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GASTRIC ADENOCARCINOMA METASTASIS TO THE BREAST- A DIFFERENTIAL DIAGNOSIS WITH PRIMARY BREAST ADENOCARCINOMA AND REVIEW OF LITERATURE.

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ABSTRACT: 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. Gastric adenocarcinoma metastasizing 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) may be helpful in differentiating these two conditions.

In this report, we present a case of adenocarcinoma of stomach with metastasis to the breast and discuss the differential diagnosis.

KEYWORDS: Adenocarcinoma stomach, extra mammary metastasis to breast, breast adenocarcinoma.

INTRODUCTION: Carcinoma of the breast is the second commonest malignancy affecting half a million women worldwide each year. It is one of 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 metastases to various organs like bone, liver,

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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. Metastasis to breast from gastric adenocarcinoma is extremely rare and in the literature only 300 cases have been described¹

CASE HISTORY:-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 contralateral 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 jejunoejejunostomy 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 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 GCDEP, CK7, S-100 protein, ER, PR, synaptophysin, 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.

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 300 cases have been described¹. Metastasis in the breast suggests that the physiological state of the breast may provide a fertile soil for metastasis.²

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

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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 tamoxifen.³

Largest series published by Georgiannos et al⁴ in his report had the files of histopathology of Department of the Royal London hospital 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 non-mammary 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.⁴

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^{5,6}. 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.^{2,7}

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. Microcalcification is not a feature of metastasis but has been observed in metastatic ovarian carcinoma with psammoma bodies. Thus the presence of spicule lesions and microcalcifications 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^{2,8}. Kwak et al considered the absence of mass lesions or microcalcification on mammography/ ultrasonography to be typical of metastatic disease in patients with adenocarcinoma (signet ring cell) of breast⁸.

Metastasis from stomach carcinomas on immunohistochemistry are usually positive for CK20, CEA but negative for GCDEP, ER, PR, CK7 strongly supports a diagnosis consistent with a primary adenocarcinoma of GIT tumor rather than a primary breast adenocarcinoma^{5,6,9}.

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 gastric cancer 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.

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Figure 1: Mediolateral oblique mammograms revealing dense glandular breast. There is no evidence of mass, architectural distortion or microcalcifications in the left breast.

Stomach adenocarcinoma metastasis to left breast.

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).