

CASE REPORT

Ovarian Cancer Metastasis to Lung Parenchyma without Peritoneal Dissemination: A Rare Case

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Abstract: Ovarian cancer is the most lethal gynecological malignancy worldwide. Despite the advances in treatment for ovary cancer, the 5-year survival rate of advanced ovarian cancer patients with peritoneal metastasis remains as high as 30%. Clinical stage is the most important prognostic factor and most patients are at an advanced stage. There is often no clearly identifiable precursor lesion; therefore, the events which lead to metastatic disease are poorly understood. Solitary lung parenchyma metastasis is extremely rare. We report a case of 39-year-old woman who was admitted with a lung mass. She had a history of high-grade serous carcinoma ovary, which was detected and treated 6 years ago with cytoreductive surgery as well as hyperthermic intraperitoneal and adjuvant chemotherapy. During the routine follow-up, positron emission tomography computed tomography scan showed two nodules of soft-tissue density in the lung parenchyma of the left lower lobe with a dimension of 2.8 × 2.5 cm. Intraoperatively, two conglomerated lung nodules seen in lung parenchyma of the left lower lobe. Deeper nodule was in close proximity to the left lower lobe bronchus and left lower lobe pulmonary artery. Video-assisted thoracoscopic surgery was conducted to perform left lower lobectomy. Postoperatively, the patient was stable. Microscopically, the tumor was classified as a high-grade serous carcinoma, and the patient was diagnosed for having an ovarian cancer metastasis. Ovarian cancer rarely metastasizes to the lung parenchyma in a relapse. However, excision of lesion with further chemotherapy showed excellent results. Surgical excision biopsy and intraoperative frozen sectioning, followed by lobectomy or segmentectomy, are both diagnostic and therapeutic.

Keywords: Ovarian carcinoma; Lung parenchyma metastasis; Lobectomy

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1. Background

Ovarian carcinoma is the second most common gynecological malignancy and it is the most common cause of gynecologic death in the resource-abundant countries^[1]. To reduce ovarian cancer mortality, a screening program which can detect ovarian cancer at an early stage should be included, because ovarian cancer mortality is closely related to the stage of cancer at diagnosis. The 5-year survival of patients with distant metastasis is 25%; with regional disease is 75–80%; and with Stage 1 disease is over 90%. The poor survival rate is because the cancer in a high percentage (around 75%) of patients spreads beyond the ovary at the time of clinical detection. Early detection efforts with imaging, which only focused on the ovaries, might have missed the detection of many tumors^[2]. A model of univocal disease, which begins in the ovaries and progresses to diffuse disease, is plausible. However, it has been proposed that a substantial number of ovarian cancers may be multifocal and extra-ovarian at their earliest recognizable state. Development of

carcinomatosis has been observed even after the removal of ovaries^[3]. Little is known about the mechanism or timing of progression of the localized ovarian cancer to disseminated ovarian cancer. The spread of ovarian cancers to only lung parenchyma after 5 years of primary disease is rarely reported^[4]. Hematogenous spread of disease is a possible mode of metastasis of ovarian cancer^[5]. In this report, we present a case of high-grade serous carcinoma of the ovary with lung parenchyma metastasis.

2. Case presentation

In 2016, a 39-year-old woman was diagnosed with high-grade serous carcinoma ovary and was treated with cytoreductive surgery (total abdominal hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic, and paraaortic lymphadenectomy, total peritonectomy, and omentectomy) and hyperthermic intraperitoneal chemotherapy (outside the hospital) in August 2016, followed by six cycles of adjuvant chemotherapy containing paclitaxel (80 mg/m²) and cisplatin on a weekly schedule. Cisplatin was used in place of carboplatin due to allergy to carboplatin. The last chemotherapy was given on March 2017 and the patient was on regular follow-up.

The patient showed an increase in cancer antigen 125 (CA 125) level from 20 to 35.60 U/ml in August 2019, which was 2 years after the disease-free interval. Positron emission tomography (PET)-computed tomography (CT) scan showed a subcutaneous deposit in right iliac fossa, and no metastasis was seen in the body. Following examination, a 3 × 2 cm, firm to hard nodule was palpable in the right iliac fossa in the subcutaneous plane, on which a wide local excision of the nodule was carried out in September 2019. Based on the final histopathology report, the nodule was suggestive of ovarian high-grade serous carcinoma. The patient was given another six cycles of liposomal doxorubicin injection 30 mg/m², 472 mg, and bevacizumab 500 mg. The last chemotherapy was given in May 2021. The patient was on regular follow-up and was asymptomatic.

