Case Report

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Ovarian cancer with breast metastasis: a rare case report

Tien Giang Dang, MD, MSc[a], Hong Quang Nguyen, MD[b], Chi Hieu Khuc, MD[a], Trung Toan Tran, MD[c], Thanh Long Nguyen, MD[a,*]

Introduction: Ovarian cancer with breast metastasis is an exceedingly rare entity. We hereby reported a case of ovarian cancer presenting with synchronous breast metastasis.

Case presentation: We report a case of a 39-year-old patient who was diagnosed with FIGO stage IV ovarian cancer, with pleural effusion and a suspected lesion in the breast. Biopsies of the breast lesion showed invasive carcinoma, immunohistochemistry stains of the breast biopsy specimen were positive for PAX-8, CA-125 markers, and negative for P53, SMA, Her2/neu, Mammaglobin. Immunohistochemistry results combined with the diagnosis of ovarian cancer helped confirm the ovarian origin of breast tumor.

Discussion: Ovarian cancer presenting with breast cancer metastasis concurrently is rare. The differential diagnosis between primary breast cancer and breast metastasis from ovarian cancer is challenging and immunohistochemistry results play a crucial role in establishing a definitive diagnosis in such cases.

Conclusion: Oncologist and pathologist should be able to identify this rare clinical scenario promptly for early diagnosis and treatment which relies on thorough examination, imaging and immunohistochemical studies. Nevertheless, owing to the extensive spread of the disease, the prognosis for this rare clinical scenario is generally poor.

Keywords: breast metastasis, case report, immunohistochemistry, ovarian cancer

Introduction

Ovarian cancer ranks third among the most common gynecological malignancies, after cervical cancer and endometrial cancer[1]. Since ovarian cancer lacks specific warning signs and effective screening strategies, patients are often diagnosed at advanced stages. Common metastatic sites of ovarian cancer include peritoneum, abdominal organs and retroperitoneal lymph nodes. However, breast metastasis is extremely rare, with only several case reports published. Further information from additional cases could be useful for physicians. In this paper, we reported a case of epithelial ovarian cancer with metastasis to the breast. This study has been reported in line with the (Surgical CAse REport) SCARE criteria[2].

Case presentation

A 39-year-old female was initially hospitalized with complaints of abdominal pain persisting for about a month, along with weight loss and difficulty in breathing. Clinical examination revealed moderate anemia, moderate right pleural effusion, ascites, and a pelvic mass measuring 8x7cm, along with a solid, well-defined breast tumor measuring 2 × 15 cm. The patient had no comorbidities, no history of smoking, drug or alcohol use, and no family history of breast or ovarian cancer.

Pelvic MRI documented bilateral ovarian lesions, peritoneal and omentum thickening and ascites. Elevated serum levels of CA-125 and CA-153 (1631 and 124 U/mL, respectively) were recorded. Thoracic CT scanning revealed pleural effusion causing partial atelectasis, mediastinal lymph nodes of 1 × 1.8 cm in size and a homogeneous enhancement breast tumor measuring 2.4 cm (Fig. 1A). Breast ultrasound and mammography indicated a hypoechoic mass measuring 20x25mm without calcification (BIRADS 4B) (Fig. 1B).

Biopsy of the breast lesion and cellblock of pleural fluid were done, which yielded invasive carcinoma for breast tumor and ovarian serous carcinoma metastasis for pleural fluid. On the HE stain breast tumor biopsy specimen (Fig. 2), the tumor tissue has a glandular structure, with areas resembling papillae or micropapillae. There were invasive cancer cells with unclear intraductal carcinoma components. Immunohistochemical staining (Fig. 3) of tumor cells was negative for mamaglobin (a marker of breast origin), while positive for PAX8 and CA-125 (ovarian origin markers). P53 negative and WT1 positive are consistent with the ovarian high-grade serous carcinoma type.

From the histopathological and immunohistochemical results of the breast tumor biopsy specimen, we determined that the patient had ovarian cancer (most likely high-grade serous carcinoma), FIGO stage IVB, with metastasis to breast and pleural effusion. Our tumor board had decided to initiate treatment with the paclitaxel 175 mg/m^2-carboplatin AUC6 regimen via intravenous infusion on day 1 of a 21-day course. After three

[a]Department of Medical Oncology No. 6, Vietnam National Cancer Hospital, Vietnam, [b]Department of Oncology, Hanoi Medical University, Vietnam and [c]Department of Pathology, Vietnam National Cancer Hospital, Vietnam

*Corresponding author. Address: Department of Medical Oncology No. 6, Vietnam National Cancer Hospital, Vietnam. Tel.: +84 345 566 577. E-mail: longnguyen.hmu@gmail.com (T.L. Nguyen).

