

METASTASIS TO BREAST FROM OVARIAN CANCER CONCURRENTLY DIAGNOSIS: A RARE CASE REPORT AND REVIEW OF LITERATURE

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ABSTRACT

Metastasis of breast cancer originating from other organs is exceedingly uncommon, accounting for merely 0.33÷6.3% of malignant breast tumors, predominantly stemming from melanoma, sarcoma, lung cancer, and renal cancer. Compared to primary breast carcinoma, metastatic breast cancer generally has a less favorable prognosis. In clinical practice, precise identification of the primary organ is imperative for devising an optimal treatment regimen. Particularly, metastasis of ovarian cancer to the breast at the time of diagnosis is even more infrequent. This article delineates a clinical case illustrating the diagnosis and initial therapeutic outcomes of ovarian cancer metastasis to the breast and reviews pertinent features in the medical literature.

Key words: Ovarian cancer; breast metastasis.

1. INTRODUCTION

Metastasis to the breast from other organs is extremely rare, accounting for approximately 0.33–6.3% of all malignant breast tumors. Most of these cases originate from contralateral breast cancer, melanoma, sarcoma, lung cancer and renal cell carcinoma [1]. Metastasis to the breast from primary ovarian carcinoma is even rarer, with the first case reported globally in 1907 [2]. According to a study by Hadju and Urban on 4,051 patients with malignant breast tumors, the rate of tumors originating from female genital organs was 0.17%, and primary ovarian cancer accounted for only 0.07% [3]. The prognosis for breast metastases is

typically very poor, and treatment approaches vary significantly depending on the site of the primary tumor. Therefore, accurate identification of the primary site is crucial for developing an appropriate treatment plan.

Typically, ovarian cancer spreads within the peritoneal cavity, as well as via the lymphatic and hematogenous routes. Common metastatic sites include the peritoneal cavity and retroperitoneal lymph nodes, while extra-abdominal organ metastases-especially to the breast-are rare. On average, breast metastases are detected about two years after the diagnosis of primary ovarian cancer [4]. Our case involves breast metastasis detected at the time of initial diagnosis, which is an extremely rare presentation globally.

Clinical Case

A 49-year-old female patient, PARA 2002, with no significant past medical history and no family history of cancer, presented to the hospital

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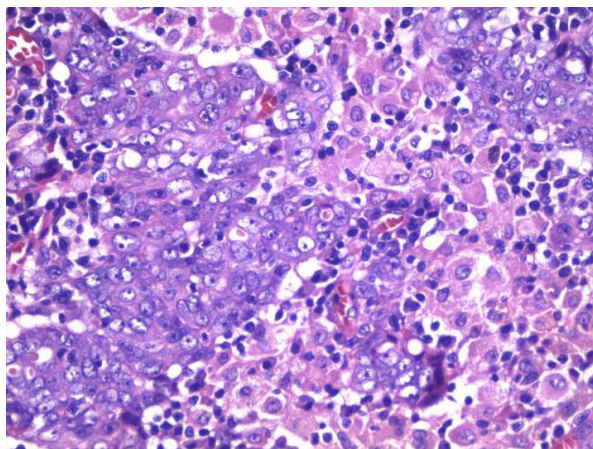
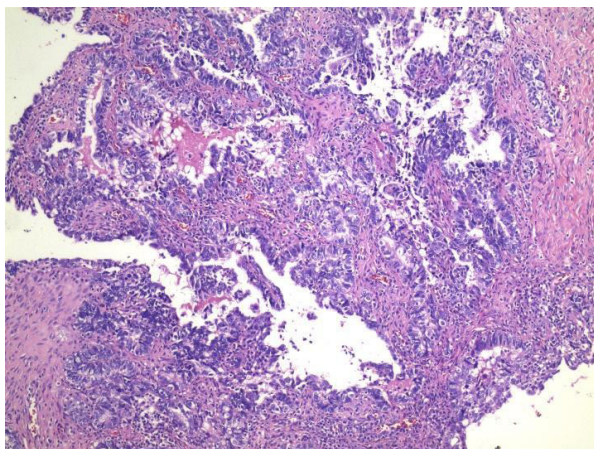
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after detecting a lump in her left breast. Clinical examination revealed a firm, poorly mobile mass in the upper outer quadrant of the left breast, measuring 3×3 cm. Additionally, a firm left inguinal lymph node measuring 3×4 cm was palpated. No

abnormalities were noted in other organs. Breast ultrasound and mammography revealed a 29×25 mm mass classified as BIRADS 4B. A 6 mm left axillary lymph node was observed with preserved hilar structure.