The CA 125 levels of the patient in January, May, and June 2022 were 7.7 U/ml, 13.5 U/ml, and 15.7 U/ml, respectively. The patient was asymptomatic, but in view of the rising CA125 level, the patient was advised for PET-CT scan. PET-CT scan, which was performed in May 2022, showed two conglomerated nodules of soft-tissue density that are F-fluorodeoxyglucose (FDG)-avid in the left lower lobe of the lung with a size of 2.8 × 2.5 cm x (Figure 1). No other signs of metastasis were seen in peritoneum or in any other parts of the body. Lung parenchyma metastasis originated from the carcinoma of ovary is very uncommon^[4]. The patient was planned for metastasectomy because of the second primary lung cancer in the patient.

Intraoperatively, diagnostic thoracoscopy was conducted and the findings are suggestive of two nodules

of 3 × 3 cm and 2 × 2 cm in the lung parenchyma of the left lower lobe. Deeper nodule was in close proximity to the left lower lobe bronchus and left lower lobe pulmonary artery branch. No other nodules were seen in the lung or pleural cavity. No pleural effusion or pleural nodules were noted. Under general anesthesia, the patient was positioned in the right lateral position. 10 mm port was inserted in the left eighth intercostal space. In view of close proximity of nodule to the left lower lobe bronchus and left lower lobe pulmonary artery branch, the procedure was converted to open anterolateral thoracotomy through incision of the fifth intercostal space muscle. The left lower lobe pulmonary artery was looped and ligated using Endo-GI-gold stapler. The left lower lobe bronchus was fixed using an Echlon green stapler and the left lower lobectomy was completed (Figure 2). Air leak was checked and hemostasis was secured. Closure was done over the left intercostal drainage tube.

The final histopathology report showed that the two tumor nodules, which are grayish white incolor, were 3 × 2 × 2.5 cm and 2.5 × 1.5 × 1.5 cm, in size (measurement in cc × tr × ap), respectively. The distance between the two discrete conglomerated nodules was 1 cm. Larger tumor

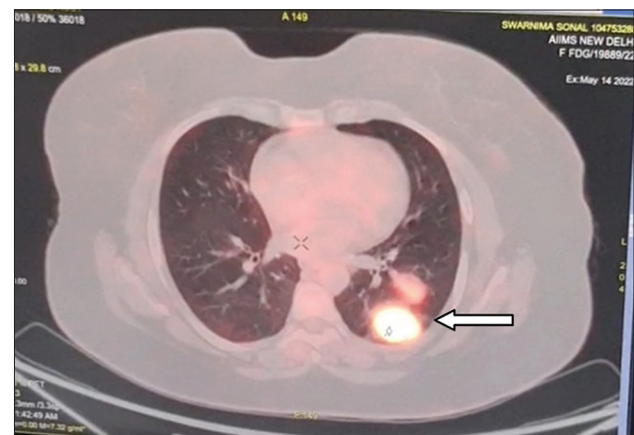


Figure 1. PET-CT scan showing two nodules in the left lower lobe of the lung (arrow), which are 2.8 × 2.5 cm in size.

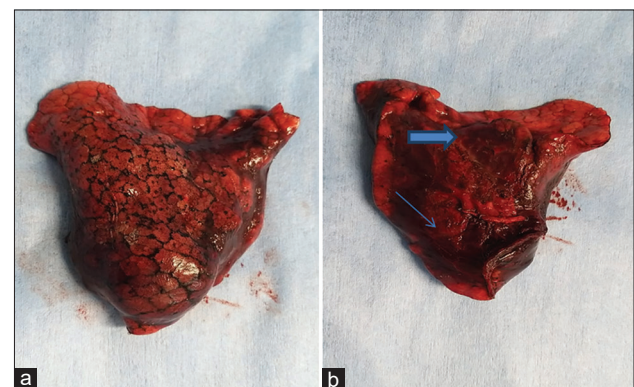


Figure 2. Specimen of the left lower lobectomy. (a) Anterior view. (b) Posterior view. Thick arrow shows a nodule in the left lower lobe, while thin arrow shows a deeper lung nodule.

