Breast as an Unusual Site of Metastasis- Series of 3 Cases and Review of Literature

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Abstract Background and objectives Metastasis to the breast from extra mammary sites is uncommon with an incidence ranging from 1.2 to 2 % in clinical reports. Approximately 300 cases of breast metastasis from extra mammary sites have been reported, mostly in small series or as a single case report. Gastrointestinal adenocarcinoma metastasising to the breast is also very rare and only 30 cases have been reported in the literature. Metastatic deposits within the breast may be difficult to distinguish from primary breast carcinoma. Radiological features and immunohistochemistry especially for steroid hormone receptors (ER/PR) and expression of gross cystic disease fluid protein (GCDFP) and presence of other immunohistochemistry protein factors in breast metastasis which are specific to primary site may be helpful in differentiating these two conditions. Materials and methods In this series of 3

cases of breast as an unusual site of metastasis, we present different cases of adenocarcinoma of stomach, sigmoid colon and kidney with metastasis to the breast and discuss the differential diagnosis and management plans. Conclusion In conclusion, secondary tumors to the breast are rare and thus differentiating primary tumors from metastatic breast carcinoma is important for rational and optimum therapy and avoidance of unnecessary radical surgery. Palpable breast lump without typical radiological signs of primary breast carcinoma in patients with known primary should be suspected of representing metastasis.

Keywords Adenocarcinoma stomach · Extra mammary metastasis to breast · Renal adenocarcinoma

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Introduction

Carcinoma of the breast is the second commonest malignancy affecting half a million women worldwide each year. It is one the major causes of death in women between 40 and 44 years age group that has become a genuine public health problem. Breast is the most common site of cancer in women. Studies have revealed that 1 in 50 women in India can develop breast cancer in their lifetime. Risk factors for breast cancer are age, early menarche, late menopause, delayed pregnancy, obesity, history of ovarian cancer, hormone replacement therapy and non breast feeding. Breast cancer is highly malignant and metastasis to various organs likes bone, liver, lung and brain. Metastasis to breast is very rare and most of them from contra lateral breast (87 %). But metastatic involvement of the breast by non mammary malignancy is extremely rare with the incidence ranging from 1.2 to 2 % of all malignant breast tumors. Out of 300 cases of breast metastasis primary from gastric adenocarcinoma is extremely rare and in the literature only 30 cases have been described[1](Figs. 1, 2, 3)

Fig. 1 Stomach adenocarcinoma metastasis to left breast and its mammogram view

Renal cell carcinoma is one of the most aggressive urological tumours and account for 3 % of also cancers in adults. It displays an extremely variable and unpredictable course both in its clinical development and its metastasis. 30 % of renal cell carcinoma has metastasis at the time of diagnosis, most commonly in the lung (70 %), lymph nodes (55 %), bone (42 %), liver (41 %), adrenal gland (15 %) and central nervous system (11 %) [2]. Breast involvement with renal cell carcinoma is also very rare. Only 3 % of secondary metastasis to breast is from renal origin. Less than 20 cases of breast metastasis from renal cell carcinoma have been reported so far, most of them are metachronous than synchronous.

Case Report 1

45 year woman presented with pain in the upper abdomen and dysphagia. Patient also complained of lump in the left breast. Physical examination revealed a firm 4x4cm lump in the upper outer and inner quadrants of left breast without evidence of axillary or supraclavicular lymphadenopathy. The overlying skin was normal. The contra lateral breast and axilla were normal. Upper GI endoscopy showed thickening of the body and fundus of the stomach which

was diagnosed as adenocarcinoma grade III on biopsy. CT scan abdomen was similar to endoscopic findings with perigastric node enlargement. Mammography revealed isoechoic lesion measuring 2x2cms in 12 'o' clock position in periareolar region of left breast. Rest of the left breast and right breast were normal. There was no significant axillary lymphadenopathy. It was reported as mostly benign lesion in left breast, correlate with FNAC. FNAC of left breast showed monolayer sheets and clusters of benign ductal cells and background shows numerous single and few clusters of malignant cells, with doubtful metastatic origin.

Considering the fact that the clinical picture was consistent with a primary cancer of the stomach with metastasis to the left breast, an exploratory laparotomy and wide local excision of the left breast lump was planned. The patient underwent total gastrectomy, oesophagojejunostomy with jejunoejunostomy and wide local excision of left breast lump. No perioperative complications were observed.

