Pulmonary Multiple Metastases of Ovarian Granulosa Cell Tumor 15 Years After Initial Diagnosis

We report a case of multiple pulmonary metastases occurring 15 years after an ovarian granulosa cell tumor was initially diagnosed. A 62-year-old woman undergoing left salpingo-oophorectomy for a granulosa cell tumor of the left ovary 15 years earlier presented with abnormal chest shadows. Computed tomography of the chest confirmed the presence of 3 well-defined nodular lesions, and Computed tomography of the abdomen and pelvis revealed a 3.5 × 2.5 cm partially solid, cystic pelvic mass. Left thoracotomy was conducted and tumors diagnosed as pulmonary metastases of a granulosa cell tumor. The pelvic mass was resected and infracolic omentectomy then conducted with total hysterectomy and right salpingo-oophorectomy including the adherent rectal segment. The pelvic mass proved to be a granulosa cell tumor. Adjuvant combination chemotherapy was started every 3 weeks and the woman has remained disease-free for 9 months.
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Key words: granulosa cell tumor, ovarian tumor, lung metastasis, metastatic lung tumor

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Granulosa cell tumors are uncommon sex cord-stromal ovarian tumors accounting for about 1.5% of all malignant ovarian tumors.[1] They are characterized by low malignant potential, local spread, late recurrence, and long-term patient survival. In contrast to that of epithelial ovarian carcinoma, the overall prognosis is very favorable. Recurrence usually occurs within the pelvis or abdomen as in epithelial ovarian carcinoma. Distant metastases of granulosa cell tumors outside the peritoneal cavity spreading hematogenously to the lungs, liver, and brain are uncommon.[2,3] We report a case of multiple pulmonary metastases of an ovarian granulosa cell tumor 15 years after initial diagnosis.

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Case

A 62-year-old woman presented with abnormal chest shadows in December 1998. Her medical history included a granulosa cell tumor of the ovary treated with left salpingo-oophorectomy in 1980, at which time no evidence of extraovarian spread was

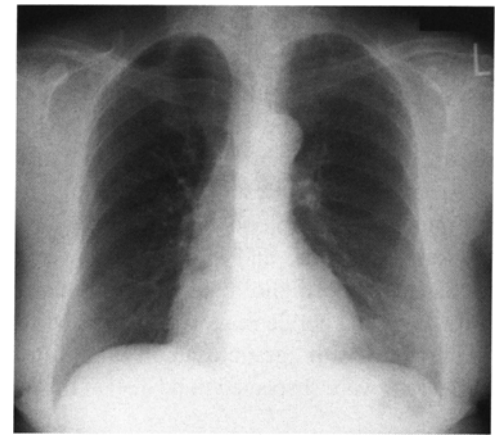

Fig. 1. Chest X-ray on admission showing 2 nodular shadows in the left lower lung field.

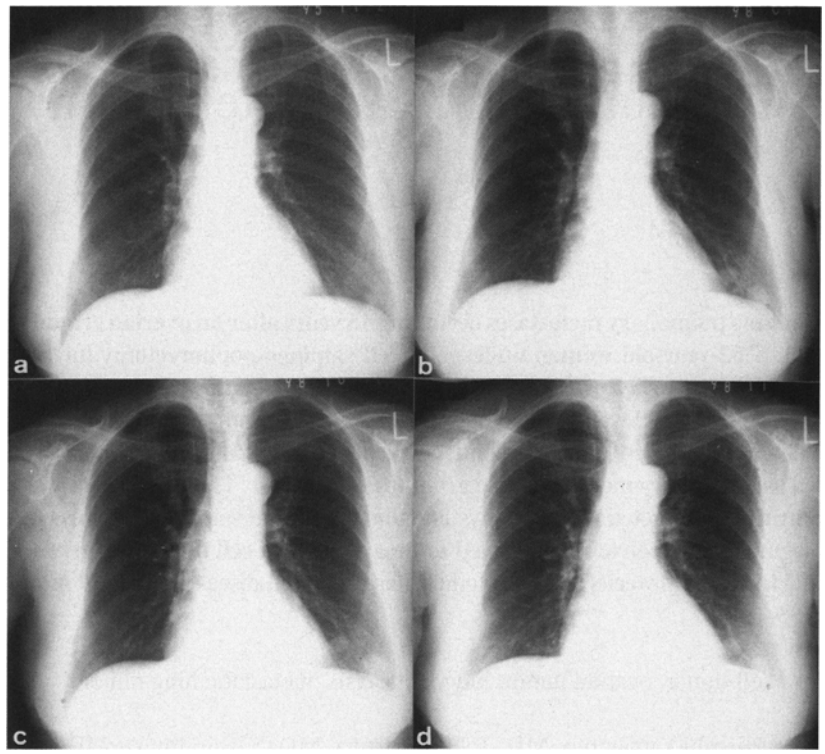

Fig. 2. Nodular shadows initially increased but later decreased in size. (a. Nov. 1995. b. Sep. 1998. c. Oct. 1998. d. Nov. 1998.)

seen and no additional therapy was prescribed. Abnormal chest shadows were noted during a regular physical examination in November 1995 and diagnosed as a benign calcified mass.

