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Original Research Paper

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PRIMARY OVARIAN CARCINOMA WITH SYNCHRONOUS ISOLATED BREAST METASTASIS: A MANAGEMENT DILEMMA

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ABSTRACT

Context. Synchronous isolated breast metastasis from primary ovarian carcinoma is rare, with few cases reported in the literature.

Case. We present a patient with isolated breast metastatis from a primary ovarian carcinoma at initial presentation. The diagnosis was confirmed by histopathology and immunohistochemistry. The histopatholgy of breast lesion was identical to ovarian mass and malignant cells from breast lesion were positive for CA-125, WT-1 and negative for ER/PR, CEA and GCDFP-15. She underwent neo-adjuvant chemotherapy followed by surgery and now undergoing completion chemotherapy.

Conclusion. Synchronous isolated breast metastasis from a primary ovarian tumor is rare. Accurate differentiation is necessary because treatment and prognosis differ significantly for patients with ovarian metastasis to the breast, as compared with patients with primary breast cancer. Ovarian metastasis to the breast is associated with poor prognosis: patient survival ranged from 13 days to 3.5 years, with a median survival of 8.1 months.

KEYWORDS : breast cancer, ovarian cancer, ovarian cancer metastasis, breast cancer metastasis.

INTRODUCTION

Isolated breast metastasis from primary ovarian carcinoma is rare. At times, it is difficult to differentiate primary lesion from metastatic lesion in the breast. Here we present a unique and rare case of isolated synchronous breast metastasis from ovarian primary and the importance of histopathology and immunohistochemistry in clinching the diagnosis.

Case Capsule

A 55-years old female was referred to our institute with FNAC from left breast lump and axillary node suggestive of ductal carcinoma and biopsy from right ovarian mass showing poorly differentiated carcinoma . She had progressively increasing left breast lump and abdominal pain for two months. On clinical examination she had 5x4 cm firm hard mass lesion in left breast which was adherent to skin with Peau'd orange appearance with 3x3 cm left axillary lymph node which was hard and partially mobile. Right breast was normal. No mass was palpable on per abdomen examination, however per vaginal and per rectal examinations revealed a hard irregular 6x5 cm right adnexal mass lesion pushing uterus to left side. Rest of the systemic examination was normal.

Investigations revealed normal hemogram, biochemistry and echocardiography. Bilateral mammosongraphy revealed multicentric breast mass lesion in left breast, diffuse skin thickening with metastatic left axillary lymphadenopathy (BIRADS V). Right breast was normal. CT scan of abdomen and pelvis was suggestive of 8x6 cms solid –cystic lesion in right adnexal region extending into pouch of douglas, right ovary not seen separately from the lesion displacing uterus to left side and abutting rectum with loss of fat plane with no pelvic or para-aortic lymphadenopathy. Rest of abdominal organs were normal and no omental caking was observed. CT- thorax was normal. Her CA-125 and CEA were 526.4 U/ml (normal 0-35) and 1.38 ng/ml (normal 0-3) respectively. She underwent core biopsy from breast lesion and USG guided biopsy from ovarian mass. Histopatholgy from ovary revealed poorly diffentiated adenocarcinoma; breast biopsy suggestive of metastatic adenocarcinoma on which IHC was done- CA-125 and WT-1 were positive and ER/PR and GCDFP15 were negative suggestive of primary ovarian carcinoma. Final diagnosis of primary ovarian carcinoma with isolated breast metastasis was made. Case was discussed in tumour board in our institute where it was decided to first subject the patient to neo-adjuvant therapy; 3 cycles of TEC (Docetaxel 75mg/m , Cyclophosphamide 500mg/m and Epirubicin 75mg/m) were administered. After 3 weeks of completion of 3 cycles of chemotherapy, her mammosonography and ultrasonography of abdomen and pelvis showed no change from previous findings. Her CA-125 was 578.2 U/ml, however serum CEA post chemotherapy was 471.8 ng/ml (increased from pre chemotherapy period). She underwent staging laparotomy with peritoneal fluid cytology, total abdominal hysterectomy and bilateral salpingo-oophorectomy, bilateral pelvic lymphadenectomy, total omentectomy, right hemicolectomy (in view of hard mass 2x2 cm at base of appendix which was partially adherent to ovarian mass) with ileo-transverse anastomosis followed by palliative mastectomy and removal of separate nodal mass from axilla (another mass was adherent to neurovascular bundles in axilla and left in situ). On post operative day 3, she developed high grade fever 2 episodes 12 hrs apart. Her NS1 AG was positive and platelets were 1.37 lacs/mm (dengue fever) with daily platelets count showed decreasing trends till her platelets came down to 42 thousands/mm. While she was recovering from dengue fever in post operative period, another complication was noted on post op day 8- minor anastomotic leak (probably due to superimposed dengue). However, she recovered on conservative management and discharged on 22nd post operative day. Final histopathology findings- a) right ovarian mass- papillary serous adenocarcinoma, poorly differentiated, 8x7 cm solid cystic mass with smooth cut surface with infiltration of capsule, right fallopian tube was normal ; b) left ovary+fallopian tube+ uterus and cervix- normal and free of tumour ; c) omentum- free of tumour ; d) right pelvic lymph nodes- all eight lymph nodes free of tumour ; e) left pelvic lymph nodes – all 6 nodes free of tumour ; f) right hemicolectomy – tumour involves full thickness of appendix near base, rest ileal and colonic mucosa free of tumour ; g) left breast with axillary nodal mass- metastatic adenocarcinoma along with skin involvement and matted mass showed metastatic tumour with perinodal extension. IHC on a)appendix- CK7, WT1, CA125- all positive and CK20, CEA, GCDFP15- all negative ; b) breast- WT1, CK7, CA125- all positive and GCDFP15, ER/PR- all negative. Hence, IHC findings was suggestive of primary ovarian carcinoma

with metastatic adenocarcinoma of breast. Her serum CA125 and CEA on 21st day of surgery were 45.1 U/ml and 4.6 ng/ml respectively.

