Metastases in the breast from extra-mammary sites are uncommon with the incidence ranging from 1.7% to 6.6% in autopsy series and 1.2-2% in clinical reports and being 2.7% in cytological series.[1] Approximately 300 cases of breast metastases from extra-mammary sites have been reported, mostly in small series or as single cases.[2] Gastric cancer metastases to the breast are rare with only 23 cases reported in the literature.[1-8]

We report an exceptionally rare case of a gastric signet ring cell carcinoma (SRCC) metastasising to the breast and discuss the features differentiating metastatic gastric SRCC from primary SRCC of the breast.

**Case History**

A 34-year-old lactating woman presented with pain in the right hypochondrium and dysphagia. The patient also complained of a lump in the left breast. A similar swelling had appeared in the right breast one month before and had subsided with lactation and manual expression of milk.

Physical examination revealed a firm, 4x3 cm lump in the upper outer quadrant of the left breast without evidence of axillary or supraclavicular lymphadenopathy. The contralateral breast and axilla were normal. Gastrointestinal endoscopy showed a submucosal infiltrative lesion involving the proximal part of the stomach diagnosed as poorly differentiated adenocarcinoma on preoperative biopsy. Computerized tomographic (CT) scan of the abdomen showed thickening of the gastric wall. Mammography revealed heterogeneously dense breasts without any evidence of mass lesions, architectural distortion or microcalcifications [Figure 1]. Ultrasonography of the left breast was normal. With the exception of elevated carcinoembryonic antigen (CEA) to the level of 3.7, the tested blood parameters were normal.

Considering the clinical picture being consistent with primary cancer of the stomach with a coexistent benign breast lesion, an explorative laparotomy and a breast biopsy were planned. The patient underwent total gastrectomy with Roux-en-Y oesophagojejunostomy via a left thoraco-abdominal approach. No operative complications were observed. Excisional biopsy of the breast lump showed metastasis of
SRCC on frozen section.

Microscopic examination of the gastrectomy specimen revealed poorly differentiated SRCC, infiltrating the full thickness of the stomach with extensive perineural invasion and one out of ten perigastric lymph nodes showing deposits of metastatic adenocarcinoma. The sections from the breast lump revealed signet ring cells infiltrating the breast stroma [Figure 2]. The tumour cells were hardly seen on routine histology but were highlighted by cytokeratin (CK) immunostaining and on staining the frozen sections with toluidine blue. In the latter, the tumour cells showed pale blue intra cytoplasmic mucin indicating metastasis from a tumour of an organ producing acidic mucin, like the stomach.

On immunohistochemistry (IHC), only a few tumour cells expressed CK 20, but all the cells were strongly positive for CK (antihuman cytokeratin, reacting to a wide range of cytokeratin), epithelial membrane antigen and CEA. GCDFP, CK 7, S-100 protein, oestrogen receptors (ER) and progesterone receptors (PR) were negative. Special stains revealed that the intra cytoplasmic mucin was mucicarmin and alcian blue positive. The special stains and the IHC profile of the stomach carcinoma were identical supporting the diagnosis of metastatic gastric carcinoma in the breast.

The patient received chemotherapy (a combination of Paclitaxel and Carboplatin). Ten days after completion of the first cycle of chemotherapy, she developed a lump in her right breast as well as an infected seroma in the operated left breast and febrile neutropenia. Antibiotics were administered and any further chemotherapy withheld. In view of poor general condition and progressive disease, only symptomatic treatment was then offered. The patient died six months after the surgery.

**Discussion**

The breast is a relatively uncommon site of metastases from extramammary primary malignancies. The average age of patients at the time of presentation of metastases is 47 years. The relatively younger age of women with metastases in the breast suggests that the physiological state of the breast may provide a fertile soil for metastases.

The metastatic lesions are usually palpable and most often located in the upper outer quadrant of the left breast. Multiple, diffuse and bilateral involvement is rare as also is the involvement of the axillary lymph nodes.

On mammography, the metastatic lesions may appear as well circumscribed masses which are difficult to distinguish from fibroadenoma or other benign solid lesions. Spicules are absent as there is little or no desmoplastic reaction associated with the metastatic lesion. Microcalcifications are not a feature of the metastases but have been observed in metastatic ovarian carcinoma with psammoma bodies. Thus, the presence of spiculated lesion(s) and microcalcifications on the mammogram is consistent with primary breast carcinoma and it practically rules out the possibility of the metastatic character of a tumour in the breast.

Kwak et al considered the absence of mass lesions or microcalcifications on mammography or ultrasonography to be typical of metastatic disease in patients with SRCC in the breast.

The histopathological features suggestive of metastases in the breast include absence of in situ carcinoma, which characterises the majority of primary breast cancers. The histological picture usually resembles the extramammary primary tumour and is not typical of breast carcinomas.

Metastases from stomach adenocarcinomas, on IHC, are usually positive for CEA and CK 20 and negative for GCDFP, ER, PR, and CK 7. By combining the results of CK 20 and ER staining, all the metastases to the breast could be properly classified in one study, as all the gastrointestinal tumors expressed the CK 20+ / ER- pattern.

SRCC of the breast is a unique variant of invasive lobular carcinoma constituting 2 to 4.5% of all types of breast cancer. It occurs more commonly in postmenopausal women and reveals high incidence of positivity for ER, PR and GCDFP (90%). Therefore, IHC expression of these markers may be useful in delineating primary and metastatic SRCC in the breast.

Differentiating primary breast SRCC from mammary metastases from a stomach primary is crucial for the management of a patient and can eliminate unnecessary procedures such as radical surgery.

In conclusion, palpable breast lumps without typical radiological signs of primary breast carcinoma in patients with gastric cancer should be suspected of representing metastases. Signet ring cell type of metastatic stomach cancer is difficult to delineate from primary signet ring cell cancer of the breast on histology. Immunohistochemical reactions, especially absence of GCDFP expression in the tumour cells are helpful in making the proper diagnosis.

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References


Cutaneous lesions on the legs

A 34-year-old woman had several symmetrically located, well-circumscribed, non-ulcerating, waxy, red-brown plaques on her lower limbs [Figure 1]. The first lesion appeared 13 years ago. She was concerned about the cosmetic appearance.

Questions
1. What is the diagnosis?
2. What is the systemic association with this dermatosis?
3. How are these lesions managed?

For the answer check page number 130

Figure 1: The first of these multiple, symmetrically located lesions appeared as a small macule 13 years previously. Inset: Close-up view of the oldest lesion shows waxy appearance and telangiectasias