Chest X-ray on admission showed 2 nodular shadows in the left lower lung field (Fig. 1). Retrospectively, the nodular chest shadows initially had grown, then decreased 1 month later, suggesting hypervascular tumors (Fig. 2). Computed tomography (CT) of the chest confirmed the presence of 3 well-defined nodular lesions at S5, S8, and S10 in the left lung (Fig. 3). CT of the abdomen and pelvis showed a 3.5×2.5 cm partially solid, cystic right-sided pelvic mass (Fig. 4). The retroperitoneum, liver, kidneys, uterus, and pancreas appeared normal. Results of laboratory investigations including full blood count, plasma electrolytes, serum creatinine, and liver function test were normal and serum estradiol concentration upper normal. Clinically, the pelvic mass was suspected to be a local recurrence of the granulosa cell tumor and pulmonary lesions were suspected to be distant metastases of it.

Transbronchial biopsy results were nondiagnostic. CT guided percutaneous aspiration cytology suggested the specimen was carcinoid. In January 1999, left thoracotomy revealed 3 tumors palpable throughout the parenchyma of the lung and 2 other lesions disseminating to the visceral pleurae at S3 and S10 that were also suspected to be distant metastases. Excisional wedge biopsies of these tumors and disseminated lesions showed macroscopically that nodules were well circumscribed, multicystic, with hemorrhagic areas and a thin fibrous capsule. Intraoperative diagnosis of frozen sections showed poorly differentiated carcinoma or a neuroendocrine cell tumor.

Postoperatively, however, microscopic examination showed a mostly microfollicular growth with Call-Exner bodies and occasional diffuse and trabecular areas (Fig. 5). Nuclei showed minimal atypia with folds and grooves resulting in a characteristic "coffee bean" appearance (Fig. 6). Immunohistochemistry studies were strongly possitive for vimentin and entirely negative for chromogranin, EMA, and S-100 protein. These morphologic findings confirmed pulmonary metastases of the granulosa cell tumor.

Laparotomy in March 1999 showed a 3.5×2.5cm retroperitoneal, partially solid, cystic pelvic mass, which we resected, following up infracolic omentec-

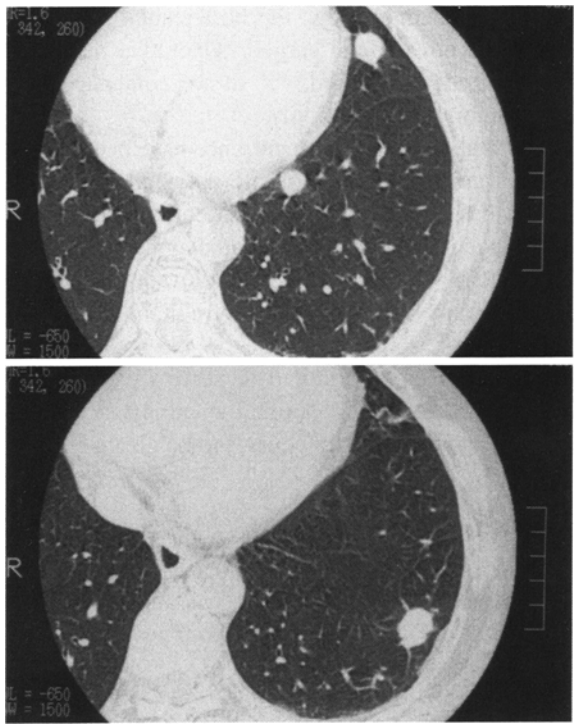

Fig. 3. Chest CT showing 3 well-defined nodular lesions in S5, S8, and S10 of the left lung.

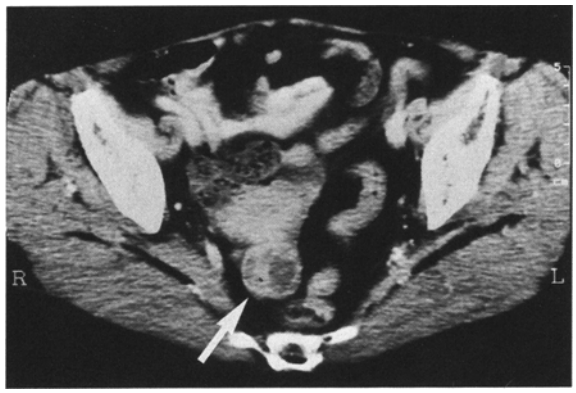

Fig. 4. CT of the pelvis demonstrating partially solid and cystic mass (arrow).

tomy with total hysterectomy and right salpingo-oophorectomy including the adherent rectal segment. The pelvic mass proved to be a recurrence of the granulosa cell tumor. Cytopathologic examination of ascites and peritoneal washings were negative.

Adjuvant combination chemotherapy was started with cisplatin (70 mg/body, day 1), epirubicin (50 mg/body, day 1), cyclophosphamide (500 mg/body, day 1) every 3 weeks, for a total of 6 courses. The patient is without evidence of recurrence 9 months later.