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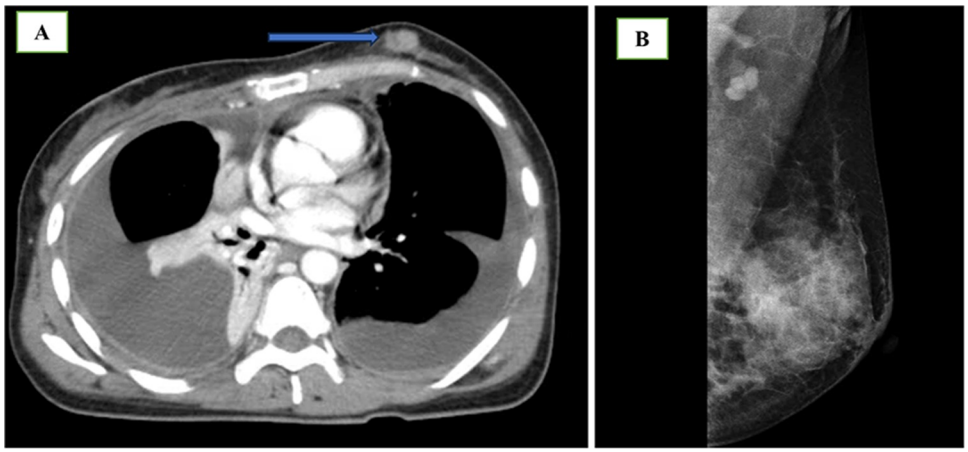

Figure 1. (A). Breast tumor on CT scan before treatment (blue arrow) and (B) breast tumor on mammography.

cycles of chemotherapy, the patient showed a partial response, with improvement on clinical symptoms, tumor markers, and imaging characteristics. Subsequently, the patient underwent an optimal debulking surgery, which included total hysterectomy, bilateral salpingo-oophorectomy and omentectomy, resection also involved the appendix, lymph nodes, breast and abdominal metastases. Ovarian tumor histopathology (Fig. 4) shows tumor tissue creates cribriform structures, with papillary or micropapillary areas. Tumor cells are round, hyperchromatic nuclei, with many mitotics consistent with high grade serous carcinoma (chemotherapy response score 2). Tumor morphology is similar to breast tumors. The post-operative course of the disease was uneventful, and the histological analysis of breast tumor confirmed high-grade serous carcinoma, further confirming its ovarian origin. No lymph node structures were found in the surgical specimen of breast lesion. The patient continued to receive 5 cycles of paclitaxel 175 mg/m^2-carboplatin AUC6 (for a total of 8 cycles both pre- and post-surgery). In Vietnam, bevacizumab is only covered by 50% by national insurance and poly-ADP ribose polymerase inhibitors are not covered, and the patient could not afford these therapies. Therefore, the patient did not have germline or somatic BRCA testing as well as homologous recombination deficiency testing since the tests had to be paid out-of-pocket.

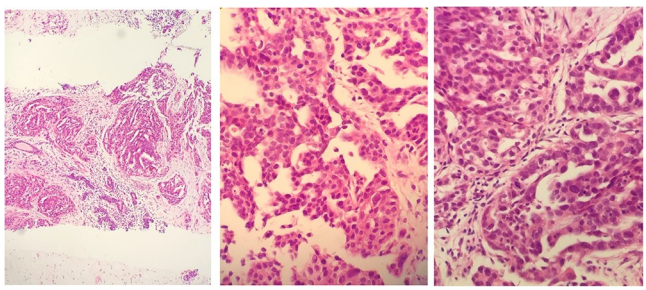

Figure 2. Results of pathology (biopsy of breast): tumor tissue invades mammary gland tissue, creating cribriform structures with papillary or micropapillary areas. Tumor cells are round, hyperchromatic nuclei, with many mitotics.