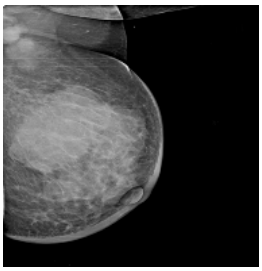

FIG 1 : Mammography of left breast

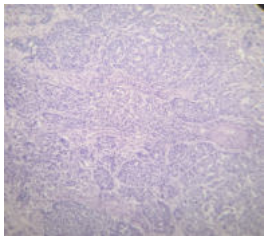

FIG 2: Section of ovarian lesion- Papillary serous adenocarcinoma

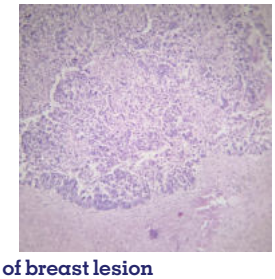

FIG 2: Section of breast lesion

DISCUSSION

Primary breast malignancy in women is a common tumour, however metastatic tumors to the breast are rare, accounting for 0.5% to 1.3% cases.[1] Majority of the metastasis are from contralateral breast, other most common extramammary sites are lymphomas, melanoma and gastrointestinal malignancies.[2] Hadju and Urban reported an overall incidence of primary gynaecologic cancers metastatic to the breast of 0.17%, with 0.07% of metastatic disease originating from a primary ovarian tumor.[3] In 1907, Sitzenfrey reported the first case of metastasis to the breast from ovarian primary.[4]

Clinical profile of patients with ovarian primary metastasis to the breast reveal that they present at a younger age, with median age of presentation is 46.28 years (range 16-70).[5] Breast metastasis is generally diagnosed an average of 2 years after the initial diagnosis of primary ovarian cancer. Metastasis to breast can also present synchronously, though rare, as seen in our case.[6] Epithelial ovarian cancer spread mainly by direct extension, by exfoliation of tumour cells or by lymphatic spread to lymph nodes. The most common site of extra-abdominal spread is pleural space (thought to occur via transdiaphragmatic lymphatics) leading to pleural effusion. Distant metastasis via hematogenous route is uncommon and mainly spreads to liver, spleen lung and brain. Isolated metastasis to breast is rare and in majority, usually patients have widespread dissemination with an average of 4 metastasis to other sites.[6,7]

The histologic variant of ovarian cancer most commonly associated with breast metastatis is papillary serous adenocarcinoma. Other histological subtypes are mucinous cystadenocarcinoma, lymphosarcoma, choriocarcinoma, dysgerminoma, endometroid carcinoma and carcinoid.[3]

Isolated breast metastasis may mimic primary breast carcinoma. Prognosis and treatment options are different in both breast metastasis and primary breast carcinoma, thereby lays the paramount importance of differentiating the two different pathologies of breast. Metastatic breast lesion mostly appear to be benign in both clinical and mammography finding. The most common form of clinical presentation is a solitary tumor with a well circumscribed, firm nodular mass with discreet border: few present with large ill-defined mass lesions with skin involvement like Peau'd orange appearance as seen in our case; presenting clinical features consistent with inflammatory breast cancer are rarity.[4]

On mammography, metastatic breast lesions frequently present as dense, well-circumscribed, non-calcified masses. Generally, spiculations, microcalcifications, architectural distortion and other skin changes are absent in metastatic lesions. However, microcalcifications may be seen with ovarian metastasis to breast, because of the presence of psammoma bodies associated with some ovarian tumours.[8]

Histopathologically, primary breast and ovarian tumors may yield similar results. However, in most cases, metastatic lesions resemble their primary ovarian tumour. Diagnosis is very difficult in poorly differentiated ovarian carcinoma. Therefore, accurate differentiation is necessary . Fine needle aspiration cytology cannot differentiate between primary tumour and metastatic lesion. Biopsy should be considered in all patients. Immunohistochemical analysis of tumour cells using cytokeratin(CK) 7, 20, gross cystic disease protein fluid (GCDPF-15), WT-1, CA-125, mammaglobin and ER/PR helps in establishing the origin of the tumour.[9]

Metastatic breast lesions should be distinguished from primary breast tumours to avoid any unnecessary surgical interventions. Ovarian metastasis to the breast should be treated as a stage IV disease, with appropriate chemotherapeutic agents. Mastectomy is best reserved for patients who are unresponsive to systemic therapy and require palliation in view of symptomatic lesions.[10]

Breast metastasis from a primary ovarian tumour is associated with a poor prognosis. In metastatic breast disease from an ovarian primary tumor, average survival is 8.1 months (range 13 days to 3.5 years).[2,10] 1-year survival rate is 40% for patients of ovarian cancer with breast metastasis, as opposed to a 4-year survival rate of 75% for patients with primary breast carcinoma.

CONCLUSION

Isolated synchronous breast metastasis from primary ovarian carcinoma is rare. Accurate differentiation is necessary because treatment and prognosis are different for patients with ovarian metastasis to the breast and primary breast cancer. Breast metastasis from ovarian primary is associated with poor prognosis. However, recently survival rates are increasing with the advent of new effective chemotherapeutic drugs.

Competing Interests

The author(s) declare that they have no competing interests.

Consent

Written patient's consent was obtained for publication of this case report.

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