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Case Report

Ovary metastasis from lung cancer mimicking primary ovarian cancer: A rare case report

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ABSTRACT

Introduction: Ovarian metastasis from lung cancer is very rare, which might lead to a misdiagnosis as primary ovarian cancer.

Case presentation: We report a 49-year-old woman presenting to our hospital because of a painful mass in the lower abdomen, with no respiratory symptoms. Her initial diagnosis was stage IVB ovarian cancer with pulmonary metastasis. Therefore, the patient underwent neo-adjuvant Paclitaxel - Carbolatin chemotherapy followed by interval debulking surgery. However, postoperative histopathology and immunohistochemistry findings confirmed the diagnosis of primary lung cancer with ovarian metastases. EGFR exon 19 deletion mutation was found by tumor analysis. Therefore, she was then treated with erlotinib and the disease achieved the partial response and remained stable for 7 months.

Conclusion: Diagnosis of lung cancer in the context of ovarian and peritoneal metastases can be difficult. In this circumstance, thorough systemic assessment and immunohistochemistry are essential to confirm the primary.

1. Introduction

Lung cancer is one of the most common malignancies and the leading cause of cancer death globally [1]. Of these, nearly half of the patients are diagnosed with stage IV. Brain, bone, liver, adrenal gland, and lymph nodes are common sites of metastasis in non-small cell lung cancer. Metastasis to other sites is rarer and accounts for less than 5%. Metastasis to the ovary is very rare, accounting for only 0.07% [2]. Differential diagnosis of the primary site of the lung or ovary is also difficult. We report a rare case of ovarian metastatic lung cancer, in which the pre-treatment clinical and paraclinical signs were more towards the primary ovarian cancer. The definitive diagnosis of lung cancer with ovarian metastasis was made with the support of histopathology and immunohistochemistry. This work has been reported in line with the SCARE 2020 criteria [3].

2. Case presentation

A 49-year-old woman was admitted to our Emergency Department due to a painful mass in the lower abdomen, which had been slowly enlarging over the past three months. She has no respiratory symptoms, and no other noticeable symptoms. She has no prior history of smoking nor family history of breast or ovarian cancer. On physical examination, she had many large non-tender mass in the lower abdomen. The cardiovascular and respiratory systems were normal. An abdominal CT scan revealed a solid, contrast-enhanced tumor of the left ovary with a diameter of 48 × 58 mm and peritoneal thickening and masses, of which the largest was 55 × 100 mm in size, along with ascites (Fig. 1).

Thoracic CT images showed multiple round nodules and masses of varying sizes in the right lung, suggesting metastatic lesions. Laboratory studies revealed: CA125 117 ng/mL; HE4 256 pmol/L; CA15-3 15ng/mL; CEA 14,1 ng/mL; Cyfra 21–1 1,67 ng/mL. The findings from gastroscopy and colonoscopy were unremarkable.

She underwent a transvaginal biopsy of her pelvic mass with a

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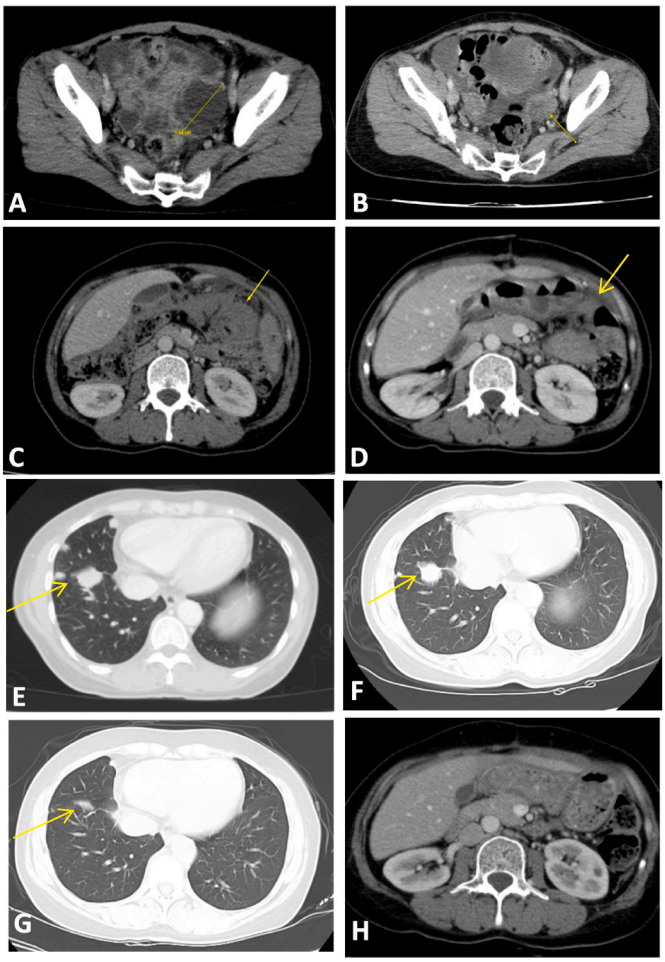

