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## Case Report

## A case of ruptured ovarian metastasis of small cell lung cancer

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## ABSTRACT

A 53-year-old woman with small-cell lung cancer (SCLC) presented at our hospital complaining of abdominal distention. Blood tests revealed rapidly progressive normocytic anemia and elevated lactate dehydrogenase levels. Pelvic magnetic resonance imaging revealed a left ovarian tumor and ascites. As her symptoms rapidly worsened, she underwent emergency surgery, which revealed a ruptured metastatic ovarian tumor of SCLC. Emergency surgery averted a life-threatening situation in this patient, and subsequent chemotherapy facilitated long-term survival. As seen from literature review, in female SCLC patients, ovarian metastasis and rupture is a rare but possible complication that should be considered because of its life-threatening nature.

## 1. Introduction

Metastatic ovarian tumors usually originate from gastrointestinal malignancies or breast cancer, and rarely from lung cancer. Among metastatic ovarian tumors, metastasis from lung cancer accounts for 0.4%, and approximately half are small cell lung cancers (SCLC) [1]. Twenty-five cases of ovarian metastasis from SCLC have been reported, and the prognosis was poor in almost all cases. Herein, we report a case of a patient with ruptured ovarian metastasis of SCLC that required emergency surgery and subsequent chemotherapy, with a good prognosis.

## 2. Case presentation

A 53-year-old woman was admitted to our hospital owing to a fast-growing ovarian mass and exacerbation of her abdominal distention. Her medical history included dyslipidemia, hypertension, and autosomal dominant polycystic kidney disease. Her regular medications included atorvastatin, tolvaptan, and olmesartan. The patient had no history of smoking. She had been diagnosed with SCLC (cT4N2M0 stage 3 B, limited disease) ten months previously and had been in complete remission (CR) after chemoradiation therapy. Four months after the CR decision, whole-body computed tomography (CT) and brain magnetic resonance imaging (MRI) revealed a small metastatic brain tumor, and she underwent stereotactic radiosurgery (SRS). Two weeks after the SRS, her carcinoembryonic antigen (CEA) level increased from 1.9 ng/mL to 40.4 ng/mL. Her serum pro-gastrin-releasing peptide (Pro-GRP) level had been within the normal range since the time of diagnosis, and the test at this time was also within the normal range. Upper gastrointestinal endoscopy and colonoscopy were performed and no abnormalities were detected. Positron emission tomography with 2-deoxy fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (18-FDG-PET/CT) revealed an abnormal

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accumulation of FDG in the left ovarian mass (Fig. 1); this was not observed with 18-FDG-PET/CT performed a year previously. Pelvic MRI showed a left ovarian tumor (150 × 92 × 116 mm) with low intensity on T1-weighted images and high intensity on T2-weighted images (Fig. 1). Two weeks after these tests, her abdomen was suddenly distended, and she was admitted to our hospital.

Her initial vital signs were as follows: blood pressure, 107/81 mmHg; pulse, 101/min; and respiratory rate, 16/min with an O<sub>2</sub> saturation of 98% on room air. The abdomen was distended with a large, palpable mass. Pelvic examination revealed a hard mass and tenderness in cervical motion. Blood tests showed normocytic anemia (hemoglobin, 7.7 g/dL; and hematocrit, 23.6%, which had been 12.4 g/dL and 37.8%, respectively, two weeks previously) and high lactate dehydrogenase (LDH) levels (782 U/L). Liver function test results and electrolyte levels were normal. All measured tumor markers were elevated (CEA, 38.3 ng/mL; CA 19–9, 60.8 U/mL; and CA 125, 299.1 U/mL). Abdominopelvic CT revealed a large mass (145 × 180 mm) in the center of the pelvis, which had enlarged rapidly since the MRI taken two weeks earlier. Multiple lymphadenopathies were also observed around the abdominal aorta.

Emergency bilateral salpingo-oophorectomy was performed the day after admission due to the extreme progression of abdominal distension, abdominal pain, and anemia (Hb decreased from 7.7 g/dL to 6.0 g/dL in 6 hours after admission). Intraoperative findings showed a large, multilobulated left ovarian tumor that had ruptured and was bleeding. Hemorrhagic ascites was also observed. No other metastatic foci were observed in the pelvis. Pathological examination of the left ovarian tumor revealed small-cell cancer with a partial glandular structure (Fig. 2). The results of immunohistochemical staining were as follows: positive for synaptophysin, CD 56, CK 7, CK 20, and MIB-1, and negative for chromogranin A, TTF-1, and napsin A. Based on these results and comparison with previous SCLC histopathological specimens, a diagnosis of ovarian metastasis of SCLC was made. Although macroscopic findings of the right ovary were normal, pathological examination revealed SCLC metastasis in the right ovary. Cytological examination of the ascites also revealed SCLC. Based on these findings, chemotherapy with carboplatin and etoposide was initiated shortly after surgery. Tumor markers (CEA, CA 19–9, and CA 125) normalized after these treatments, and 10 months after surgery, the patient remained in good health with no evidence of recurrence.