was 1.2 cm from the end of bronchial resection, 3 cm from the end of vascular resection, and 0.5 cm from the parenchymal stapled margin. Multiple sections examined from both nodules showed features of a metastatic carcinoma. Following immune histochemistry, tumor cells showed a strong positive staining for paired box gene (PAX8) and Wilms tumor protein (WT1), while negative for thyroid transcription factor 1 (TTF1); the staining of tumor protein p53 was strong and diffuse, indicating a mutant profile. No lymphovascular/perineural invasion was seen. All peripheral resection margins of lung parenchyma were within normal limits. Four nodes were identified in final histopathology examination, and all four of them were free of tumor. A lung specimen from the left lower lobe indicated metastatic high-grade serous carcinoma of the ovary (**Figure 3**).

3. Discussion

The present report describes a case of solitary metastatic high-grade serous carcinoma of the ovary. The clinical presentation of epithelial ovarian carcinoma is acute or subacute, and in some cases, the carcinoma could be found incidentally during examination, imaging, or surgery. Acute presentation is typically in those with advanced disease who are presented with a condition that requires urgent intervention and management (e.g., ascites, pleural effusion, bowel obstruction, and venous thromboembolism). Commonly, the disease presents

in a subacute fashion (e.g., pelvic or abdominal pain, bloating, and gastrointestinal symptoms). The type or severity of symptoms does not correspond to the disease stage. In patients with advanced disease, these symptoms are typically due to the presence of ascites and omental or bowel metastases. Dyspnea is occasionally present due to a pleural effusion. However, studies have found that symptoms occur in many patients even at an early stage of the disease^[6]. The goal of early detection is to reduce mortality, when the disease is confined to ovary rather than in advanced stages, which are when the 5-year survival rate is less favorable. Unfortunately, almost 80% of patients have distant metastases at the time of diagnosis^[7], but the disease is confined within the peritoneal cavity in 95% patients^[8]. For this reason, early identification of symptomatic patients has become the goal of the disease.

The secondary goal is detection and treatment of advanced disease as early as possible. Cure rates of this disease are twofold for patients in whom optimal cytoreduction (<1 cm of gross residual disease following surgery) was performed, compared to those who did not have optimal surgery (30–40% vs. 15–20%)^[9]. However, significant advancement in ovarian cancer treatment may lead to an increased incidence of metastases in uncommon sites^[10]. Despite initial therapy (usually consisting of surgical cytoreduction and platinum-taxane combination therapy), the majority of women with advanced stage ovarian cancer will relapse and require additional treatment.

The typical course of metastatic ovarian cancer is intra-abdominal spread manifesting as peritoneal carcinomatosis, whereas the most common sites of distant metastases are liver, pleura, lung as pleural effusion, and lymph nodes. Ovarian cancer usually presents at an advanced stage, but the disease confined within the peritoneal cavity in 85% of the cases^[8].

Lung metastasis from ovarian cancer is uncommon^[11], and cases on pulmonary metastasis after 6 years of primary diagnosis and treatment have never been reported. Breast carcinoma, colon carcinoma, and renal adenocarcinoma are the most common tumors associated with lung metastasis^[12]. Almost 50% of ovarian carcinoma metastases to thorax, mainly as pleural involvement (cytologically proven pleural effusion is considered stage 4a), are probably direct dispersion from peritoneal cavity through diaphragmatic lymphatic vessels^[13].

The most common cancers with pulmonary metastases are malignant melanoma, sarcoma, and carcinoma of the bronchus, colon, breast, kidney, and testis^[14]. The pulmonary nodules that are FDG-avid are biopsied or excised. A surgical excisional biopsy is the gold standard for diagnosing pulmonary nodule and can be curative for some malignancies. During video-assisted thoracoscopic surgery (VATS), nodules targeted for resection are usually located by visual inspection. However, for deeper lesions, digital palpation can be performed to increase