Fig. 1. Figure A, C: Pre-treatment abdominal computed tomography image showing left ovarian tumor and peritoneal thickening (yellow arrow). **Figure B, D**: A respectively computed tomography image of the abdomen after neoadjuvant chemotherapy shows a reduced left ovarian and peritoneal tumor size (yellow arrow). **Figure E, F**: A computed tomography image of the chest before (E) and after neoadjuvant chemotherapy (F) shows a slight decrease in tumor size. (yellow arrow) **Figure G, H**: Computed tomography of the chest and abdomen after erlotinib treatment showed a near-complete response to the lung tumor, with no image of abdominal peritoneal thickening. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

pathological diagnosis of carcinoma. The diagnosis of FIGO stage IV ovarian carcinoma (with lung metastasis) was established. She underwent neoadjuvant chemotherapy with paclitaxel/carboplatin combination prior to interval debulking surgery. After three cycles of chemotherapy, she was evaluated with a partial response.

Interval debulking surgery was performed, including completion hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and excision for suspicious peritoneal nodules. The primary surgeon is a leading gynecological oncology surgery specialist with 20 years of experience. The macroscopic appearance of the tumor showed uterine appendages on both sides have many large white masses 0.5–3cm in size with solid density, no longer distinguishable salpinx tubal tissue and ovarian tissues. On HE stains, epithelial cells are proliferated, with round, irregular nuclei, rough chromatin, clear nuclei, multiple nuclei, and disordered tumor cells (Fig. 2).

The postoperative pathological examination revealed adenocarcinoma. Postoperative histopathology was not consistent with ovarian cancer as initially diagnosed. Therefore, immunohistochemistry was performed to confirm the diagnosis.

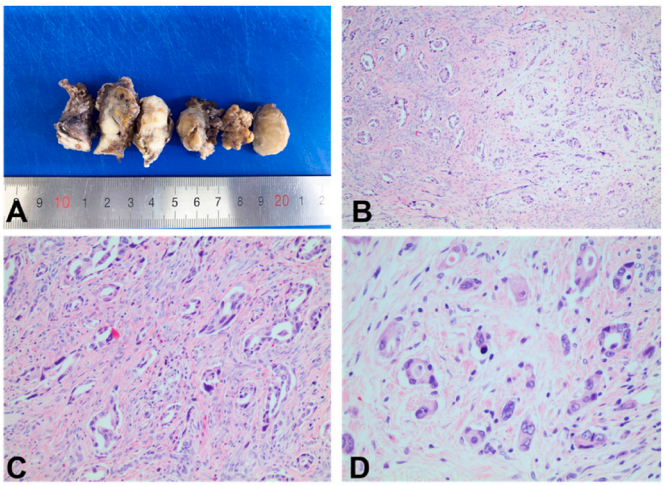

Fig. 2. Histopathological image after surgery of ovarian tumor. A. Gross ovary, Bx100, Cx200, Dx400. On HE stains, epithelial cells are proliferated, with round, irregular nuclei, rough chromatin, clear nuclei, multiple nuclei, and disordered tumor cells.

