Case Reports

A case of granulosa cell tumor of the ovary detected from metastatic foci

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Summary

The authors report a case of granulosa cell tumor of the ovary that followed a rare clinical course, where the primary focus did not appear as a mass, and disseminated foci grew in the abdominal cavity. In 2008, a 70-year-old patient, gravida 6 and para 3, was diagnosed with a perihepatic mass, peritoneal dissemination, and an abdominal wall mass as confirmed by computed tomography (CT) scanning. There was no mass lesion in the pelvis. The pathological diagnosis based on the resected mass in the abdominal wall was malignant mesothelioma. During follow-up, abdominal bloating developed from April 2009. CT scans indicated growth of the intraperitoneal lesions. Therefore, the patient received two cycles of combination therapy with cisplatin and pemetrexed. The treatment was discontinued due to lack of efficacy. The intraperitoneal lesions grew but the clinical course was slow and inconsistent with that of malignant mesothelioma. Central pathological review was requested in April 2011, and a granulosa cell tumor was diagnosed. The patient was referred to the department for detailed examination and treatment. The patient underwent incision of the intraperitoneal tumors, simple total hysterectomy, bilateral salpingo-oophorectomy, and omentectomy. The final pathological diagnosis was normal-size adult-type granulosa cell tumor originating from the left ovary. It was a case of granulosa cell tumor without ovarian enlargement where growth of the metastatic foci was the major observation. As complete surgical resection was achieved and no additional therapy was given, the subject was followed on an outpatient basis and no recurrence was identified.

Key words: Granulosa cell tumor; A rare clinical course; Debulking surgery.

Introduction

Granulosa cell tumors of the ovary account for 1.9% of primary ovarian tumors and 6.0% of malignant ovarian tumors [1, 2]. The prognosis in general is considered good in the early stages, however, there are some studies reporting that late recurrence more than ten years after surgery is not uncommon [3-5]. Postoperative follow-up is necessary for a long period of time. Metastases outside the ovary usually remain within the pelvis, with distant metastases that are apparently rare [6]. The authors report a case of granulosa cell tumor of the ovary with an unusual clinical course, where the primary focus did not appear as a mass, and disseminated foci alone grew in the abdominal cavity.

Case report

The patient was a 70-year-old female, gravida 6 and para 3, who underwent menopause at the age of 50 years. The patient had undergone an appendectomy at the age of 20 years and had goiter surgery at 30 years.

The patient noticed an abdominal mass in 2008 and consulted a medical practitioner. A perihepatic mass, peritoneal dissemination, and an abdominal wall mass were detected on CT scans. A pelvic mass was not noted at that point. The patient was referred to the department of gastroenterological surgery at a general hospital for detailed examination. The mass in the abdominal wall was resected for diagnostic purposes. Subsequent histopathology findings indicated a diagnosis of malignant mesothelioma. On this basis, the patient was to be followed without postoperative treatment. In 2009, abdominal bloating developed. Another CT scan confirmed an apparently enlarged perihepatic lesion along with the peritoneal dissemination. The patient requested chemotherapy and other treatment and visited the department of medical oncology at our hospital for consultation in April 2009. The patient was to be followed as an outpatient as progression of the disease was slow. Periodic CT scans identified further enlargement of the intraperitoneal lesions. Accordingly, the patient was started on a treatment regimen for malignant mesothelioma. This consisted of two cycles of combination therapy with cisplatin and pemetrexed. However, the treatment was discontinued due to lack of efficacy. Right lower quadrant abdominal pain developed from the Spring of 2010. Simultaneously, enlargement of the intraperitoneal lesions were identified by a CT scan. However, the clinical course was not consistent with that of malignant mesothelioma, which is often rapidly fatal. The histopathology was re-examined. As a result of the central pathologic review, a granulosa cell tumor was diagnosed (Figure 1A). The patient visited our department for detailed examination and treatment in April 2011. The patient was to undergo surgery for adult-type granulosa tumor, although the primary lesion was unidentified.