### 3. Discussion

SCLC accounts for approximately 15% of all lung cancers, is a fast-growing, highly malignant tumor [2], and is characterized by high sensitivity to radio- and chemotherapy. SCLC has a high potential for metastasis and is generally considered an advanced-stage disease. The common sites of metastasis from SCLC are the liver, brain, bone, and adrenal glands, with few reports of metastatic ovarian tumors. Conversely, metastatic ovarian cancer accounts for 5–30% of malignant ovarian cancers [3]. The common sites of primary origin are the breast, endometrium, and gastrointestinal malignancies [3,4]. The frequency of ovarian metastasis of lung cancer is very low, accounting for 0.4% of metastatic ovarian cancers. The routes of ovarian metastasis include hematogenous, lymphangitic, and peritoneal seeding, with hematogenous and lymphangitic metastases being more common in lung cancer. The most common histology is small cell carcinoma (44%), followed by adenocarcinoma (34%) [1]. Ovarian metastasis due to SCLC was reported in 10 papers with 25 cases [1,5–13] (Table 1), and the median age of these patients was 42 years (range, 24–71 years). Although SCLC is more common in older adults, ovarian metastasis is more likely to occur in younger age groups. Almost all reported patients

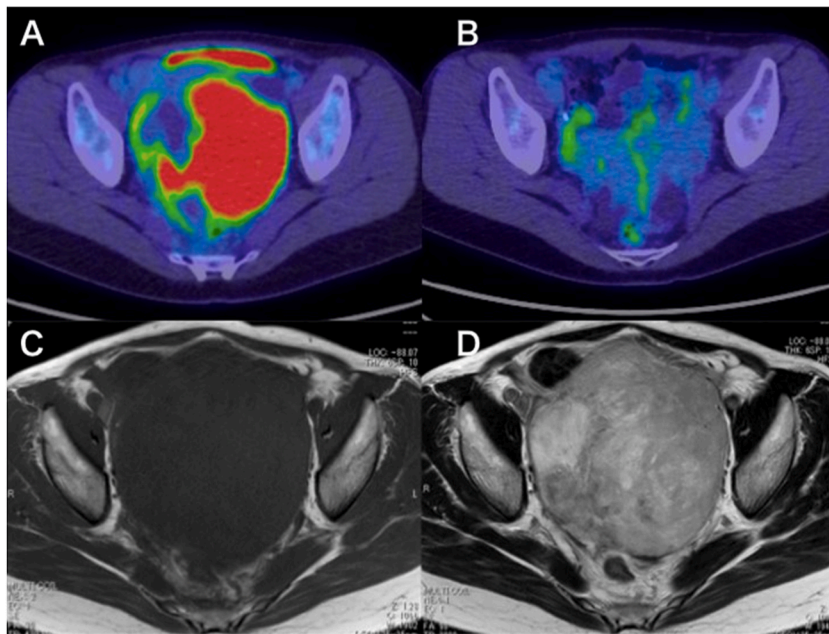
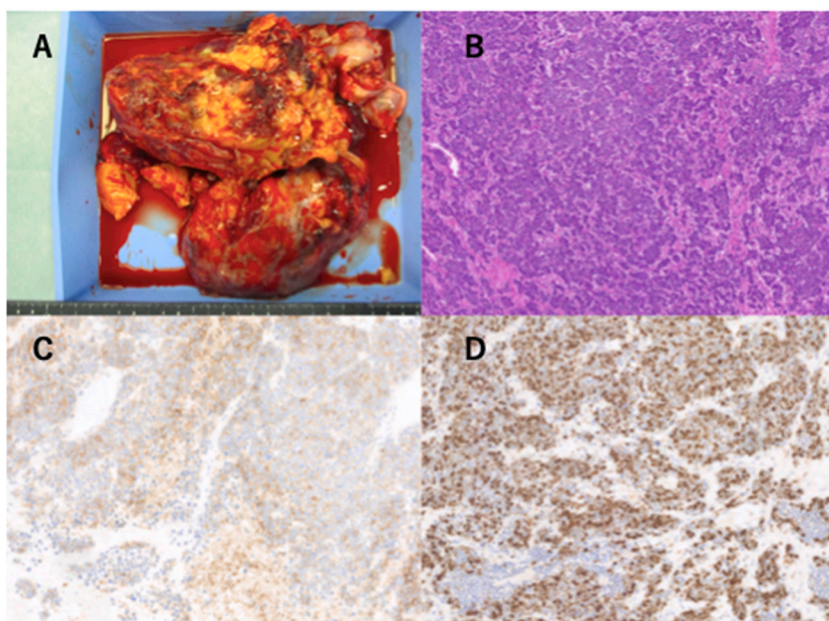


Fig. 1. Positron emission tomography (PET) showed abnormal accumulation of FDG in left ovary (A). This finding was not present a year ago (B). Pelvic magnetic resonance imaging (MRI) showed left ovarian tumor (150mm × 92mm × 116mm) with low intensity on T1-weighted image (C) and high intensity on T2-weighted image (D).



