



EXTRAMAMMARY MALIGNANCY PRESENTING AS PRIMARY BREAST LESION - AN INTERESTING CASE REPORT.

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Abstract :

Primary breast cancers are the most common malignancies in clinical practice and literature. Breasts are also sites of secondary carcinomatous deposits but rare as presenting symptom of extramammary malignancy. We present a case of signet ring cell gastric cancer presenting as breast lesion in a premenopausal female where metastatic evaluation revealed the primary gastric lesion and systemic metastases.

Keyword : Signet ring cell carcinoma, Breast metastases, Gastric cancer.

INTRODUCTION:

Primary breast cancer is the commonest malignancy reported in literature presenting with breast lumps. However, it also constitutes approximately 0.5 – 6.6 % of extramammary cancers metastasizing to breast [1,2,3] , most commonly lymphoma, melanoma, rhabdomyosarcoma, lung, ovarian cancer, etc [4]. Primary gastric cancer with breast metastases is a rare presentation. This case assumes significance as

the presentation masqueraded the primary lesion which was subsequently diagnosed on further investigations

CASE HISTORY:

32 year old premenopausal female presented with complaints of right breast lump noticed for a period of 2 months with abdominal distension, loss of appetite and easy fatigability. Her performance status was Eastern Cooperative Oncology Group (ECOG) 2. General examination revealed pallor. There was a 9 x 7 cm breast lump almost occupying whole of the right breast without any clinical evidence of axillary and supraclavicular lymphadenopathy. Contralateral breast examination was normal. Systemic examination revealed moderate ascites.

Blood parameters revealed decreased hemoglobin of 6 gm% with hypochromic microcytic anemia. Initial evaluation with ultrasound revealed antropyloic thickening and moderate ascites. Chest X ray was unremarkable. Biopsy from right breast lesion was reported to have multiple atypical cells with abundant foamy cytoplasm

with signet ring appearance surrounded by intact preserved lobules and ducts. Immunohistochemistry (IHC) for Estrogen receptor (ER), Progesterone receptor (PR) and Her 2 were negative. Endoscopic evaluation revealed an antropyloric growth and histopathology revealed poorly differentiated diffuse type gastric adenocarcinoma. IHC revealed positive pan Cytokeratin (CK), CK 7, CDX 2, E-Cadherin and negative CDK 20. This IHC panel was performed on breast biopsy tissue and was found similar. Histopathology and IHC Images are enclosed in Fig 1 - 9. PET/CT imaging was done for metastatic evaluation which revealed diffuse F-18 deoxy glucose (FDG) uptake in breast parenchyma, hypermetabolic circumferential wall thickening in antro-pyloric region with omental, mesenteric, bone and lymph nodal metastases (Fig 10 – 14). A final diagnosis of metastatic signet cell adenocarcinoma of stomach with systemic metastases has been made and started on palliative chemotherapy (with Paclitaxel and Carboplatin) and supportive care. She had minimal response to chemotherapy. She completed 4 cycles of chemotherapy and lost for follow up subsequently.