Due to grade 2 peripheral neurotoxicity and repeated neutropenia even after dose reduction, chemotherapy was stopped after discussions with the patient. Her CT scan after chemotherapy is shown in Fig. 5, and the CA 125 level was 459 U/mL. After 1.5 months she was hospitalized due to worsening clinical symptoms and elevated tumor marker. Her CT scan showed multiple peritoneal lesions and increased pleural effusion, which required drainage. At that time, she had an ECOG Performance Status score of 2. Our tumor board decided to treat her with Liposomal Doxorubicin 50 mg/m^2 via intravenous infusion on day 1 of a 28-day cycle. Unfortunately, after just one cycle, the patient's condition deteriorated significantly, with excessive pleural effusion affecting both lungs leading to atelectasis. The patient and her family decided to discontinue chemotherapy and transition to supportive care only. She passed away 10 months after initial diagnosis.

Discussion

Ovarian cancer cells usually metastasize within the peritoneal cavity or, less commonly, to supraclavicular lymph nodes through retroperitoneal and diaphragm lymphatics[3]. Meanwhile, hematogenous metastasis is uncommon and usually occurs in advanced stages, often leading to metastases in the liver parenchyma, lung or brain[3]. The prognosis of ovarian cancer patients with distant metastasis is generally poor[4]. Among them, the overall incidence of primary gynecologic tumor metastases to the breast is 0.17%[5]. The most common type of ovarian malignancy that metastasizes to the breast is serous carcinoma, accounting for 72% of cases[6]. Similar to primary breast carcinoma, the most frequent site of breast metastases is the upper outer quadrant, affecting 62% of patients[7]. Both ovary and breast cancers share various risk factors, including environmental factors and mutations in genes such as BRCA1and BRCA2[8].

Metastasis of ovarian cancer to the breast is rare and distinguishing primary from metastatic breast lesion is significantly challenging due to nonspecific imaging features. Certain pathological and imaging characteristics which may suggest a breast metastasis include distinct margins, absence of microcalcifications on mammography. Additionally, most lesions of this type are found in the subcutaneous layer of breast mammary gland[9].

