ovarian Tumor in a 43-Year-Old Woman

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A 43-year-old African American woman, gravida 5 para 5, presented with abdominal pain and was found to have a pelvic mass on radiologic examination. An endometrial biopsy specimen revealed normal proliferative-phase endometrium. She underwent right salpingo-oophorectomy; a specimen was sent for frozen section. Based on the frozen section diagnosis, a completion hysterectomy, left salpingo-oophorectomy, and staging laparotomy were performed.

The right ovary showed a 15 × 15 × 5-cm, hemorrhagic, multiloculated cystic tumor, with peripheral yellow-white solid areas (Figure 1). The cysts varied in size from 0.3 to 1.8 cm in diameter. The cyst walls varied in thickness from 0.1 to 0.5 cm. Microscopic examination of the right ovary showed large areas of necrosis. The viable tumor cells were present in sheets and ill-defined solid nests interspersed with microcystic foci (Figure 2). No Call-Exner bodies or follicular areas were identified. The tumor cells had scant cytoplasm, round-to-oval vesicular nuclei with small eosinophilic nucleoli, and irregular nuclear contours. No ''coffee-bean'' nuclei were noted, and nuclear clefts and grooves were rare. The mitotic activity was focally brisk, with an average of 8 to 10 mitoses per high-power field in these areas (Figure 3). The tumor cells showed positive staining with antibodies to α-inhibin (Figure 4) and were negative for chromogranin. Prognostic markers performed on the tumor showed the following results: diploidy, 19% positivity for Ki-67 (MIB-1), 46% positivity for progesterone receptor, 4% positivity for p53; and negative staining for estrogen receptor and Her-2/*neu* (c-erbB-2).

The left ovary showed a mature cystic teratoma. There were leiomyomata in the myometrium, and the endometrium was in the proliferative phase. There were tumor deposits in the peritoneum.

What is your diagnosis?

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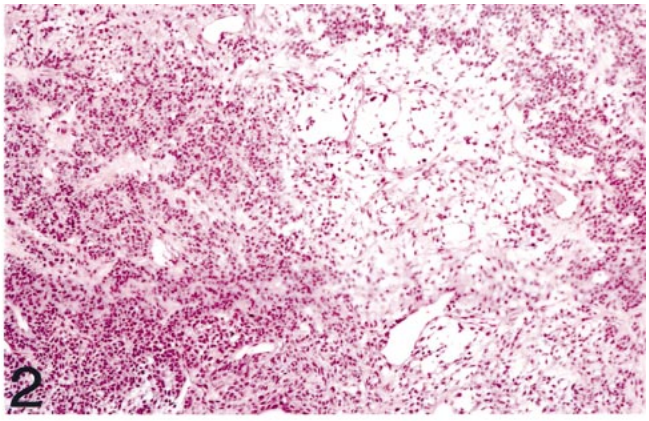

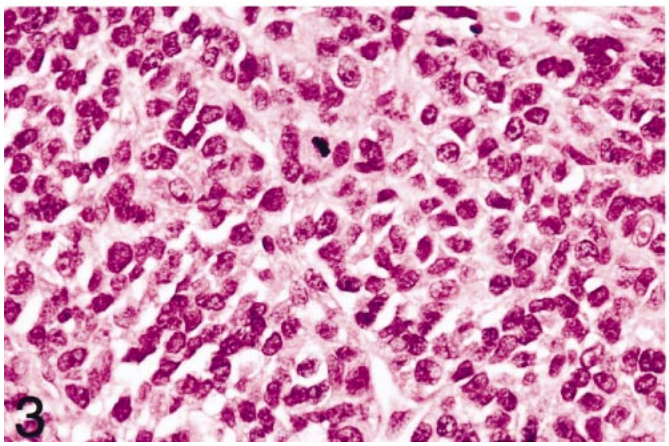

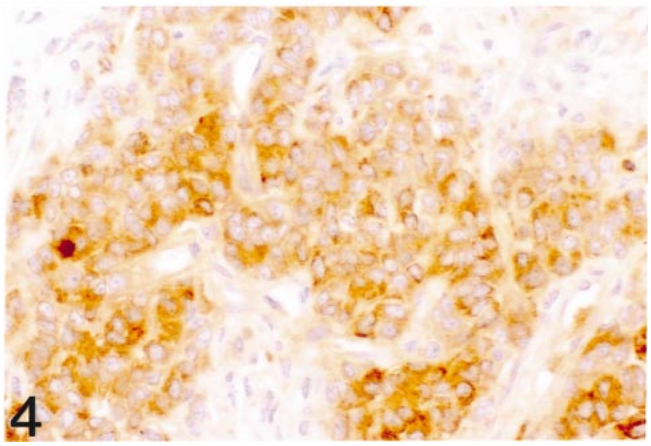

Pathologic Diagnosis: Cystic Juvenile-Type Granulosa Cell Tumor of the Ovary in an Adult

Granulosa cell tumors constitute 1% to 2% of all ovarian neoplasms but are the most common malignant neoplasms among the sex cord–stromal tumors and occur in women aged 50 to 55 years.[1] Juvenile granulosa cell tumor (JGCT), a distinct histologic subtype, most commonly occurs before 10 years of age, and in one series, 97% of cases were present before 30 years of age, with most occurring in the first 20 years.[2] The adult granulosa cell tumor (AGCT) most commonly presents with abnormal uterine bleeding (63.9%) and abdominal pain (45.4%).[3] In contrast, the clinical manifestations of JGCT depend on whether the patient is prepubertal or postpubertal. In a large series, 82% of prepubertal patients with JGCT presented with isosexual pseudoprecocity, whereas older patients presented with nonspecific symptoms such as abdominal swelling and pain.[2]

Both AGCT and JGCT secrete sex steroid hormones, usually estrogens and rarely androgens.[4] Clinical evidence of estrogen production in AGCT can be found in the form of endometrial hyperplasia (14.4% to 56.2% cases) and endometrial carcinoma (2.1% to 12.5% cases).[3,5,6] There is also a 50% incidence of nulliparity in women with granulosa cell tumor before the age of 45 years and 23% after the age of 45 years.[5] The sexual precocity in patients with JGCT is also due to excessive estrogen production.

