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Case Report

Ovarian Cancer and Breast Metastases: A Diagnostic Dilemma

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Abstract

Metastases of ovarian carcinoma to the breast are uncommon. The incidence of ovarian metastasis to the breast ranges from 0.5% to 1.2%. Nevertheless, its detection and distinction from other primaries, especially primary breast carcinoma, is important as treatment and prognosis differ significantly. We report the case of a 38-year-old Tunisian woman with bilateral metastases to breast from ovarian carcinoma. Through a review of literature, we discuss the clinical, radiological and histological characteristics of ovarian metastases to the breast.

Keywords: Breast, Diagnosis, Metastases, Ovarian cancer

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Introduction

Ovarian carcinoma (OC) is limited to the peritoneum in 85% of cases.[1] Metastases of OC to the breast are almost exceptional. About 2% of malignant neoplastic breast lesions are of secondary origin and they most commonly originate from primary contralateral breast tumors.[2] Clinical studies have revealed that the incidence of breast metastases varies from 0.5% to 1.2 %.[3] Breast metastases have diverse characteristics and tumor appearance depending on the site of the primary tumor. Nevertheless, they can sometimes mimic a primary breast cancer.

Case Report

A 38-year-old woman, with a personal history of primary infertility treated with hormone replacement therapy during one year, presented to the gynecologic department in August 2017 with abdominal distension and discomfort. She underwent pelvic ultra-sound examination and abdominopelvic computed tomography (CT) which showed bilateral ovarian masses with peritoneal lesions. There were no lymph nodes, nor intra-thoracic metastases. She underwent exploratory laparotomy. During intra-operative exploration, the surgeons noted two solid-cystic ovarian masses as well as diffuse peritoneal carcinomatosis. Biopsies were taken. Histological study showed a poorly differentiated ovarian adenocarcinoma. On immunohistochemical staining, the tumor cells were positive for cytokeratin, PAX8, CA 125, estrogen receptor (ER), progestin receptor (PR) and vimentin, and negative for calretinin-synaptophysin and chromogranin. The final pathologic diagnosis was stage IIIc poorly differentiated adenocarcinoma of ovaries. The CA 125 level was elevated to 130 U/mL. The patient received paclitaxel-carboplatin combination chemotherapy. The CA 125 level decreased to 30 U/mL after three cycles. After four courses of CT, 4 cm non-fixed breast masses were found located in the superior external quadrant of each breast. There was no nipple discharge and no skin infiltration of the breasts. She also had a solid fixed 2 cm axillary lymph node with 2 cm left supra-clavicular lymph node. We noted the presence of cutaneous nodules disseminated on the chest wall and on the periumbilical region (Figure 1). Mammography showed scattered fibro-glandular densities of the breasts, without architectural distortion or micro-calcifications. Breast ultra-sonography demonstrated a right non-vascularized ductal dilatation with no associated masses, a left axillary lymph node of 20 mm and a left supra-clavicular node of 15 mm.

The CA125 level had risen to 150 U/mL. The CA 15-3 level was within normal ranges. CT revealed new mediastinal lymph nodes, bilateral pleurisy with pulmonary metastases.

With regard to the breast masses and the disseminated cutaneous lesions, we suspected primary breast cancer. Therefore, biopsies were taken from the two breast masses and skin lesions. Histopathological study reported dermal and mammary involvement by a poorly differentiated carcinoma (Figure 2). Immunohistological study of both

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Figure 1. Breast Masses (Blue Star) and Skin Nodules (Black Arrow).