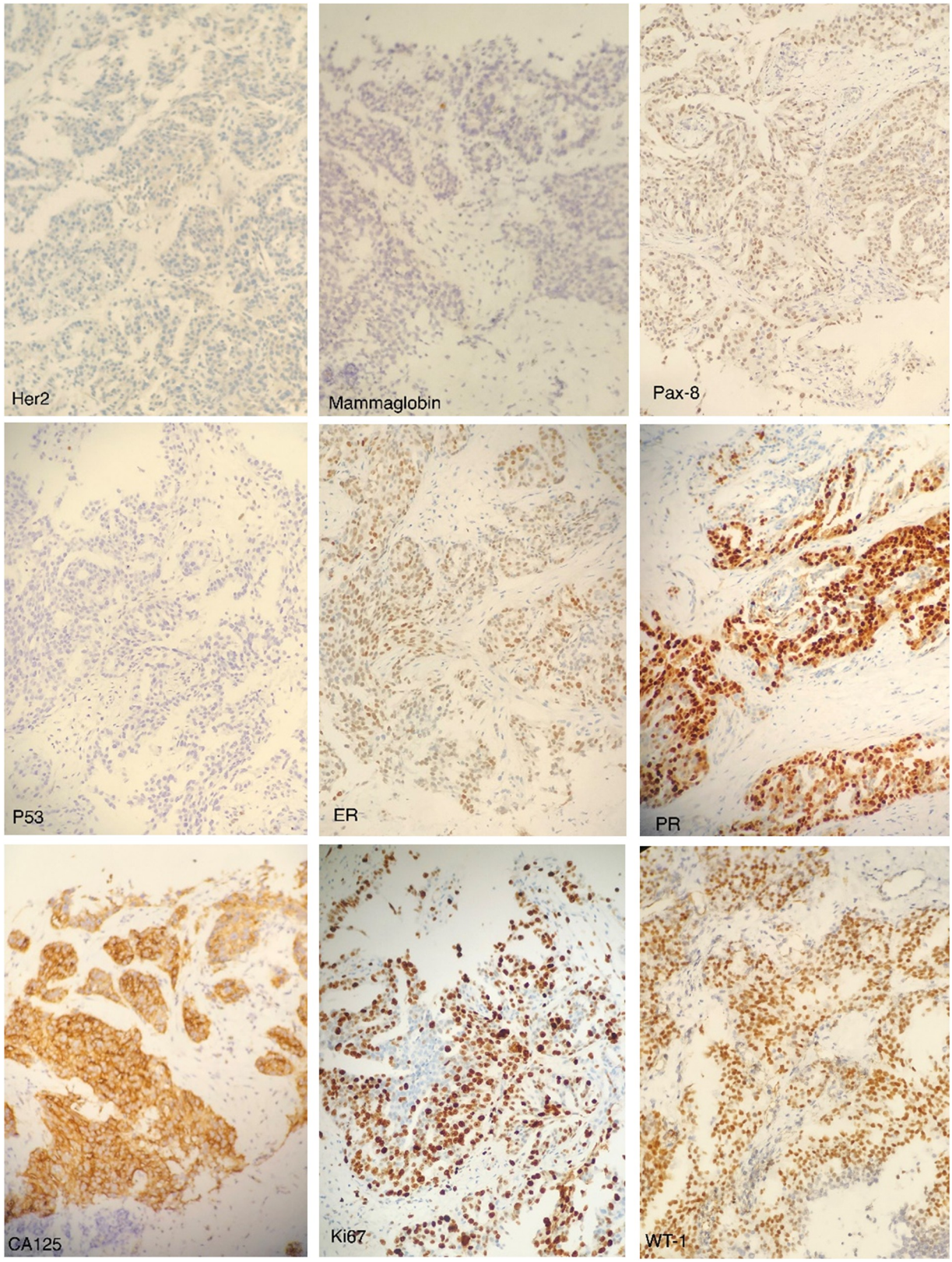

Figure 3. Results of immunohistochemistry: marker p53 (negative); marker ER (1+; 70%); marker PR (3+; 80%); marker Her 2 (negative); marker Ki67 (positive, 70%); marker mammaglobin (negative); marker PAX-8 (positive); marker CA125 (positive), marker WT-1 (positive).

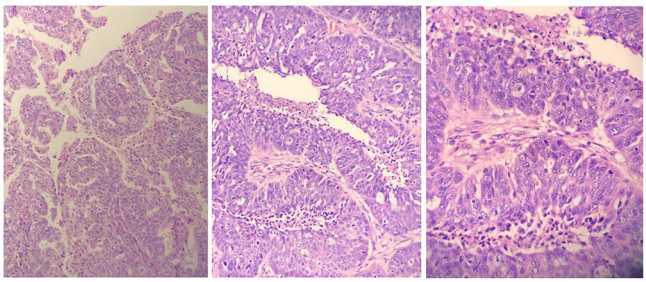

Figure 4. Results of pathology (ovary tumor): Tumor tissue creates cribriform structures, with papillary or micropapillary areas. Tumor cells are round, hyperchromatic nuclei, with many mitotics. Tumor morphology is similar to breast tumors.

However, pathology and immunohistochemistry (IHC) results, incorporating markers such as mammaglobin, PAX-8, CA-125, can aid in identifying the origin of the tumor. PAX-8 is a transcription factor Paired box8 which is a marker of the Fallopian tube secretory cell lineage. Its expression is also crucial for organogenesis of thyroid gland, kidney, nervous system and Mulerrian system[10]. PAX-8 is expressed in 99% high grade serous ovarian carcinoma and 100% low grade serous ovarian carcinoma and borderline tumors[11]. According to Ryan *et al*, the sensitivity and specificity of PAX-8 in diagnosing ovarian cancer was 90% and 100%, respectively[12]. Besides, PAX-8 represents a useful marker for diagnosis of primary or metastatic neoplasms given its negative in mammary and lung tissue[13]. CA-125 is a transmembrane glycoprotein that is expressed on surfaces derived from coelomic epithelium including the female reproductive tract, respiratory tract, and ocular surfaces[14]. Therefore, CA-125 is an essential marker for the diagnosis of ovarian malignancy. Besides, mammaglobin expression is highly specific for tumors originated from the breast, female genital tract and salivary glands. Mammaglobin is detected in 91% of the breast cancer cases, independent of stage and histological type[15].

In our patient, PAX-8 positivity, CA125 positivity along with mammaglobin negativity confirmed the diagnosis of metastatic ovarian carcinoma. On the other hand, ER and PR markers can be expressed in both primary epithelial tumors of the breast as well as primary epithelial tumors of the ovary. In this patient, ER and PR had a high expression rate and HER2 is negative. This immunophenotype, if it is a primary breast tumor, usually belongs to the group of patients with low Ki67. However, the Ki67 of this case was very high (70%), favoring the origin of the ovary.