Immunohistochemistry showed that the malignant cells were positive for TTF1 and cytokeratin 7 (CK7), and negative for WT-1, cytokeratin 20 (CK20), estrogen receptor (ER), progesterone receptor (PR), CDX2, and Vimentin, which supported an ovarian metastasis from the lung (Fig. 3).

The patient recovered well, and the postoperative course was uneventful. She underwent the remaining three cycles of chemotherapy paclitaxel – carboplatin regimen. While undergoing chemotherapy, we tested the tumor specimen which revealed an EGFR exon 19 deletion. Therefore, targeted therapy with erlotinib was commenced. After seven months of treatment, she was evaluated with partial response disease.

3. Discussion

Lung cancer is the second most common after breast cancer. Approximately 50% of patients are diagnosed at the metastatic stage [4]. The ovary is a extremely rare metastatic site of lung cancer, accounting for only 0.07%. In contrast, ovarian cancer often metastasizes to the lung, accounting for 28.4% [5].

Secondary ovarian lesions account for 13.6% of malignancies in the

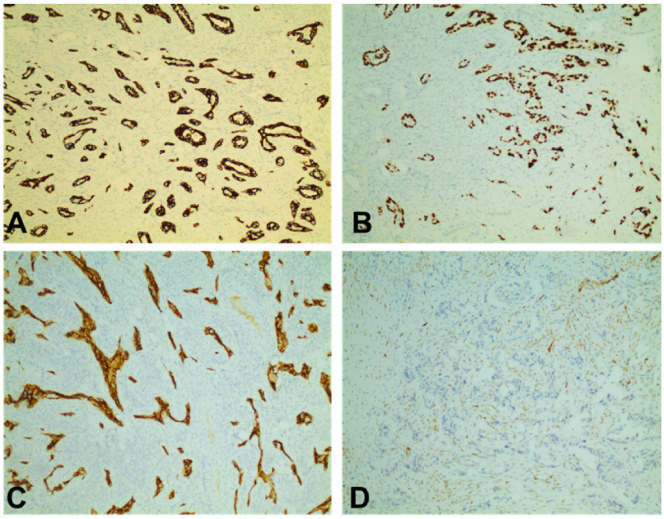

Fig. 3. Immunochemical stain. The tumor cells were positive for CK7 (A), TTF1 (B), CEA (C), but negative WT1 (D) (A, B, C, D x100).

ovary, in which metastasis from cancer of the gastrointestinal tract is the most common, accounting for more than 70%, and metastases from lung cancer was only recorded in 0.4% cases [6]. However, this rate has been increasing due to the prevalence of lung cancer in women over the past decades. Although secondary ovarian tumors are common, primary location is difficult to determine, up to 42% of ovarian metastases are found before primary cancer is diagnosed [7].

Clinical symptoms of stage IV lung cancer patients may manifest only in metastatic sites. Therefore, the differential diagnosis is essential because the prognosis and treatment are entirely different. Our patient's case is complex because the patient was admitted to the hospital with abdominal pain mass and abdominal distension symptoms but absolutely no respiratory system signs. CA125, HE4 concentrations increased. Computed tomography revealed images of ovarian tumor and peritoneal metastases, and pelvic mass biopsy showed carcinoma. Moreover, the lung lesions were atypical of the primary cancer. In addition, ovarian cancer with lung metastases is often seen clinically, which was why the diagnosis of lung cancer was not considered. These difficulties are also mentioned in the literature, in a study of 54 patients with ovarian metastatic non-genital cancer, only 30% of patients were diagnosed with the primary tumor site before surgery, and among them the primary site is mainly breast [8].

Regarding the clinical features of lung cancer with ovarian metastasis, Irving's study analyzing 32 cases in the literature, the mean age was 47 (26–76). Ovarian metastases are usually detected within one year of a primary lung cancer diagnosis. Only 31% of patients with ovarian metastases were detected at the time of diagnosis. The most common histopathological types of ovarian metastatic lung cancer are small cell carcinoma and adenocarcinoma of the lung, accounting for 43.8% and 34%, respectively [9].