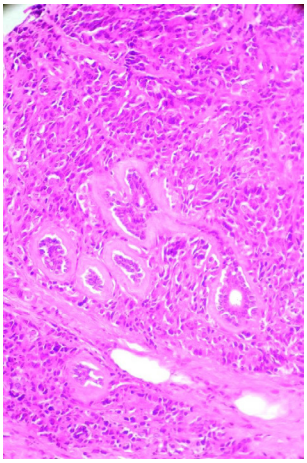

Figure 2. Breast Involvement by a Poorly Differentiated Carcinoma (Hematoxylin and Eosin Stain x400).

cutaneous and breast biopsies were positive for ER, PR, and PAX 8. It was negative for GATA binding protein 3, mammaglobin, WT1, Her2/neu oncoprotein and the prolactin-induced protein, also named gross cystic disease fluid protein-15 (GCDPF15) (Figure 3). The final diagnosis was breast and skin metastases from OC. The patient received one cycle of second line chemotherapy type Gemcitabine. However, the disease evolution was rapidly fatal because of respiratory failure.

Discussion

Metastases of OC to the breast are infrequent, accounting for almost 110 reported cases in the literature[4] and only 1.9% of cases. Metastatic lesions of the breast from extra mammary origins are rare, accounting for 0.5 to 1.2% of malignant breast tumors.[3] A contralateral primary breast tumor represents the most common origin of breast metastases.[5] Hajdu and Urban studied 4051 patients with malignant breast lesions. The overall incidence of breast metastases from primary gynecologic cancers was 0.17%, with only 0.07% originating from ovarian cancer.[6] Usually, breast metastases are well-circumscribed, as in the case of

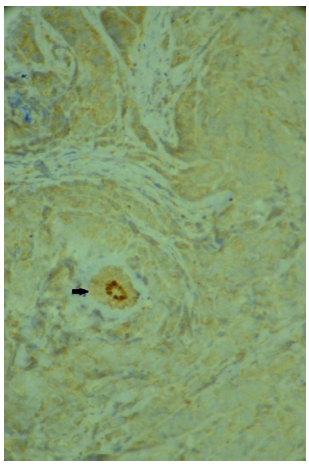

Figure 3. Negative Immunostaining of Tumor Cells for GATA3 (GATA3 x400) with Positive Immunostaining in the Normal Mammary Gland (Black Arrow).

our patient.[7] Mammography shows a well-circumscribed, non-calcified dense mass with no spiculations, micro-calcifications or architectural distortion.[8] On ultra-sound, micro-lobulated margins and posterior enhancement are visualized. In our case, breast ultra-sonography demonstrated a right non-vascularized ductal dilatation with no associated masses.

Differentiation between metastases of OC to the breast and a primary breast cancer needs a combination of histology and immunohistopathological study. Yet, both entities can yield similar results. Breast and ovarian cancers are usually positive for cytokeratin 7 and ER.[8] The antigen expression pattern of the epithelial membrane is typical for serous papillary carcinoma.[9] WT-1 expression in the cell nuclei occurs in 70% of OC. However, less than 10% of breast cancers express this marker.[10] GCDFP-15 expression is found in approximately 40% of BCs. Its expression is negative in triple negative carcinomas.[8] CA125 staining is present in 60% to 90% of OCs. PAX 8 is also a useful marker in differential diagnosis as it is positive in 87% of OCs and totally negative in mammary carcinoma.[11] Primary and metastatic mammary carcinomas may express GATA 3 (80–90%); however, its expression is lower in triple-negative tumors (67%). GATA 3 expression is also detected in 86% of urothelial carcinomas but in none of OCs.[11] In the present study, the breast and cutaneous lesions were positive for ER, PAX 8 and negative for GATA 3.

In conclusion, breast metastases from ovarian cancer are exceedingly rare. Histology and immunohistological study are of great help in recognizing histological patterns and distinguishing them from *de novo* breast carcinoma.

Authors' Contribution

WBK: Analysis and interpretation of data, drafting of the manuscript and critical revision of the manuscript for important intellectual content; SS: Acquisition of data, analysis and interpretation of data and drafting of the manuscript; SC: Acquisition of data, analysis

and interpretation of data; NT, TB and KC: Interpretation of data; AK: Interpretation of data and critical revision of the manuscript for important intellectual content.

Conflict of Interest Disclosures

None.

Ethical Statement

Informed consent was obtained from the patient to publish these images.

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