Grossly, AGCTs can be cystic (30.3% of cases), solid (27.8% of cases), or of a mixed consistency (41.7% of cases). Tumor rupture occurred in 21.6% and metastasis at the time of diagnosis in 12.4% of cases.[3] In addition, JGCTs show similar gross features. Microscopically, many different architectural patterns are characteristic of AGCT: microfollicular, macrofollicular, trabecular, insular, watered silk, and diffuse.[1] The most characteristic features are Call-Exner bodies (small cavities lined by well-differentiated granulosa cells) and grooved ''coffee-bean'' nuclei (representing deep indentation of the nuclear membrane).[1] In contrast, JGCTs are characterized by microcysts or irregular follicles, hyperchromatic round-to-oval nuclei that are usually not grooved, and a high mitotic rate,[2] all of which were present in the current case. The average mitotic count in JGCTs has been reported to be 7 per 10 high-power fields.[2] In our case, mitotic activity was high focally, reaching up to 10 mitoses per high-power field. In addition, JGCTs can show focally prominent luteinization.[2]

The differential diagnoses of granulosa cell tumor may include undifferentiated carcinoma, small cell carcinoma of the ovary, endometrial stromal sarcoma, thecoma, cellular fibroma, large solitary luteinized follicle cyst of pregnancy, endometrioid carcinoma with sex cord–like patterns, steroid cell tumor, carcinoid tumor, gonadoblastoma, sex cord stromal tumor with annular tubules, metastatic melanoma, and metastatic lobular carcinoma of breast.[3,7] The differentiation of granulosa cell tumor, which is a low-grade malignancy from its mimics, some of which are highly malignant neoplasms, can be aided by immunohistochemical analysis using recently described markers, including α-inhibin, CD99, mullerian inhibiting substance, and melan-A.[8] Of these, α-inhibin appears to be the most specific for sex cord–stromal differentiation and helps to differentiate granulosa cell tumor from its mimics of non–sex cord–stromal differentiation.[8]

The most striking feature of our case was the absence of typical features of AGCT, such as Call-Exner bodies, follicular areas, and ''coffee-bean'' nuclei. Instead, there were prominent microcystic areas interspersed with nests of round-to-oval cells more akin to JGCT. In some areas, the microcysts were clustered together, creating alternating solid and microcystic pattern. However, JGCT is rare in adults older than 30 years, with 97% of cases occurring in the first 3 decades in one large series.[2] Thus, the current case brings out the point that AGCT and JGCT can show a significant morphologic overlap and that these 2 tumors perhaps represent the 2 ends of a morphologic spectrum. This viewpoint is further supported by the fact that both morphologic types show positive immunostaining with inhibin and similar cytogenetic profile.[9,10]

References

1. Czernobilsky B, Lifschitz-Mercer B, Roth LR. The ovary and fallopian tube. In: Silverberg SG, DeLellis RA, Frable WJ, eds. *Principles and Practice of Surgical Pathology and Cytopathology.* 3rd ed. New York, NY: Churchill Livingstone Inc; 1997:2547–2550.
2. Young RH, Dickersin GR, Scully RE. Juvenile granulosa cell tumor of the ovary: a clinicopathological analysis of 125 cases. *Am J Surg Pathol.* 1984;8:575–596.
3. Cronje HS, Niemand I, Bam RH, Woodruff JD. Review of the granulosa-theca cell tumors from the emil Novak ovarian tumor registry. *Am J Obstet Gynecol.* 1999;180(2 pt 1):323–327.
4. Caron PJ, Cogne M, Rumeau JL, Hoff J. Androgenic granulosa cell tumor of the ovary: in vivo hormonal studies. *J Endocrinol Invest.* 1993;16:545–548.
5. Unkila-Kallio L, Tiitinen A, Wahlstrom T, Lehtovirta P, Leminen A. Reproductive features in women developing ovarian granulosa cell tumor at a fertile age. *Hum Reprod.* 2000;15:589–593.
6. Aboud E. Adult granulosa cell tumors of the ovary. *Eur J Gynaecol Oncol.* 1997;18:520–522.
7. Sex cord-stromal and steroid cell tumors. In: Clement PB, Young RH, eds. *Atlas of Gynecologic Surgical Pathology.* Philadelphia, Pa: WB Saunders Co; 2000:364–367.
8. McCluggage WG. Value of inhibin staining in gynecological pathology. *Int J Gynecol Pathol.* 2001;20:79–85.
9. Halperin D, Visscher DW, Wallis T, Lawrence WD. Evaluation of chromosome 12 copy number in ovarian granulosa cell tumors using interphase cytogenetics. *Int J Gynecol Pathol.* 1995;14:319–323.
10. Lindgren V, Waggoner S, Rotmensch J. Monosomy 22 in two ovarian granulosa cell tumors. *Cancer Genet Cytogenet.* 1996;89:93–97.