Microscopic image of the lesion in the right ovarian tumor

Cytological analysis showed malignant epithelial cells in both the left breast tumor and left inguinal lymph node, while the left axillary lymph node was benign. A biopsy of the left breast tumor and left inguinal lymph node was performed. Histopathological results indicated grade III invasive carcinoma in the breast and metastatic carcinoma in the inguinal lymph node. The initial diagnosis was left breast cancer with metastasis to the left inguinal lymph node. To assess metastases in other areas, the patient underwent a whole-body CT scan and bone scintigraphy. Imaging revealed a well-defined right ovarian mass measuring 38×52 mm. Multiple enlarged lymph nodes were observed along the abdominal aorta, bilateral pelvic vessels, and left groin, with the largest measuring 39×52 mm and showing loss of hilar architecture. No abnormalities were found in other regions. Gastroscopy and colonoscopy were also performed and yielded normal results. At this point, three differential diagnoses were considered: (1) Primary breast cancer, (2) Primary ovarian cancer, (3) Synchronous primary cancers of both the breast and

ovary. To distinguish between these possibilities, immunohistochemistry (IHC) was performed on both the left breast tumor and the left inguinal lymph node specimens. Results showed both lesions were positive for estrogen receptor (ER), negative for progesterone receptor (PR), negative for human epidermal growth factor receptor 2 (HER2), positive for GATA binding protein 3 (GATA3), positive for p53, positive for Wilms' tumor 1 (WT1), and positive for paired box gene 8 (PAX8). This immunoprofile is consistent with high-grade serous carcinoma of ovarian origin. Thus, the definitive diagnosis was stage IV ovarian carcinoma with metastases to the left breast, pelvic lymph nodes, para-aortic lymph nodes, and left inguinal lymph node.

The patient received neoadjuvant chemotherapy with a regimen of Paclitaxel 175 mg/m² and Carboplatin AUC 5, administered every three weeks for three cycles. This regimen is known to be effective against both breast cancer and ovarian cancer. After three cycles, the left breast tumor decreased in size from 29×25 mm to 7×11 mm;

multiple lymph nodes along the para-aortic, bilateral pelvic chains, and left inguinal region (initially up to 39×53 mm) were reduced to 16×19 mm; the right ovarian mass decreased from 38×52 mm to 33×35 mm; and the tumor marker CA125 declined significantly from 2,817 U/mL to 57.3 U/mL.

The patient was evaluated as having a partial response to neoadjuvant chemotherapy and was subsequently indicated for interval debulking surgery. Intraoperative findings included: A left breast lesion measuring 1×2 cm, cystic and degenerative in nature; A left inguinal lymph node measuring 1.5×2 cm, firm; A right ovarian tumor measuring 3×4 cm; Peritoneal implants in the pelvic cavity with nodular masses up to 2 cm in size; Enlarged, soft bilateral pelvic and para-aortic lymph nodes measuring 1–2 cm. The diaphragmatic peritoneum, paracolic gutters, and mesentery appeared smooth and uninvolved. The patient underwent the following procedures: Total hysterectomy, Bilateral salpingo-oophorectomy, Omentectomy, Pelvic peritonectomy, Excision of the left inguinal lymph node, Left breast tumor resection. Postoperative histopathology findings: The right ovarian tumor was confirmed to be high-grade serous carcinoma, grossly presenting as a thin-walled cystic lesion containing yellowish fluid, measuring 5×3.5×3 cm. Microscopic examination showed tumor cells arranged in solid sheets and papillary structures, with areas of degeneration. Metastatic carcinoma was identified in the right pelvic, para-aortic and left inguinal lymph nodes, with some areas showing signs of tumor degeneration. No residual malignancy was detected in the left breast tumor or pelvic peritoneum. The greater omentum, left adnexa, and entire uterus were free of tumor cells. Postoperative recovery was uneventful. The patient is currently planned for adjuvant therapy following surgery.