Microscopic examination of the gastrectomy and breast specimen revealed adenocarcinoma grade III. The tumor showed infiltration into the serosa. Lymphovascular tumor emboli were not identified. 12/12 lymph nodes showed metastatic carcinoma with extra nodal spread. Proximal, distal and circumferential resection margins were free of tumor. Wide

Fig. 2 Infiltration of stomach by tumor cells (upper left). Similar cells infiltrating benign breast ductal cells (upper right) (low power H and E stain). Breast metastasis negative for ER and PR by immunohistochemistry (lower left and right)

Fig. 3 Renal cell carcinoma with left breast (chest wall) metastasis. CT scan and microscopic view

local excision of breast showed a similar tumor. Tumor cells showed pale blue intracytoplasmic mucin indicating metastasis from a tumor of an organ producing acidic mucin like stomach. On immunohistochemistry only few tumor cells expressed CK20 but all the cells are strongly positive for CK, CEA. But GCDFP, CK7, S-100 protein, ER, PR, syatophysin, chromogranin, mamoglobin negative. Special stains revealed that intracytoplasmic mucin was mucicarmine and alcian blue positive. Special stains and immunohistochemistry profile of the stomach adenocarcinoma were identical supporting the diagnosis of metastatic gastric carcinoma in the breast. Considering the stage of the disease and age of the patient she was offered palliative chemotherapy.

Case Report 2

A 38 years female patient previously treated for adenocarcinoma sigmoid colon with surgery and 6 cycles of chemotherapy presented with right breast lump after 1 year of chemotherapy. On clinical examination diffuse lump of size 3X3 cms. was present in outer and upper quadrant of right breast

with no palpable axillary nodes. Mammography revealed well circumscribed mass in outer and upper quadrant of right breast without micro calcification and no obvious axillary nodes and reported as BIRADS IV (Breast Imaging Reporting And Data System). Fine needle aspiration cytology showed malignant signet ring cells under the background of normal ductal cells. Excision biopsy of the lump revealed microscopic features similar to signet ring cell adenocarcinoma of sigmoid colon. These cells are again positive for CK 20, CEA and negative for CK 7, GCDFP, ER and PR which confirmatory for GIT primary. In view of progressive disease and no other site of metastasis another 6 cycles of chemotherapy was planned for this patient.

Case Report 3

50 year old man presented with mass in the left breast since 3 months and pain abdomen since 2 months. On clinical examination hard lump was palpable in the central quadrant of the left breast measuring about 10X10 cm. There was no infiltration to the underlying structure and to the skin. Axillary

nodes were not palpable. On examination of the abdomen a huge left kidney was palpable. CT scan of the thorax and abdomen revealed irregular heterogeneously enhancing mass measuring 15X13X8 cms. arising from upper pole of the left kidney. Another well defined heterogeneously enhancing mass was seen left anterior mid chest wall with multiple pulmonary nodule. All these suggestive of left renal cell carcinoma with bilateral pulmonary and left chest wall/breast metastasis. Bone scan revealed multiple vertebral metastasis. True cut of both left renal mass and breast mass revealed conventional clear cell renal cell carcinoma. There was no evidence of in situ ductal or lobular disease in breast tissue. These tumour cells were positive of vimentin and CK and negative for GCDFP, CK 7, ER and PR. indicating primary was from kidney. In view of multiple metastasis and performance status II ECOG (Eastern Cooperative Oncology Group) surgery was not offered. The patient was treated with targeted therapy, oral tyrosine kinase inhibitor sorafenib with good tolerance. The patient died after 1 year of diagnosis and treatment.

Discussion

Breast carcinoma is the most common tumor of the adult women in most parts of the world. But metastatic involvement of the breast by non mammary malignancy is extremely rare with the incidence ranging from 1.2 to 2 % of all malignant breast tumors. Metastasis to breast from gastric adenocarcinoma is extremely rare and in the literature only 30 cases have been described [1]. Metastasis in the breast suggests that the physiological state of the breast may provide a fertile soil for metastasis [3].

