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Case Report

Recurrent ovarian cancer presenting with isolated axillary lymph node metastasis: A rare case report

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ABSTRACT

Introduction: Ovarian cancer with metastatic axillary lymph node is a very rare entity. This study aims to report a case of recurrent ovarian cancer presenting with isolated axillary lymph node metastasis.

Case presentation: We report a case of a 58-year-old patient with recurrent ovarian cancer in the axillary node and a suspected lesion in the ipsilateral breast. One year before recurrence, the patient was diagnosed with FIGO stage IIIC ovarian cancer and was treated with primary debulking and paclitaxel-carboplatin adjuvant chemotherapy. Biopsies of the breast lesion, right and left axillary lymph node yielded a fibroadenoma in the breast and a metastatic carcinoma in the axillary node. Immunohistochemistry stains of the left axillary node biopsy specimen was positive for CK7, P53 and PAX-8 markers, and negative for CK20 and GCDFP-15 markers. Immunohistochemistry results combined with a history of ovarian cancer helped confirm the ovarian origin of axillary lymph node metastasis.

Clinical discussion: Recurrent ovarian cancer presenting with isolated axillary lymph node metastasis is rare. Immunohistochemistry combined with medical history is essential for definitive diagnosis in this situation. PAX-8 and GCDFP-15 help to differentiate the origin from the breast or the ovary.

Conclusion: Oncologists and pathologists should recognize this rare clinical scenario for early diagnosis and treatment. Detailed medical history, imaging, and immunohistochemical studies on biopsy specimen should help reach accurate diagnosis.

1. Introduction

Ovarian cancer ranks third among the most common gynecological malignancies, after cervical cancer and endometrial cancer [1]. Since ovarian cancer does not have specific warning signs and there are no effective screening strategies, patients are usually diagnosed at advanced stages. The common metastatic sites of ovarian cancer include the peritoneum, abdominal organs and retroperitoneal lymph nodes. However, axillary lymph node metastasis is extremely rare with only several case reports have been published [2,3]. Information from further cases could be useful for physicians when encountering this clinical entity and provide data for evidence synthesis. In this paper, we presented a case of epithelial ovarian cancer with solitary metastasis to axillary lymph node. This work has been reported in line with the SCARE 2020 criteria [4] (see Figs. 1–4).

2. Case presentation

A 58-year-old female was initially diagnosed with high grade serous ovarian carcinoma, FIGO stage IIIC. The patient had no comorbidities, no history of smoking, drug or alcohol use. Her mother and sisters do not have breast or ovarian cancer. BRCA1/2 genes testing of the tumor specimen showed no mutations. She underwent primary debulking surgery and 6 cycles of adjuvant chemotherapy with Paclitaxel-Carboplatin. Afterwards, she was discharged with complete response on CT scan and normal CA 125. After 1 year, the patient came back to hospital because of axillary lymphadenopathy. On examination, there was a left axillary lymph node of 1 × 1.5 cm in size, which is hard and relatively fixed. A similar right axillary lymph node of 1 × 1 cm in size was also documented. Breast and gynecological examination revealed no abnormalities.

On breast MRI, a suspicious left breast lesion of 10mm in size was

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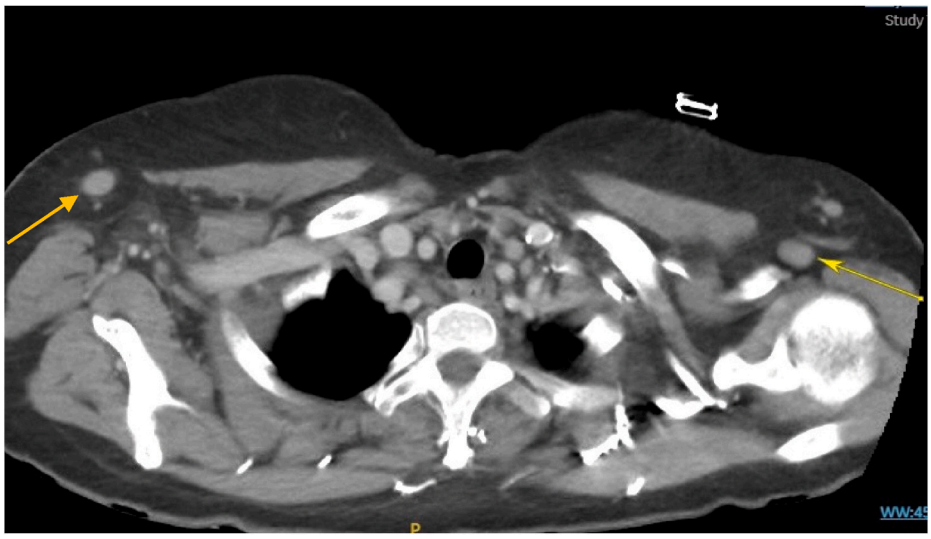