**Fig. 2.** Gross finding of ovarian tumor (A). Small cell carcinoma cells with a high N/C ratio were found and are accompanied by glandular structures containing intracellular mucus (B). Immunohistochemical staining of the metastatic ovarian tumor cells was positive for CD56 (C) and MIB-1 (D).

had undergone surgery for ovarian tumors, and in four cases [7,8,12], ovarian tumors were discovered before the lung cancer was detected. Differentiating between primary and metastatic ovarian tumors is paramount because of the differences in treatment. However, determining whether an ovarian tumor is primary or metastatic preoperatively is challenging because the clinical and imaging findings are similar. Regarding the localization of tumors, 52.6–54.5% of cases with metastatic ovarian cancer had bilateral ovarian involvement [3,4]. A history of malignancy [2], tumor size <9 cm [14], and normal or mildly elevated CA 125 levels [15] suggested a secondary ovarian tumor. The presence of ovarian primary SCLC requires careful differentiation from metastatic ovarian

**Table 1**

Literature review of previously reported cases with metastatic ovarian cancer due to small cell lung cancer.

References	Age	Size	Laterality	Smoking history	Immunocytochemistry	Treatment to ovarian metastasis
Kitazawa J et al. [5]	42	4cm	L	+	TTF-1 (+) Synaptophysin (+) chromogranin A (+)	Surgery
Moro F et al. [6]	24	R:20cm L:3cm	B	NA	neuroendocrine markers (+)	Surgery + chemotherapy
Antonio C et al. [7]	24	NA	B	+	TTF-1 (+)	Surgery + chemotherapy
Garcia V et al. [8]	54	4.8cm	L	+	Synaptophysin (+) chromogranin A (+) p53 (+)	Surgery + chemotherapy
Kadiev S et al. [9]	53	20cm	L	+	NA	Surgery + chemotherapy
Sukumvanich P et al. [10]	42	R:7.2cm L:4.4cm	B	-	NA	Chemotherapy
Bing Z et al. [11]	62	R:19.5cm	R	+	TTF-1 (+) chromogranin A (+)	Surgery + chemotherapy
Young RH et al. [12]	40 (range, 26–42)	8.5–10cm	R: 1 case B: 1 case L: 1 case	+: 1 case NA: 2 cases	NA	Surgery: 2 cases Surgery + radiation therapy: 1 case
Malviya VK et al. [13]	40	19cm	R	+	NA	Surgery
Irving JA et al. [1]	46 (range, 26–71)	0.15–26cm	R: 4 cases B: 5 cases L: 5 cases	+: 4 cases NA: 10 cases	TTF-1 (+): 4 cases	Surgery: 14 cases
Our case	53	L:15cm	Bilateral	-	synaptophysin (+) chromogranin A (-) CD56 (+) TTF-1 (-) Napsin A (-) CK7 (-) CK20 (+), MIB-1 (+)	Surgery + chemotherapy

R: right, L: left, B: bilateral, NA: not available.

tumors. Although they present with similar histological and immunohistochemical findings [16], TTF-1, CK 7, and CK 20 staining are useful for distinguishing primary and metastatic ovarian cancer from small cell cancer [17–19].

In our case, a history of SCLC and the consistency of immunohistochemical staining between the lung and ovary lead to a diagnosis of metastatic ovarian cancer from SCLC. Our patient was relatively young, as previously reported, but was unique in that she had rapid progressive anemia and circulatory failure due to ovarian tumor rupture. Emergency surgery was performed to save her life.

The risk of metastatic ovarian tumor rupture has not yet been reported because of its rarity. Ovarian surface involvement is infrequent in metastatic ovarian cancer [1]; however, in our case, the lesion extended to the surface of the ovary, which was also considered a risk factor for rupture. For liver tumors, chemotherapy can trigger rupture due to tumor necrosis [20]; however, since no chemotherapy was administered prior to rupture in our case, rapid enlargement was the likely cause.

Even though the role of local treatment in patients with SCLC is limited, Kitazawa et al. reported a better clinical course in SCLC patients with metastasis to the ovary after surgical treatment [5]. Surgery is a possible alternative to chemotherapy for prevention of rupture and improvement of the prognosis for cases with ovarian metastasis. Our patient achieved partial recovery after surgery and subsequent chemotherapy.

To the best of our knowledge, this is the only reported case of emergency surgery for metastatic ovarian tumor rupture in a patient with SCLC. Although recent reports indicate that the 2-year survival rate for SCLC is only approximately 14–15% [21], immunotherapy and other treatments are under development to improve the prognosis. Therefore, the frequency of observation of ovarian metastases due to SCLC may increase. Clinical history, histology, and immunohistochemistry are essential for the accurate diagnosis of metastatic ovarian cancer.

#### 4. Conclusion

In conclusion, our case highlights the importance of awareness of small-cell ovarian metastases and the risk of rupture. Early intervention may reduce the risk of rupture and prolong prognosis.

#### Informed consent

Informed consent was obtained from the patient.

#### Declaration of competing interest

There are no conflicts of interest to declare.

#### Acknowledgements

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