The levels of tumor markers were within the normal range, except for a slightly elevated CA-125 of 69 U/ml. The estradiol level was 38.4 pg/ml, considered high for her age. No abnormalities were detected in other blood data. A transvaginal ultrasound (TVUS) at the initial consultation did not identify endometrial thickening or ovarian enlargement. As ascites retention was detected in Douglas' pouch, aspiration biopsy cytology

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Fig. 1A

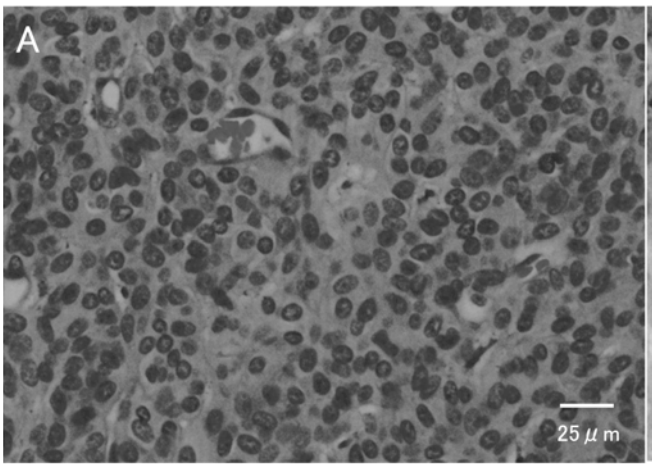


Fig. 1B

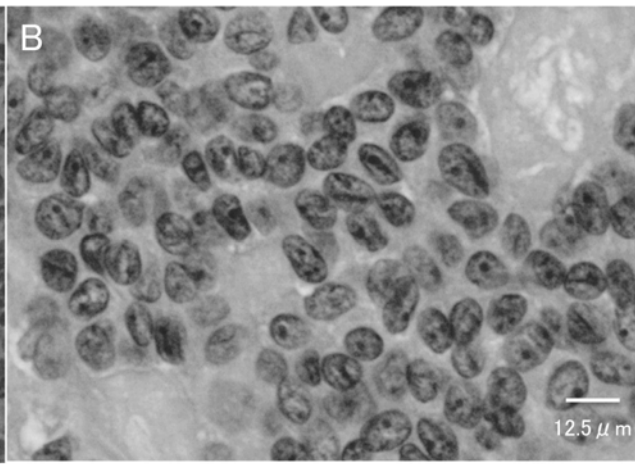


Fig. 2A

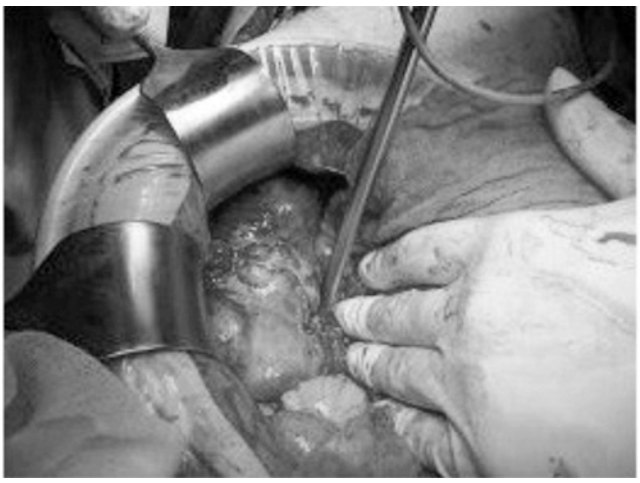


Fig. 2B

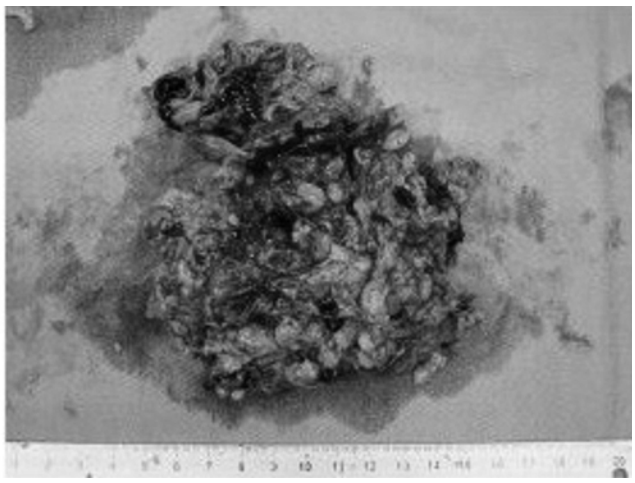
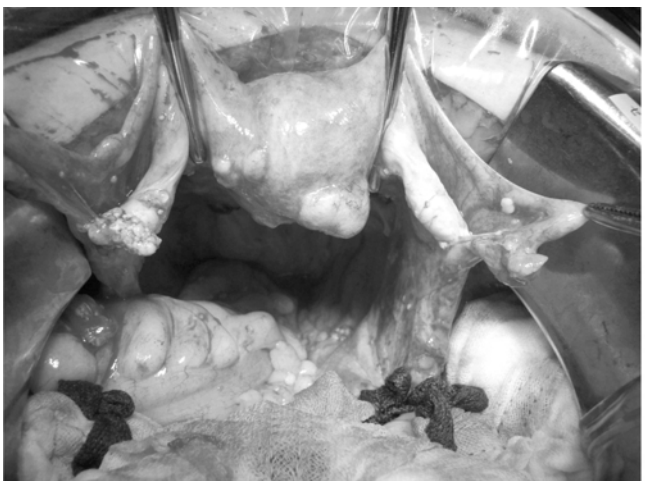


Fig. 3



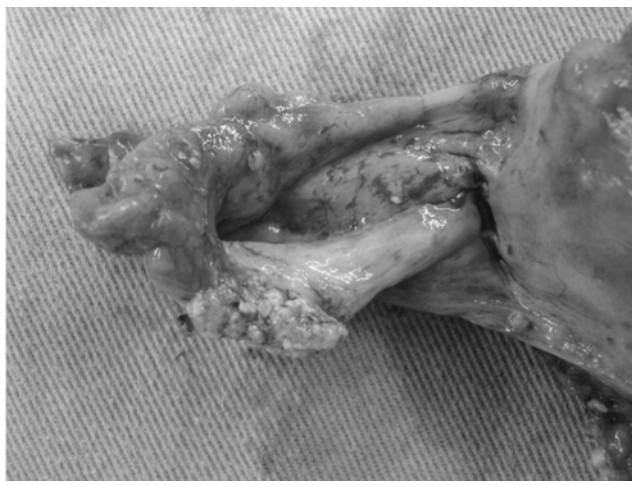


Figure 1. — A) Pathological findings in the abdominal wall mass. B) Pathological findings in the left ovarian lesion. The tumor cells are relatively large, and near-circular coffee-bean nuclei are found. Call-Exner body-like structures can be identified in any specimen.

Figure 2. — A) Metastatic peritoneal mass near the ileocecal region. B) Macroscopic finding on the resected surface of the mass. It is solid, yellow, and fragile mass.

Figure 3. — Macroscopic findings in the internal genitalia. An apparent mass lesion was not detected, however, a yellowish lesion growing outward from the left ovary can be seen.

was performed. Atypical cells were not detected. A comparison of the images from an abdominopelvic CT scan performed in 2008 and in 2011 prior to surgery suggested that the masses under the right diaphragm, in the ileocecal region, and left lower abdominal quadrant, tended to enlarge and increase in number, however, progression of the mass was slow. No apparent enlargement in the ovaries was seen in any CT scans.

Laparotomy was performed in July 2011. A peritoneal mass around the ileocecal region (Figure 2A), a peritoneal mass under the right diaphragm, and an omental mass were found. The resected surfaces showed that all were solid, yellow, and fragile masses (Figure 2B). There were no apparent mass lesions in the internal genitalia, however, a yellowish lesion growing outward from the left ovary was detected (Figure 3). Incision of the intraperitoneal tumors, a simple total hysterectomy, bilateral salpingo-oophorectomy, and omentectomy were performed. Complete debulking surgery without any residual mass was achieved.