Fig. 1. CT scan demonstrating left axillary lymph node enlargement (yellow arrow) and right axillary node (orange arrow).

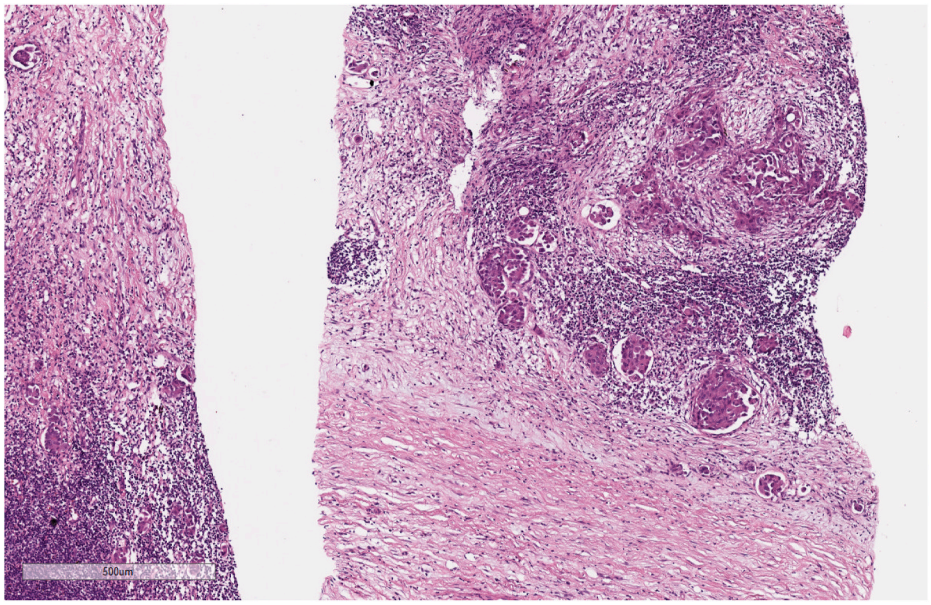

Fig. 2. On HE-stained axillary lymph node specimens showed metastatic carcinoma suggesting originate from the ovary.

documented (BIRADS 4a). No other lesions were observed on chest and abdominopelvic CT scan. Serum CA 125 was slightly elevated (41.2 U/L). Biopsy of the breast lesion, right and left axillary lymph node, which yielded a fibroadenoma for the breast and a metastatic carcinoma for the axillary node. Immunohistochemistry stains of the left axillary node biopsy specimen came positive for CK7, P53 and PAX-8 markers, and negative for CK20 and GCDFP-15 markers. This IHC result confirmed the ovarian origin. Our tumor board had decided to treat the patient with of Paclitaxel-Carboplatin regimen. After six cycles of chemotherapy, the patient had a complete response. She could not afford to pay for Olaparib maintenance and was then followed up for every three months afterwards. After six months of follow-up, there are no signs of recurrence.

3. Discussions

Ovarian cancer cells mainly metastasize within the peritoneal cavity, or sometimes to supraclavicular lymph nodes via retroperitoneal and diaphragm lymphatics. Hematogenous spread is not common and is usually seen in advanced stages, leading to with liver parenchyma, lung and brain metastases [5]. The mechanism of axillary lymph node metastasis in ovarian cancer is unclear, with two hypotheses proposed. Firstly, the cancer cells could travel through the diaphragm via superior diaphragmatic lymph nodes to the internal jugular vein, subclavian vein or subclavian lymph trunk and eventually to the axilla. The second route is via the deep lymphatic vessels inferior to the diaphragm (iliac, para-aortic, and mesenteric) and the superficial lymphatic vessels inferior to the level of umbilicus, to the thoracic duct and finally to the junction of the left subclavian and internal jugular vein [6].

