Ovarian serous carcinoma in which mediastinal recurrence of the cancer was resected 16 years after surgery: A case report

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Abstract
We report a rare case of ovarian carcinoma in which a mediastinal recurrence was resected 16 years after the initial operation. A 72-year-old woman underwent hysterectomy with adnexectomy for stage IIIIC ovarian serous carcinoma after neoadjuvant chemotherapy. Six courses of adjuvant chemotherapy were administered. Three years after surgery, left supraclavicular lymph node metastasis occurred, and radiotherapy and two courses of chemotherapy were administered. Six years before presentation, a metastasis at the right cardiophrenic lymph node was resected, and six courses of chemotherapy were administered. During follow-up, a retrosternal tumour was found. The metastatic lesion in contact with the diaphragm was thought to result from pleuropertitoneal communication, and it increased in size. Although high-grade serous carcinoma is aggressive, its sensitivity to chemotherapy may suppress early recurrence, contributing to good outcomes, but with late recurrence. Multidisciplinary therapy including surgery is required for improved long-term prognosis for mediastinal metastasis of ovarian serous carcinoma.

KEYWORDS
late recurrence, mediastinal recurrence, ovarian cancer, serous carcinoma

INTRODUCTION
Recurrence of ovarian cancer often occurs in the abdominal cavity, but there are only a few reports of its recurrence in the thoracic cavity and mediastinum. Here, we report a case of ovarian serous carcinoma in which a mediastinal recurrence was resected 16 years after the initial operation.

CASE REPORT
A 72-year-old Japanese woman presented with an abnormal shadow on chest computed tomography (CT). Sixteen years previously, peritoneal dissemination was observed when laparotomy was performed based on a diagnosis of ovarian cancer. After four courses of chemotherapy consisting of carboplatin and paclitaxel, hysterectomy with adnexectomy was performed. The pathological finding was stage IIIIC serous cystadenocarcinoma. Six courses of adjuvant chemotherapy composed of the regimen mentioned above were administered. Three years after surgery, left supraclavicular lymph node metastasis occurred, and the patient was irradiated (70 Gy/35 fractions) after two courses of chemotherapy composed of carboplatin and paclitaxel. Six years before presentation, a metastatic lesion at the right cardiophrenic extrapulmonary area suspicious of lymph node metastasis was resected under the complete video-assisted thoracic

FIGURE 1 Chest computed tomography image showing a mediastinal tumour over 6 years
surgery, and six courses of chemotherapy also composed of carboplatin and paclitaxel were administered at another hospital.

During follow-up, a tumour that kept increasing in size was found in the inferior retrosternum of the anterior mediastinum, and the patient was referred to our department. Chest CT revealed a tumour sized 52 × 21 mm that was not detected 6 years previously (Figure 1). Thymoma or ovarian cancer metastasis was suspected. The tumour was removed via a median sternotomy; it was strongly adhered to the diaphragm, which was resected along with the tumour. The tumour was an adenocarcinoma, with a similar histology to that of the ovarian cancer resected 16 years ago (Figure 2). Immunostaining revealed that the mediastinal metastasis of ovarian cancer that was p53-positive, WT1-positive, partially ER-positive and napsin A-negative. The stainability was same as that of the ovarian cancer. No obvious infiltration was observed in the diaphragm. Six courses of adjuvant chemotherapy with carboplatin and paclitaxel as well as radiotherapy were administered, and no metastasis or recurrence was observed 10 months after the operation (Table 1).

**DISCUSSION**

Serous carcinoma is the most common histological type of ovarian cancer, accounting for 40% of all cases of ovarian cancer. A recent study showed that it originates from the fallopian tube epithelium and secondarily involves the ovary.\(^1\) Serous carcinoma is classified into low-grade and high-grade types. The former exhibits slow progression with borderline malignancy as a precursor lesion, and the prognosis is good. The latter has no precursor lesions and exhibits aggressive progression, often leading to peritoneal dissemination, and it has a poor prognosis.\(^1\) Our case had a pathological diagnosis of high-grade serous carcinoma.