The current standard treatment for advanced ovarian cancer primarily involves upfront or interval debulking surgery and cytotoxic chemotherapy, although targeted therapies are also widely used. Poly ADP-ribose polymerase inhibitors and antiangiogenics have demonstrated improved outcomes in both the frontline and recurrent settings for selected patients. However, data regarding the treatment approach for ovarian cancer metastasis to the breast at initial diagnosis are lacking. Patients with confirmed metastasis to the breast have, by definition, stage IVB disease. Although the role of debulking surgery in patients with stage IVB is still controversial, a number of studies have shown that complete resection without any residual disease is an independent prognostic factor for survival outcomes[16-18]. Therefore, distant metastasis, including breast metastasis, should not refrain efforts to achieve optimal cytoreduction surgery, and neoadjuvant chemotherapy followed by interval debulking surgery might be a potential option[19]. Although bevacizumab might improve survival outcomes in patients with stage IV disease or ascites as shown in the GOG-218 and ICON7 trials[20,21], its role in neoadjuvant therapy is less well defined, with the ANTHALYA trial demonstrating an encouraging complete resection rate, while the GEICO1205 trial did not[22,23].

In a series of 169 patients with confirmed metastases to the breast from solid organ tumors, Williams *et al* found that the median survival time from the diagnosis of breast metastasis was 10 months, with significantly higher survival time observed in patients who underwent surgical resection for breast metastases[24]. Conversely, according to Micha *et al*, ovarian cancer metastatic to the breast should be managed with systemic chemotherapy, supplemented by local treatments such as mastectomy or lumpectomy for palliative purposes in patients who are unresponsive to systemic medication[25]. Breast metastasis from ovarian cancer may be disseminated widely and it is associated with a poor prognosis. The mean-survival time was reported to range from 13 days to 3.5 years, with a 1-year survival rate of approximately 40%[26]. In one series, over 90% of patients succumbed, with a median survival time of 15 months after diagnosis[27].

In regard to our patient, despite a significant response following neoadjuvant therapy and she had an optimal debulking surgery, her overall survival was only 10 months from initial diagnosis due to unresolved pleural effusion and subsequent respiratory failure. This evolving course of this patient reflects the fact that ovarian cancer metastasis to breast presents a disseminated disease with a poor prognosis.

Conclusions

While breast metastasis from ovarian cancer is exceedingly rare, clinicians should remain vigilant regarding this clinical condition,

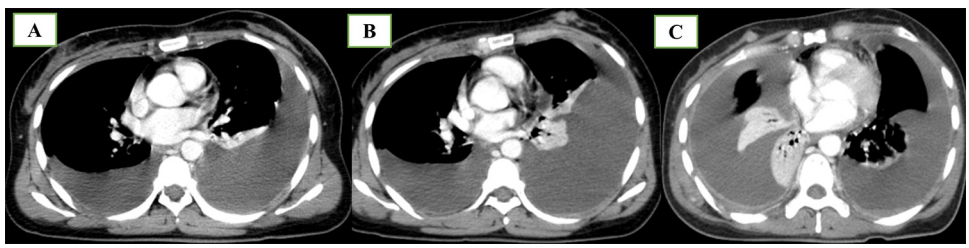

Figure 5. (A) CT scan after neoadjuvant therapy, (B) after three cycles of paclitaxel-carboplatin and (C) at the end of primary treatment.

and thorough evaluation is essential for differential diagnosis to establish a precise treatment plan. Immunohistochemistry plays a crucial role in identifying the ovarian origin and in ruling out breast and other primary cancers. In general, metastatic ovarian cancer to the breast is associated with a poor prognosis in spite of timely diagnosis and treatment.

Ethical approval

This study was approved by the ethics committee of Vietnam National Cancer Hospital.

Consent

Written informed consent was obtained from the patient for publication and any 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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Author contribution

D.T.G., N.H.Q., K.C.H., T.T.T., and N.T.L.: contributed to diagnosis and management of the case, performing literature search, writing the paper and approved the manuscript.

Conflicts of interest disclosure

No potential conflicts of interest relevant to this article were reported.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

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Data availability statement

Data is provided upon reasonable request.

Provenance and peer review

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