Lymph node metastasis occurs in about 14–70% of patients with ovarian carcinoma and distributes mainly in the pelvic and aortic region [7]. In a study of Blanchard et al. on 640 patients, there were only 27 cases with distant lymph node metastasis and 55% of which were at supraclavicular lymph node [8]. Metastasis to axillary lymph node or breast is extremely rare in ovarian cancer, in which the prevalence is about 0,03–0,6% [2]. Recine et al. reported a series on 18 serous ovarian

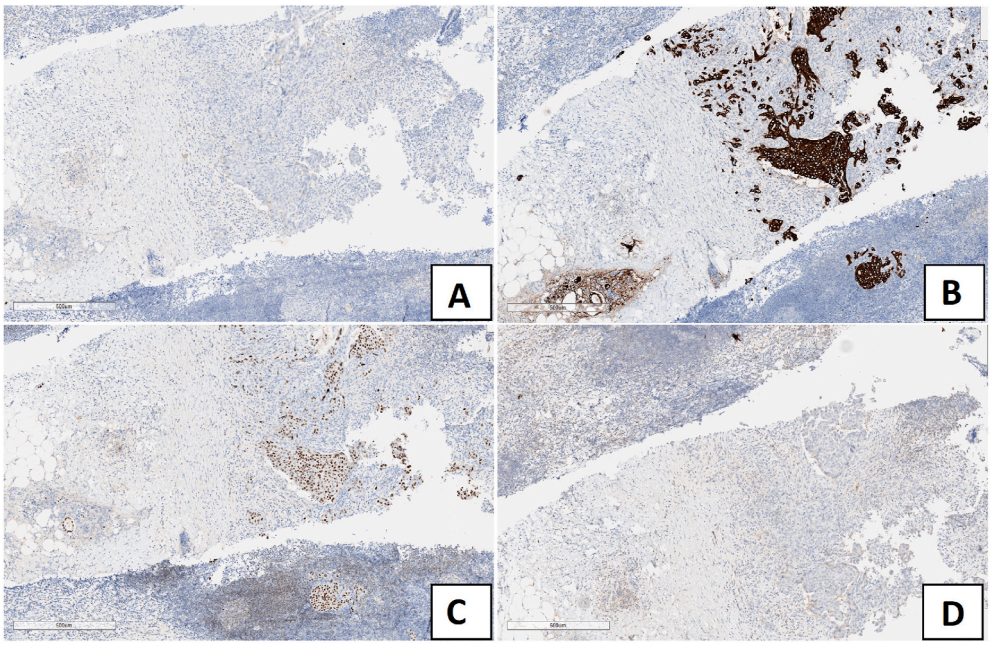

Fig. 3. Immunohistochemical imaging of axillary lymph nodes, CK20 negative (A), CK7 positive (B), Pax8 positive(C), GCPF-15 negative (D).