To our knowledge, there are only seven reports of mediastinal metastasis from ovarian cancer other than mediastinal lymph nodes metastasis, including our case, and all seven were cases of serous carcinoma (Table 2). The reports clearly stated that mediastinal lymph node metastasis were

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**FIGURE 2** Histological findings of mediastinal tumour resembled those of primary ovarian serous carcinoma

**TABLE 1** Timeline of treatment

| Date  | Clinical findings | Treatment |
|-------|-------------------|-----------|
| X-16  | Ovarian cancer    | Laparotomy; peritoneal dissemination Four courses of chemotherapy (CBDCA + PAC) Hysterectomy + adnexectomy |
| X-13  | Left supraclavicular LN metastasis | Two courses of chemotherapy (CBDCA + PAC) Radiotherapy 70 Gy/35 fractions |
| X-6   | Metastasis at the right Cardiophrenic area | Resection Six courses of chemotherapy (CBDCA + PAC) |
| X     | Mediastinal metastasis | Resection |

Abbreviations: CBDCA, carboplatin; LN, lymph node; PAC, paclitaxel.

**TABLE 2** Mediastinal metastasis from ovarian cancer

| First author | Histological type | Time to recurrence (years) | Part of mediastinum with recurrence | Recurrence site | Number of metastases | Treatment |
|--------------|-------------------|----------------------------|------------------------------------|----------------|----------------------|-----------|
| Montero\(^2\) | Low grade Serous | 0                          | Anterior                           | Inferior Retrosternum | Oligo                | Resection |
| Lu\(^3\)     | Papillary Serous  | >20                        | Anterior                           | Cardiophrenic ~Thymus  | Multiple             | Resection |
| Chase\(^4\)  | Psammoma Serous   | 0                          | Anterior                           | Cardiophrenic ~Superior mediastinum | Multiple             | Hormonal Cyberknife |
| Scarci\(^5\) | High grade Serous | 0                          | Middle                             |                | Oligo                | Resection |
| Inoue\(^6\)  | Papillary Serous  | 29                         | Anterior                           | Cardiophrenic      | Oligo                | Resection |
| Omura\(^7\)  | Low grade Serous  | 33                         | Anterior                           | Thymus            | Oligo                | Resection |
| Present      | High grade Serous | 16                         | Anterior                           | Inferior Retrosternum | Oligo                | Resection |

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\(^1\) MIURA ET AL.
excluded. In all cases but one, thymic metastasis was in contact with the diaphragm. One case involved a cystic mass abutting the pericardium in the middle mediastinum. A tumour reported by Lu and Goldblatt was speculated to invade to the diaphragm according to their operative findings. Of the seven cases, tumours were present in the cardiophrenic area in three cases. In two cases including our case, a tumour was found in the anterior mediastinum at the inferior retrosternum. In our case, a tumour located at the right cardiophrenic lesion suspicious of lymph node metastasis was found 6 years previously and was resected at another hospital. Lymph nodes were originally found at the site of the cardiophrenic lesion, and the tumour that metastasized to this lymph node may have increased in size and replaced the lymph nodes. Lopes et al. performed cardiophrenic lymph node resection in 29 of 456 patients with stage IIIC–IV epithelial ovarian carcinoma and found lymph node involvement in 24 patients. Twenty-two of the cases were high-grade serous carcinoma. In addition to lymph node metastasis, the metastatic lesion in contact with the diaphragm was thought to be due to pleuroperitoneal communication and the migrated tumour cells attached to the diaphragm.

Inoue et al. reported a case of ovarian serous carcinoma that metastasized to the anterior mediastinum 29 years after the initial treatment. In addition, they referred to the literature about ovarian cancer that recurred more than 20 years after surgery, and all of them involved serous carcinoma.

Although high-grade serous carcinoma is aggressive, it is responsive to chemotherapy. Conversely, chemotherapy was not associated with improved survival for low-grade serous carcinoma. Serous carcinoma is common in epithelial ovarian cancer, and its sensitivity to chemotherapy may suppress early recurrence, contributing to good outcomes but with late recurrence. Multi-disciplinary therapy including surgery is required for improved long-term prognosis in mediastinal metastasis of ovarian serous carcinoma.

AUTHOR CONTRIBUTION
Dr Hiroyuki Miura and Dr Shinichi Goto helped in the conception and design of the work and the acquisition and analysis or interpretation of data for the work. Dr Jun Miura drafted the work and revised it critically for important intellectual content. Dr Tomoko Yamamoto diagnosed this cancer pathologically. All authors contributed to the final version of this manuscript and approved it to be published.

CONFLICT OF INTEREST
None declared.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT
Appropriate written informed consent was obtained for the publication of this case report and accompanying images.

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