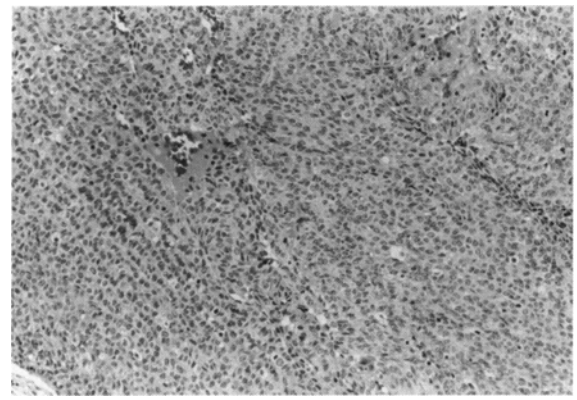

Fig. 5. Microfollicular growth with Call-Exner bodies and occasional diffuse and trabecular areas (H-E stain, × 40).

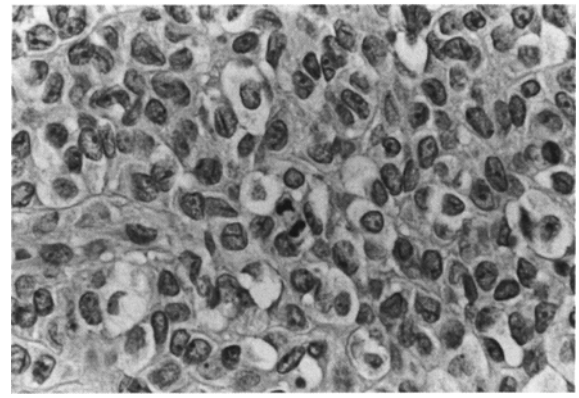

Fig. 6. Nuclei showing minimal atypia with folds and grooves resulting in the characteristic "coffee bean" appearance (H-E stain, × 400).

Discussion

The vast majority of granulosa cell tumors occur in adult women, with one-third in women of reproductive age and the remainder mostly in postmenopausal women. The mean age at diagnosis is 46.9 years.[1,3,4] Tumors are unilateral in 95% of cases, averaging about 12 cm in diameter.[1]

Granulosa cell tumor relapse occurs an average of 6 years after initial diagnosis,[2] but recurrences more than 20 years later have been reported. The latest reported recurrence was 37 years after initial diagnosis.[5] Although tumors may also spread hematogenously and metastases develop in the lungs, liver, and brain years after initial diagnosis, we could find few reports of cross-sectionally occurring metastatic granulosa cell tumors of the lung.[2,3,6–8] In our case, a recurrence in the pelvis occurred 15 years after initial diagnosis and rare multiple lung metastases were found simultaneously. We believe that the pelvic lesion arose from

the remaining right ovary and spreaded hematogenously to the lung.

When multiple lung lesions are detected in patients previously treated for malignant disease, all such lesions are generally assumed to be metastases. Since pulmonary metastases may be a manifestation of terminal disease, metastasectomy plays an important role in the management for selected patients. Surgery for metastatic lung tumors from a variety of primary sites has been aggressive. Pulmonary metastatic granulosa cell tumors are seldom reported in the literature and appear to be extremely rare, so treatment for granulosa cell tumors has not been standardized.

Metastatic tumors in the peripheral lung field usually show nodular shadows with compact components CT images. In our case, the nodular shadows initially had increased but decreased 1 month later, suggesting hemorrhagic components in tumors. Surgically resected specimens revealed a multicystic mass with evidence of hemorrhagic areas, and that is most common gross pathologic appearance of the granulosa cell tumor.

If a granulosa cell tumor is limited and localized to 1 or both ovaries, surgery alone is adequate and definitive and further adjuvant treatment is usually not needed. In our case, only surgery was conducted at initial diagnosis. Evans et al.[2] reported 56% of patients underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy, and more conservative unilateral salpingo-oophorectomy was often conducted in younger women to preserve reproductive function.

The extent of the initial surgical procedure affects recurrence rates statistically, with 6% of women undergoing total abdominal hysterectomy and bilateral salpingo-oophorectomy had recurrence, but those with less extensive procedure having a recurrence rate of 25%.[2] In our case, 15 years after unilateral salpingo-oophorectomy, local recurrence and pulmonary metastases occurred. Adequate treatment for granulosa cell tumors must be defined as total abdominal hysterectomy and bilateral salpingo-oophorectomy.

Although recurrent disease may respond to radiotherary or chemotherapy, the best results have been obtained from optimal surgery. Operative debulking is most commonly used,[2,3,5,7] so we conducted both thoracotomy and laparotomy.

Metastatic lesions and recurrence have been treated with a variety of antineoplastic drugs. Complete response has been reported for patients treated with a single agent, and in those treated with combinated VAC and CAP.[4] We conducted adjuvant combinated chemotherapy with cisplatin, epirubicin, and cyclophosphamide. Reported studies to the present, however, have been too limited to serve as a basis for conclusions regarding optimal combinated chemotherapy or the number of courses to be given.

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