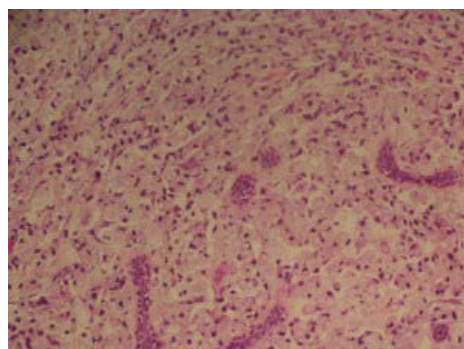


Fig 1 - 4x10 magnification - Breast tissue infiltrated by tumour

Fig 2 - 20x10 magnification - Breast tissue infiltrated by tumour

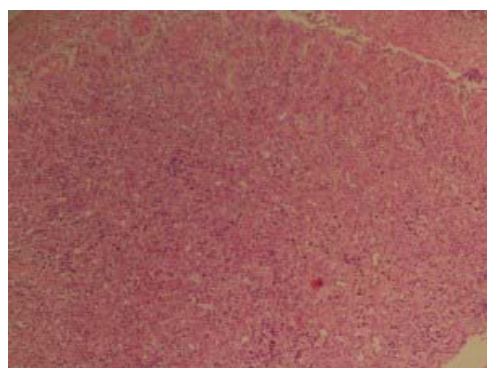


Fig 3 - 4x10 magnification - Gastric Biopsy

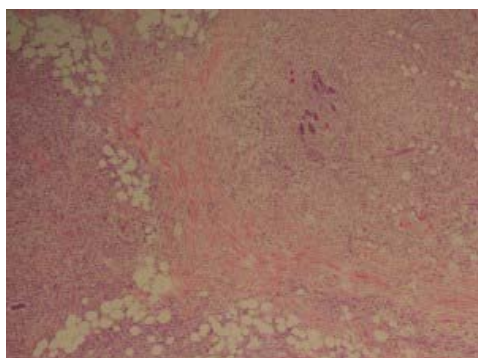
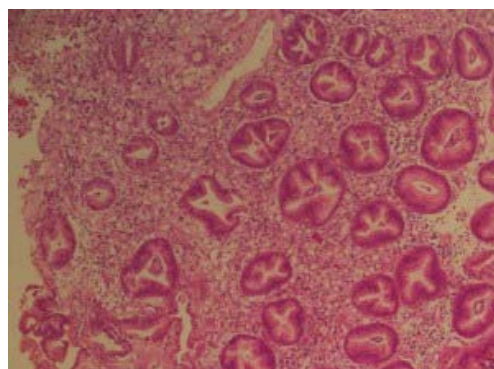


Fig 4 - 10x10 magnification - Gastric biopsy with signet ring carcinoma

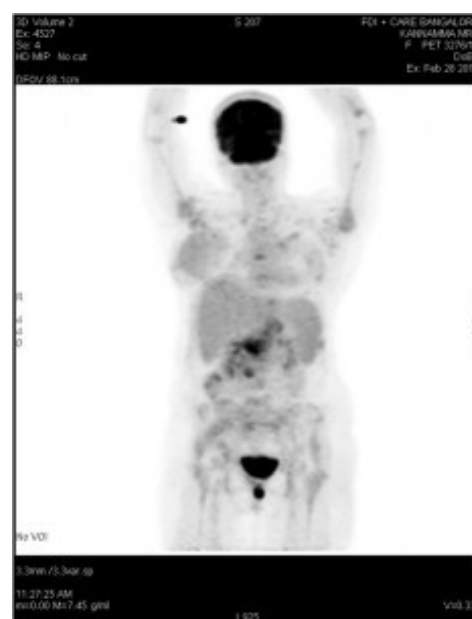
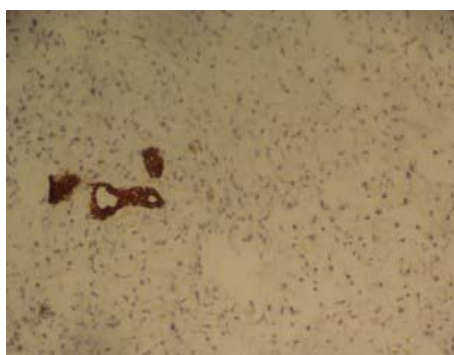
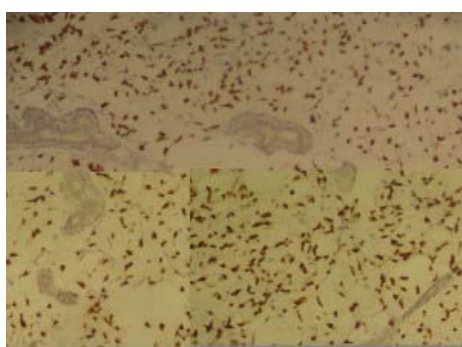
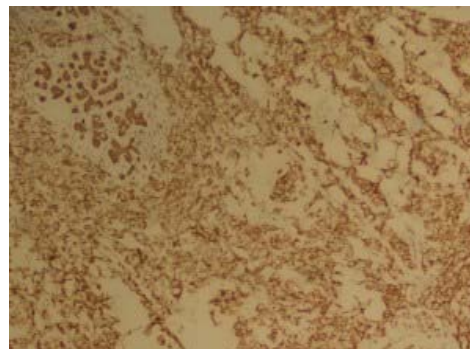
Fig 5 - 40x10 magnification - Gastric biopsy with tumour