However it must be remembered that carcinoma of the stomach is not always a primary lesion. Walker and associates reported three patients in whom primary gastric carcinoma of linitis plastica was initially confidently diagnosed. All three patients previously had been treated for breast carcinoma and, in two of the patients the disease was bilateral. A review of the original histopathology showed infiltrating nodular breast carcinoma of a similar type to that seen in the stomach. In one case the disease responded well to tomosifine [4].

Largest series was published by Georgiannos et al. [5]. In this report, the files of histopathology department of the Royal Landon hospital were reviewed including all surgical and postmortem materials during the period 1907–1999. It was found that 450 malignancies (3.2 %) had involvement of breast by secondary tumors, most of which (390 malignancies 87 %) were considered metastasis from the contra lateral breast. It was also found that remaining 60 malignancies (13 % of secondary malignancies and 0.4 % of total breast malignancies) were nonmammary metastasis. Involvement of the breast by hematological malignancies like leukemia and

lymphoma were becoming relatively more common. Only 4 of the 60 patients had adenocarcinoma of the stomach [5].

Clinically metastatic lesions are not distinct from primary tumors. Thus differentiating primary from metastatic breast carcinomas important for rational and optimum therapy and avoidance of unnecessary radical surgery [6,7]. The metastatic lesions of the breast are usually palpable and most often located in the upper outer quadrant of the left breast. Multiple diffuse and bilateral involvement is rare also is the involvement of the axillary nodes [3,8].

On mammography, the metastatic lesions may appear as well circumscribed mass which are difficult to distinguish from fibroadenoma or any other benign lesions. Spicules are absent as there is little or no desmoplastic reaction associated with metastatic lesion. Micro calcification is not a feature of metastasis but has been observed in metastatic ovarian carcinoma with psammoma bodies. Thus the presence of spicule lesions and micro calcifications on the mammogram is consistent with primary breast carcinoma and it particularly rules out the possibility of the metastatic character of a tumor in the breast [3,9]. Kwak et al considered the absence of mass lesions or micro calcification on mammography/ultrasonography to be typical of metastatic disease in patients with adenocarcinoma (signet ring cell) of breast [9].

Metastasis from stomach carcinomas on immunohistochemistry are usually positive for CK20, CEA but negative for GCDFP, ER, PR, CK7 strongly supports a diagnosis consistent with a primary adenocarcinoma of GIT tumor rather than a primary breast adenocarcinoma [6,7,10].

Breast metastasis from a renal tumour is also extremely rare, accounting for 3 % of breast secondaries [11]. The metastatic behavior of renal cell carcinoma is frequently bizarre and unpredictable. The clinical literature includes a surprisingly high number of organs involved in metastasis, the number is even higher in autopsy series, which include metastatic sites never or rarely reported in clinical studies [12]. The majority of presentations (80 %) have been metachronous metastasis which has been found to carry a better prognosis than the synchronous metastasis [13]. There have been less than 20 cases of metastasis renal cell carcinoma to the breast reported so far. Among them 12 cases were breast metastasis identified between 1 and 18 years after nephrectomy, including bilateral breast metastasis in a 14 year old girl [14]. Breast metastasis was the initial presenting symptom in 2 cases as in our case report. A crude survival rate of 11 months has been reported after detection of metastasis [15].

Clinically, metastatic lesions in the breast presents as painless swelling with rapid growth. Unlike primary tumour skin is not involved and axillary node involvement is rare. Mammographically it shows well circumscribed lesion without micro calcification and should be suspected of secondaries in breast with preexisting or known primary elsewhere [16].

Conclusion

In conclusion, secondary tumors to the breast are rare and are reported only in approximately 2 % of all malignant breast tumors. Thus differentiating primary tumors from metastatic breast carcinoma is important for rational and optimum therapy and avoidance of unnecessary radical surgery. Palpable breast lump without typical radiological signs of primary breast carcinoma in patients with primary somewhere else should be suspected of representing metastasis. Immunohistochemistry that is positive for CK20, CEA but negative for CK7, GCDFP, ER, PR helps in the diagnosis of primary GIT tumor metastasis to breast.

Declaration We hereby declare that the work entitled “Breast as an unusual site of metastasis- series of 3 cases and review of literature” is a bonafide and genuine research work carried out by us.

Conflict interest None declared

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