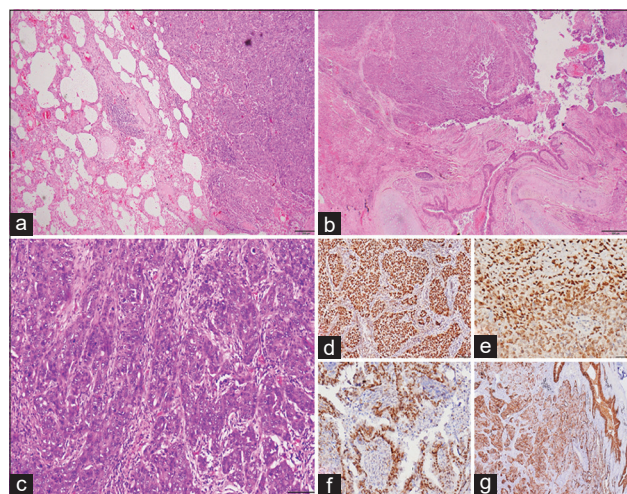


Figure 3. (a and b) Low-power images of tumor invading lung parenchyma with mild inflammation and congestion in the alveolar septa (H&E; ×40). (c) A high-power view of adenocarcinoma with cells having high nuclear-cytoplasmic ratio and prominent nucleoli (H&E; ×400). (d) More than 90% tumor cells show nuclear immune positivity for p53 IHC, ×200; 1:300; Santa Cruz Biotechnology). (e) More than 80% tumor cells show nuclear immune positivity for WT1 (IHC; ×200; 1:200; BioSB). (f) More than 80% tumor cells show nuclear immune positivity for PAX8 (IHC; ×200; 1:100; MJ Genome). (g) More than 80% tumor cells show membranous immune positivity for CK7 (IHC; ×200; 1:200; BioSB).

diagnostic yield. The diagnosis is typically established intraoperatively with the use of frozen section^[15]. If the diagnosis indicates malignancy, preferably, oncological pulmonary surgery should be indicated as lobectomy is a gold standard procedure.

In our case, intraoperative frozen section shows metastatic high-grade carcinoma, and lung lesions can be easily removed by VATS converted to open thoracotomy and left lower lobectomy. Moreover, PET-CT scan showed no findings of relapse of the primary tumor in the peritoneal cavity or any other sites. The time involvement from the diagnosis of primary tumor to lung involvement was 6 years. According to a retrospective chart review, which is conducted on 162 patients with ovarian cancer, distant metastasis is a late complication that occurs in about 30% of ovarian cancer patients, and the median interval time between diagnosis of ovarian cancer and metastatic disease was 3.5 years^[16]. Unlike other malignancies, ovarian cancer rarely metastasizes through vascular route, which is a possible explanation of lung metastasis in ovarian carcinoma^[10].

Once ovarian cancer relapses, the nature of therapeutic modality should change from curative to palliative. However, palliative treatment may be effective in prolonging the survival rate and improving quality of life. Measurement of CA 125 level serves as a key mode for monitoring disease during follow-up, but CA 125 measurement has limited diagnostic role in the context of relapse and should be supported by further imaging studies. Therefore, treatment should only be initiated on confirmation of diagnosis using imaging and physical examination^[17]. In the present case of a patient with Stage 4b ovarian cancer, cytoreductive surgery, hyperthermic intraperitoneal chemotherapy, and long-term multiple chemotherapy following surgery controlled the disease effectively. Appropriate treatment should be selected on the basis of the patient's condition to maximize the therapeutic efficacy. Postoperatively, the patient was on a regular follow-up and started on further chemotherapy. At present, the patient receives one cycle of paclitaxel and carboplatin.

4. Conclusion

Ovarian cancer rarely metastasizes to lung parenchyma in a relapse. Excision of lesion with further chemotherapy showed excellent results. As ovarian cancer is a highly recurrent disease, both clinicians and patients should be cautious about the timing of follow-up as early detection improves the treatment outcome. Possibly, the metastasis of high-grade ovarian carcinoma to lung parenchyma is through hematogenous route. After 6 years, it would be confusing to the clinicians to distinguish between isolated pulmonary parenchymal metastasis and primary lung cancer^[4]. Surgical excision biopsy intraoperative frozen sectioning, followed by lobectomy or segmentectomy, is both diagnostic and therapeutic.

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Conflicts of interest

The authors declare no conflicts of interest.

Author contributions

S.S. wrote and edited this case report and assisted in the surgery. N.K.G. and J.S. assisted in the surgery. R.R. contributed to final histopathology report and pathology findings in this case. S.A. helped with the pathology reporting of the case. M.R. was the primary operating surgeon for this case.

Ethics approval and consent to participate

Consent from patient was obtained before participation.

Consent for publication

Consent for publication from patient was obtained.

Availability of data and materials

Not applicable.

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