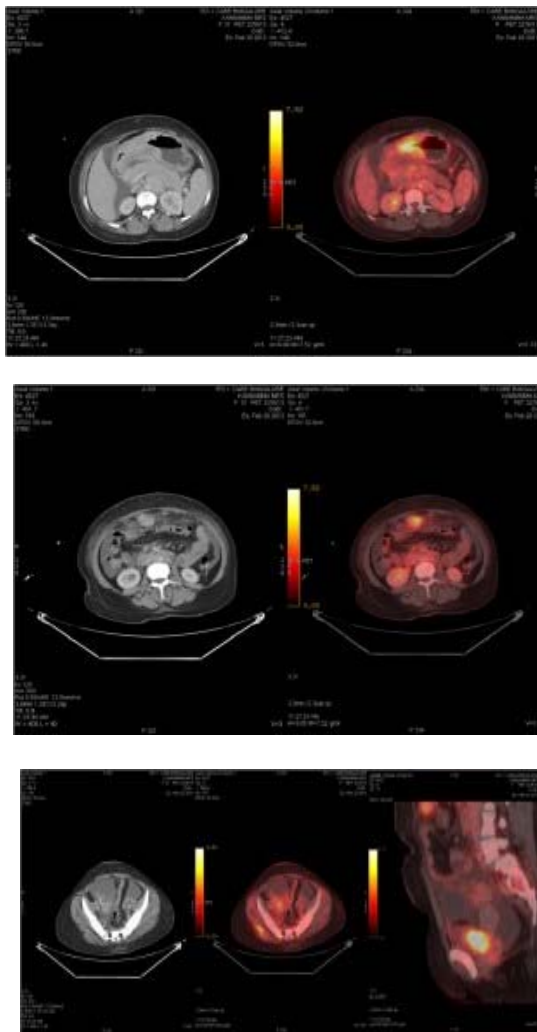
Fig 6 - Breast CDX-2 IHC

Fig 7 - Breast CK7 IHC

Fig 8 - Breast CK20 IHC

This micrograph displays a section of testis tissue stained with hematoxylin and eosin (H&E). The image shows several seminiferous tubules, which are the structures where sperm are produced. The tubules are filled with developing sperm cells at various stages of maturation. The interstitial space between the tubules contains various cells, including Leydig cells and fibroblasts, which are responsible for producing and secreting testosterone.





DISCUSSION:

The breast is one of the most common unusual sites of secondary cancer deposits from extra mammary primary malignancies. Nearly about 500 cases of breast as secondary metastatic site had been reported in literature [5,6]. However there are very few cases with gastric cancer, especially signet ring cell carcinoma as primary malignancy with breast metastases either as synchronous or metachronous disease. The rarity of breast metastasis along with pelvic and omental spread without liver involvement which is the usual solid organ for secondary spread, underscores the basis

of this case report. A short review of all cases of primary gastric cancer with secondary breast deposits is given in Table 1. Evidence supports breast metastases in younger women with average age at the time of presentation as 47 years [24]. As molecular mechanisms for site specific metastases are evolving, hormonal milieu and physiological status are also implicated as reasons for “soil and seed” hypothesis. Exact pathways of spread still remain as unsolved enigma. Clinico-radiological features help in differentiating primary and metastatic lesions of the breast. Fibrous connective tissue proliferation around the tumour adds to the size of the lesion. Lack of desmoplastic reaction in metastatic disease results in similar size noted clinically and mammographically. However, primary breast cancers have elicited fibrous reaction and may differ in clinical and radiographic size. Metastatic lesions may not be associated with thickening and retraction of skin and nipple until very advanced stages. Nipple discharge is also a differentiating clinical point for identifying primary breast cancer which is uncommon in metastatic lesions[7].

Though many extra mammary malignancies are commonly associated with breast deposits, signet ring cell carcinoma of the stomach forms the major differential diagnosis for primary signet cell carcinoma of the breast. This specifically makes a clear distinction between the two entities. Microscopically secondary deposits can be differentiated with intact lobules and breast ducts as evident in this case. Associated breast disorders like ductal in-situ lesions may be absent and the histological picture would resemble the primary malignancy. Differentiating the primary and secondary deposits

would define the treatment intent and guide management decisions.

Immunohistochemistry adds to the distinction by positive reaction for CK 7, CDX 2 and E-cadherin. Most Stomach primaries are CK 20 negative. Literature support for IHC confirmation can be obtained from 2 studies done by O'Connell et al [8] and Park et al [9]. CDX 2 (+), CK 7 (+), CK 20 (-) and TTF 1 (-) has a sensitivity 26%, specificity 99.2% and positive predictive value 85.7%. Breast cancers are typically positive for CK7 and negative for CK 20. Estrogen (ER) and progesterone (PR) receptors are expressed in 80% and 60% of the tumors respectively. Gross cystic disease fluid protein-15 (GCDFP 15) though specific for breast cancers (70% expression), is also expressed in salivary gland and skin tumors. In our case, microscopic picture was corroborative of secondary deposit and IHC for ER, PR, Her 2, CK 20 were negative and CK 7, CDX 2 and E-cadherin were positive. An additional specific marker for gastric adenocarcinoma is MUC – Mucin Glycoprotein Antigens which includes mucin glycoprotein antigen 2, MUC3, MUC5AC and MUC6 expressed in 54%, 36%, 71% and 39% respectively. As other features were consistent with gastric primary, IHC for mucin glycoprotein was not done in our case.

Table 1: Literature evidence for metastatic lesions to breast from Gastric primaries.

Treatment options for metastatic disease had always been of palliative intent with systemic chemotherapy. Survival is limited from days to months based on tumour biology and response to chemotherapy. Kim et al had analysed the time of survival for cases reported over decades which ranged from 3 days (gastric primary) to 19 months (endometrial primary). Prognosis is generally poor for the subset of patients with signet ring cell gastric primary with survival reported until 6 months [40].

CONCLUSION:

Though primary breast cancer is the most common malignancy, metastatic lesions should also be considered in younger female patients presenting with systemic symptoms. A careful clinical examination with attention to patients' symptomatology and exhaustive investigations will help in identifying the primary malignancy based on clinical, radiological, histological and immunohistochemical features.

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