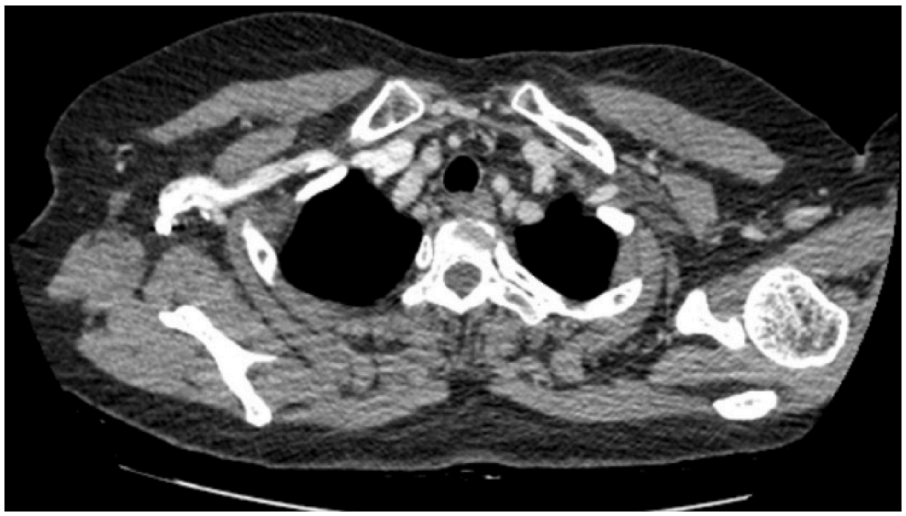

Fig. 4. On computed tomography image of the patient after treatment: no bilateral axillary lymph nodes.

carcinoma patients with breast and/or axillary lymph node involvement in 14 years from 1990 to 2003, which showed that most patients were initially diagnosed stage III disease, had high grade carcinoma and the median time to metastasis was 20 months [9]. In this report, only 6 patients with solitary axillary lymphadenopathy and without breast metastasis were documented [9]. Therefore, our case is among very few cases reported to date. Although the BIRADS-4A lesion in the breast was confirmed to be fibroadenoma, diferrential diagnosis between breast and ovarian origins of the axillary node was essential because axillary metastasis from the breast is much more common than from ovary. Differentiating between ovarian and breast origin in this situation is essential in management strategy.

Immunohistochemistry can help to identify the primary of the axillary node. CK7+/CK20- might suggest a breast or ovarian origin [10], GCDFP-15 is a useful marker which is a protein isolated from the contents of mammary apocrine cysts and is strongly expressed in apocrine breast carcinoma [11]. GCDFP-15 is highly sensitive and specific in diagnosing breast origin, with a specificity and sensitivity of 95% and 74% respectively [12]. Monteagudo et al. showed that 71% cases of ovarian metastasis from breast cancer were GCDFP-15 positive, while no cases with ovarian epithelial carcinoma had GCDFP-15 stain [13]. Besides, PAX-8 is also an important marker in identifying ovarian origin [14], in which it is expressed in 99% high grade serous ovarian carcinoma and 100% low grade serous ovarian carcinoma and borderline tumors. According to Ryan et al. the sensitivity and specificity of PAX-8 in diagnosing ovarian primary was 90% and 100% respectively [15]. In our patients, GCDFP-15 negativity and PAX-8 positivity, along with the history of advanced stage ovarian cancer confirm the diagnosis of metastatic ovarian carcinoma.

For platinum-sensitive recurrent ovarian cancer can be considered for secondary cytoreductive surgery, especially if the patient has a positive AGO-score (PS ECOG 0, ascites $\leq$500 ml, and complete resection at initial surgery) [16]. However, data on patients with isolated axillary lymph node relapse is limited and the benefit of surgery is unclear in this case. Besides, although bevacizumab and poly ADP-ribose polymerase (PARP) inhibitors (PARPi) have shown benefits in

platinum-sensitive recurrent ovarian cancer, these drugs are not fully covered by the insurance in our country and the patient could not afford these treatments [17]. In such patients with limited financial capability, early diagnosis and treatment of recurrence play a key role. Although rarely encountered, the prognosis of ovarian cancer patients with solitary axillary metastasis is considerably good, with median survival from documentation of recurrence of 26 months[8]. In a study of Euscher et al. on 35 ovarian cancer cases with lymphadenopathy, the median survival of patients with lymph node metastasis and minimal peritoneal spread was 120 months compared to 24 months in those with overt peritoneal diseases [18].

4. Conclusions

Although axillary lymph node metastasis from ovarian cancer is an extremely rare, clinician should be aware of this clinical entity and careful evaluation is necessary for differential diagnosis. Immunohistochemistry is helpful in identifying the ovarian origin and in ruling out breast and other primaries.

Ethical approval

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

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Author contributions

Huyen T. 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.

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

Trial registry number

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

Guarantor

Huyen Thi Phung, MD, PhD.

Provenance and peer review

Not commissioned, externally peer reviewed.

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.

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.

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