Differential diagnosis of primary lung tumors and pulmonary metastases is sometimes difficult, such as in our case report. Computed tomography scan plays a certain role in distinguishing between them. In most cases, pulmonary metastases are hematogenous in origin, and they tend to predominate in the lung bases which receive more blood flow than the upper lobes. Nodules tend to be varied in size, sharply marginated in most cases, and round or lobulated in contour. In contrast, primary lung tumors frequently appearing as solitary nodules which may appear solid, round or lobulated and have irregular and spiculated margins. However, imaging tests cannot confirm the differential diagnosis [10,21].

The diagnosis of pulmonary origin often relies on immunohistochemical markers. In our case, both TTF1 and cytokeratin 7 (CK7) were strongly expressed, while tumor cells were negative for WT1, p53, ER, and PR. Thyroid transcription factor (TTF-1) is a 38-KD protein located primarily in the nuclei of type II pneumocytes and Clara cells. It is widely used as a specific and sensitive marker for the majority of bronchopulmonary adenocarcinomas and pulmonary small cell carcinoma in addition to thyroid carcinomas [22]. TTF-1 is expressed in 73–95% of primary lung adenocarcinomas, whereas the expression is lacking in most lung metastases [11]. According to some previous studies, strongly expressed TTF-1 is a favorable factor associated with improved survival in primary lung carcinomas [12]. Tumor cells expressed TTF-1 have a higher incidence of EGFR mutations [13].

CK7 is expressed in 63% of lung tumors and only 5% of gastrointestinal tumors [14]. In contrast, gastrointestinal tumors have a high frequency of CK20 expression. The combination of CK7 (+)/CK20 (−)/TTF-1 (+) immunophenotype is highly specific for primary pulmonary tumors (specificity 100% and sensitivity 50%) [14,15]. WT-1 expression is a hallmark of serous ovarian carcinomas (93% of cases), and is considered an important marker used to distinguish ovarian carcinomas from other types of carcinomas [16,17].

Metastatic pulmonary carcinoma has a poor prognosis, with a 3-year overall survival rate of approximately 10%–20% [18]. Survival depends on the site of metastases, in which hepatic metastasis has the worst prognosis [19]. Ovarian metastasis from the lung is rare and has been described through several case reports, and there is limited data on survival outcomes. Systemic therapies including chemotherapy, targeted therapy, and immunotherapy are considered at this stage.

Does surgical treatment of ovarian metastases in patients with lung cancer improve survival outcome? This is still an unanswered question. However, several previous studies have shown that cytoreduction surgery improved survival in metastatic gastrointestinal cancer (Krukenberg tumors) [20]. Patients often presented to the hospital with bowel obstruction due to ovarian metastases. At this point, surgery plays a role in resolving symptoms and making the diagnosis [21–23]. In our case, surgery not only helped to confirm the diagnosis of the disease but also to resolve abdominal pain symptoms and reduce the tumor burden.

4. Conclusion

Ovarian metastasis from lung cancer is very rare and clinical symptoms are difficult to distinguish from primary ovarian cancer. The diagnosis of pulmonary primary often relies on immunohistochemical markers.

Ethical approval

The manuscript approved by ethical committee of Viet Nam National cancer hospital.

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Author contributions

Huyen Thi Phung: primary doctor who treated the patient, revised manuscript.

Anh Quang Nguyen: doctor who treated the patient, wrote manuscript.

Tung Van Nguyen: doctor who treated the patient, revised manuscript.

Trong Van Nguyen: Follow up the patient, revised manuscript.

Long Thanh Nguyen: Follow up the patient, revised manuscript.

Khuyen Thi Nguyen: provided histological imaging diagnosis to the article, revised manuscript.

Ha Dieu Thi Pham: the doctor operated on the patients, revised manuscript.

All authors read and approved the final manuscript to submit.

Declaration of competing interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this paper. All authors read and approved the final manuscript for publication.

Trial registry number

This is not a first-in-human study, thus it is not needed.

Guarantor

Huyen Thi Phung, MD.

Provenance and peer review

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Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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