A 26-Year-Old Woman With Right Ovarian Mass

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A 26-year-old woman presented with abdominal pain and bilateral upper chest pain. She started noticing some lower abdominal discomfort/pain, which became more persistent for the last week and radiated to the upper abdomen and chest. Her medical history was significant for supraventricular tachycardia diagnosed 5 years previously that was treated medically for 3 years. The laboratory studies of the blood revealed a white blood cell count of 7.3 cells/μL; platelet count, 331 × 10^3 cells/μL; hemoglobin level, 13.6 g/dL; serum urea nitrogen level, 19 mg/dL (6.783 mmol/L); creatinine level, 1.1 mg/dL (97.24 μmol/L); potassium level, 3.5 mEq/dL; calcium level, 12.8 mg/dL (3.2 mmol/L); albumin level, 4.1 g/dL; thyroid-stimulating hormone level, 5.62 μU/mL; parathyroid hormone level, 4 pg/mL; and CA 125 level, 252 U/mL. The liver function test results were within normal limits. Transabdominal and transvaginal pelvic ultrasound revealed a large complex partially cystic and partially solid right adnexal mass, measuring 12.7 × 10.1 cm, with findings consistent with an ovarian neoplasm, possibly carcinoma. Computed axial tomography scan also suggested a focus of intraperitoneal metastatic disease. The bone scan showed no evidence of osseous metastasis. During exploratory laparotomy, a smooth-surfaced right ovary, measuring 12.0 cm in the longest dimension, was seen. The intraperitoneal exploration was grossly normal.

The specimen received by the pathology laboratory labeled “right ovary” was an ovoid mass, weighing 477 g and measuring 14 × 12 × 8 cm. The surface was smooth, with a prominent vascular pattern. Serial sectioning showed a predominantly solid tumor with gelatinous areas, foci of hemorrhage and necrosis, and small foci of cystic degeneration. The solid areas were soft and pale tan to gray (Figure 1). No residual ovarian tissue was seen.

Histologically, the sections showed a highly cellular neoplasm composed of small-to-medium–sized cells with scant cytoplasm and round-to-oval nuclei with focal spindling. The cells were arranged as solid sheets with numerous mitotic figures. Areas of necrosis, fibrin, and hemorrhage were seen. Ectatic blood vessels and occasional follicle-like spaces containing eosinophilic material were present (Figures 2 and 3). No vascular invasion or surface involvement was identified. Immunohistochemical studies revealed the tumor cells were immunoreactive for vimentin (Figure 4); focally immunoreactive for pan-cytokeratin (AE1/AE3/PCK26), CAM 5.2, and epithelial membrane antigen; and were immunonegative for α-inhibin, S100, chromogranin, and desmin.

What is your diagnosis?
Pathologic Diagnosis: Small Cell Carcinoma of Ovary, Hypercalcemic Type

Abstract

Small cell carcinoma of the ovary, hypercalcemic type (SCC-HT), is rare. It generally occurs in young women between 10 and 40 years of age (mean age, 23 years), although it has been reported in an 8-year-old girl. It is usually unilateral, but bilateral familial cases have been reported. Patients usually present with abdominal pain and swelling, and two thirds of the cases are associated with hypercalcemia.

Gross examination usually shows a large mass, between 6 and 26 cm (average, 15 cm). The tumor is typically solid, and pale white to gray. Areas of hemorrhage, necrosis, and cystic degeneration may be present. Microscopic examination shows tumor cells growing in a diffuse pattern (most common), or as small islands/nests, trabeculae, and cords. Follicle-like spaces containing eosinophilic fluid are present in 80% of the cases. The tumor cells are small and round with scant cytoplasm, hyperchromatic nuclei, and small nucleoli. Characteristically, there is brisk mitotic activity and there are foci of necrosis. Fifty percent of the tumors have a large-cell component, with eosinophilic cytoplasm, intracytoplasmic eosinophilic globules, eccentrically located vesicular or clear nuclei, and prominent nucleoli. Twelve percent of the tumors are associated with benign or malignant mucinous epithelium.

Immunohistochemical studies typically show immunoreactivity for one or more epithelial markers (pan-cytokeratin, epithelial membrane antigen, or CAM 5.2). Variable immunoreactivity for vimentin, neuron-specific enolase, parathyroid hormone–related protein and chromogranin has been observed. α-Inhibin, S100, B72.3, and desmin are generally immunonegative.

The differential diagnosis is broad and includes adult and juvenile granulosa cell tumor, primitive germ cell tumor, malignant lymphoma, primitive neuroectodermal tumor, neuroblastoma, desmoplastic small round cell tumor, small cell carcinoma (pulmonary type), and metastatic small cell carcinoma. Thorough sampling of the tumor with attention to the characteristic clinical, microscopic, and immunohistochemical features of these other tumors should allow distinction from SCC-HT.

In contrast to SCC-HT, adult granulosa cell tumors usually affect middle-aged to postmenopausal women, and are not associated with hypercalcemia. Microscopically, cells with grooved nuclei in a microfolllicular pattern and Call-Exner bodies are characteristic, and are not seen in SCC-HT. Granulosa cell tumors are immunoreactive for α-inhibin.

Juvenile granulosa cell tumor and SCC-HT can both occur in young women and can both have follicle-like structures microscopically, but juvenile granulosa cell tumor is commonly estrogenic, is not associated with hypercalcemia, and is almost always stage I. Conversely, SCC-HT is never estrogenic and only approximately half of the cases are stage I. Microscopically, these 2 tumors have some common features, but SCC-HT generally has a much higher mitotic rate. In difficult cases, immunohistochemistry for α-inhibin can be helpful in making this distinction.

Metastatic small cell carcinomas and small cell carcinomas of pulmonary type are very similar tumors. They differ from SCC-HT in that they usually occur in much older women, they display the characteristic cytologic features of small cell carcinomas (finely stippled chromatin and molding), and they are immunoreactive for thyroid transcription factor-1.

The prognosis for SCC-HT is generally poor. Surgery is the mainstay of therapy, with adjuvant chemotherapy, and radiation is often used as well. In the review of Young et al., 33% of the patients with stage IA disease were alive and free of tumor for an average of 5.7 years postoperatively. In contrast, only 10% of patients with stage IC disease and 6.5% of patients with stages II, III, and IV disease were alive without recurrence at the last follow-up. In their study, favorable prognostic factors for stage IA tumor included age older than 30 years, normal preoperative calcium level, tumor less than 10 cm, and the absence of a large-cell component.

References