Pathological findings were that Call-Exner body-like structures were detected in the specimens of the abdominal wall mass (Figure 1A) and left ovarian lesion (Figure 1B), and in the mass cells relatively large and near-circular coffee-bean nuclei were detected. Immunostaining showed positive results for α-inhibin and calretinin. The lesion was considered to be an adult-type granulosa cell tumor originating from the left ovary.

The postoperative course was good. The patient was discharged 18 days after surgery. The postoperative estradiol level one month after surgery dropped below five pg/ml, lower than the measurement sensitivity level. The case was diagnosed as Stage IV granulosa cell tumor of the ovary. Complete surgical resection was achieved and the patient did not require additional treatment. The estradiol level remained low, and no recurrence or metastases were clinically found as of March 2012.

Discussion

The authors dealt with a case of granulosa cell tumor of the ovary with a clinical course that was quite rare in terms of the following: a granulosa cell tumor was diagnosed from the metastatic focus, while the disseminated foci were growing in the abdominal cavity and the primary focus did not appear as a mass.

Granulosa cell tumors are categorized as gonadostromal borderline malignancies. These tumors are characterized by slow progression and have a relatively good prognosis. However, recurrence more than ten years after surgery has been reported [3]. In rare cases, malignant courses such as intraperitoneal dissemination and hepatic metastases have also been reported [6]. Ninety percent of the patients with granulosa cell tumor present with a Stage I tumor. Approximately 95% of cases are unilateral [7].

First-line therapy is surgical treatment. The same treatment for malignant ovarian tumors is adopted in most cases. Simple total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and staging laparotomy are recommended for the initial operation [8]. For patients in which fertility must be preserved and the lesion is confined to the ovaries, unilateral salpingo-oophorectomy alone will be performed. In such a case, patients must be placed under strict postoperative management [9]. More than 95% of young patients are in Stage IA, and unilateral salpingo-oophorectomy is selected for such patients. The five-year survival rate in Stage I and II is good, at 95%, while that in Stages III and IV is not as good, at 59% [9]. If an appropriate staging is achieved, surgical treatment alone may be sufficient for initial treatment in Stage I. As in the presented case, however, recurrence occurs in 20% to 30% of adult-type granulosa cell tumors. A ruptured tumor, Stage IC, low differentiation and tumors not less than 10 cm to 15 cm in diameter are considered risk factors for recurrence in Stage I. Postoperative treatment such as chemotherapy is recommended for Stages IC, II and more advanced stages [10]. Chemotherapy regimens such as BEP (bleomycin, etoposide, and cisplatin) therapy, PVB (cisplatin, vinblastine, and bleomycin) therapy, and TC (paclitaxel and carboplatin) therapy demonstrate relatively high response rates [11, 12]. However, phase III clinical trials of chemotherapy for the treatment of granulosa cell tumors have not been conducted, and effective therapies have not yet been established. Where there are residual lesions or the patient is at high-risk of recurrence or where recurrence has already occurred, chemotherapy, including use of platinum-containing drugs, is considered to be indicated.

The patient in this case was diagnosed with a Stage IV granulosa cell tumor. Since the surgery in this case was performed successfully, leaving no residual tumor, additional treatment, such as postoperative chemotherapy, was not necessary. The association between the presence or absence of residual lesions and patient prognosis has been recognized in multiple studies [13-16], although multivariate analysis is not often performed. It has been suggested that total resection in debulking surgery significantly prolongs disease-free survival in cases of recurrence or metastasis. In cases such as this with a slow clinical course, disease-free status may be maintained for a long period, even in Stage IV, as long as a complete surgical resection is achieved. The patient in this case did not appear to have clinical signs of recurrence or metastasis, but a long follow-up period is considered necessary, due to the very slow tumor progression, insufficient data on prognosis, and the unusual clinical course.

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