2. DISCUSSION

Malignant breast tumors are predominantly primary breast carcinomas, with most secondary

breast malignancies originating from the contralateral breast [5]. Advanced-stage ovarian cancer typically presents with widespread peritoneal involvement or retroperitoneal lymph node metastasis within the abdominal cavity. Distant metastases are rare, though the disease can occasionally spread to the liver, pleura, and lungs, with such cases generally associated with poor prognosis [6].

Metastasis of primary ovarian cancer to the breast is extremely rare. In a study of 4,051 patients with breast malignancies, the incidence of ovarian cancer metastasizing to the breast was only 0.07% [3]. Since the first reported case by Sitzenfrey in 1907 [2], a literature review by Tempfer et al. in 2016 identified over 110 reported cases [7], and by 2020, the number had increased to 120 cases, according to Caruso et al [8].

Unilateral breast involvement is more common than bilateral metastases in ovarian cancer. In our case, metastasis was confined to the left breast. According to a 2022 study by Arif Musa et al., only 10 cases of bilateral breast metastases from primary ovarian cancer have been reported.

The median time to breast metastasis detection after a primary ovarian cancer diagnosis is approximately two years. In contrast, our patient presented with breast metastasis at the time of initial diagnosis, which is extremely rare. According to Ferrari et al. (2020), only 18 cases of synchronous breast metastases at the time of ovarian cancer diagnosis had been reported [4].

Our case was histopathologically identified as high-grade serous carcinoma (HGSC) of the ovary. This histological subtype accounts for approximately 72% of ovarian cancer metastases to the breast, according to Antuono et al. [2]. Among the patients in the Ferrari study with breast metastases at the time of ovarian cancer diagnosis, 61% were HGSC [4].

Differentiating between primary and metastatic breast tumors is crucial, as it directly impacts both prognosis and treatment strategies. Typically,

metastatic breast tumors present as well-defined masses without architectural distortion, as was seen in our case. On mammography, metastatic lesions often appear as solid, well-circumscribed masses without spiculations or skin retraction. On ultrasound, ovarian metastases to the breast may show lobulated margins, well-defined borders, and posterior acoustic enhancement. Due to the psammoma bodies (calcifications) seen in ovarian carcinoma, calcifications on imaging may not reliably distinguish primary breast cancer from ovarian metastases [2].

Histopathology and immunohistochemistry (IHC) are critical in differentiating between primary breast carcinoma and ovarian metastasis to the breast. Both tumors are commonly positive for cytokeratin 7 and estrogen receptor (ER). Wilms' tumor 1 (WT1) nuclear expression is present in about 70% of ovarian carcinomas, but in less than 10% of breast cancers. Paired box gene 8 (PAX8) is another useful marker, being positive in 87% of ovarian cancers and consistently negative in breast cancers. Both primary and metastatic breast tumors may show GATA3 positivity in 80–90% of cases, though this rate is lower in triple-negative breast cancers (around 67%). GATA3 can also be expressed in 86% of urothelial carcinomas but is rarely seen in ovarian cancers. p53 mutation marker, frequently positive in ovarian carcinoma, is a key factor in distinguishing the origin of the malignancy [9]. In our case, IHC staining showed positivity for ER, PAX8, WT1, GATA3, and mutant p53, supporting a diagnosis of metastatic ovarian serous carcinoma.

Our patient underwent three cycles of neoadjuvant chemotherapy, with a partial clinical response, followed by maximal cytoreductive surgery, and is planned to continue with adjuvant chemotherapy. According to various studies, the overall survival following diagnosis of breast metastasis from ovarian carcinoma is limited, ranging from 13 days to 3.5 years, with most patients succumbing to the disease within one year [10].

3. CONCLUSION

This is an extremely rare clinical case of ovarian cancer metastasizing to the breast, identified at the time of initial diagnosis a phenomenon seldom reported both in Vietnam and globally. Accurate determination of the primary site of metastasis is of paramount importance, as it directly influences the patient's prognosis and therapeutic strategy. Diagnosis should be based on a combination of clinical presentation, radiological findings, and, most critically, the use of histopathology and immunohistochemistry, which play a pivotal role in establishing a definitive diagnosis and distinguishing between primary breast cancer and metastasis from ovarian origin.

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