



Breast cancer metastasis from Gastric Carcinoma in a young female

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ABSTRACT

Gastric cancer is a disease of elderly patients and mainly metastasizes to liver, lung, and peritoneum, while signet ring cell is a variant of gastric cancer and commonly metastasizes to peritoneum and lymph nodes. Metastasis to mammary is a rare condition which accounts for 3% and has a poor prognosis. Generally extra mammary carcinoma precedes breast metastasis by 2 years. It's uncommon to have breast metastasis as a first manifestation of extra mammary malignancies. There is no age limit and presentation may mimic primary breast cancer. Due to the rarity of this condition there are no consensus about clinical, radiological and histological features which make it a challenging task to distinguish primary from metastatic breast neoplasm. The case below is a young woman with diagnoses of diffuse-signet ring cell gastric cancer. First presentation was right breast edema with ascites, peritoneal nodules, and enlarged enhancing ovaries on imaging. Biopsy from each site confirmed involvement by metastatic adenocarcinoma with signet ring pattern. Her condition progressed after 5th cycle of EOX.

Keywords: Gastric cancer, breast metastasis, young age

INTRODUCTION

Gastric cancer at young ages is rare. The median age at diagnosis is 71 years and is the second most common cause of death worldwide (1).

Incidence of signet ring cell gastric cancer ranges from 3.4% in Japan to 39% in western countries (2,3) and accounts for 29% of gastric cancers, it occurs most commonly in women and mainly younger age groups, it is less chemo-sensitive with poor prognosis than intestinal type (4,5). Diffuse-signet ring cell type exhibits very little cell cohesion with predilection for extensive sub-mucosal spread and early metastasis (6), diffuse form's main carcinogenic event is loss of E-cadherin expression through mutation of CDH1 gene (7).

Carcinoma of stomach can spread by local extension, hematogenous spread, lymphatic dissemination or seeding of peritoneal surface, wide spread metastasis may involve any organ, especially liver, lung and peritoneum (6,8,9), while signet ring cell subtype's main metastatic sites are peritoneum and lymph nodes rather than liver (10).

Metastatic lesions to the breast from extra-mammary neoplastic lesions are unusual with poor prognosis. The most common reported sources are malignant melanomas, lymphoma/leukemia group, contralateral breast carcinoma, lung carcinoma and carcinoid tumors (11,12). There is no consensus on a distinct clinical and radiologic presentation (12,13). Although diagnosis of primary malignancy usually precedes detection of the breast lesion in some cases may have no history of malignancy (13).

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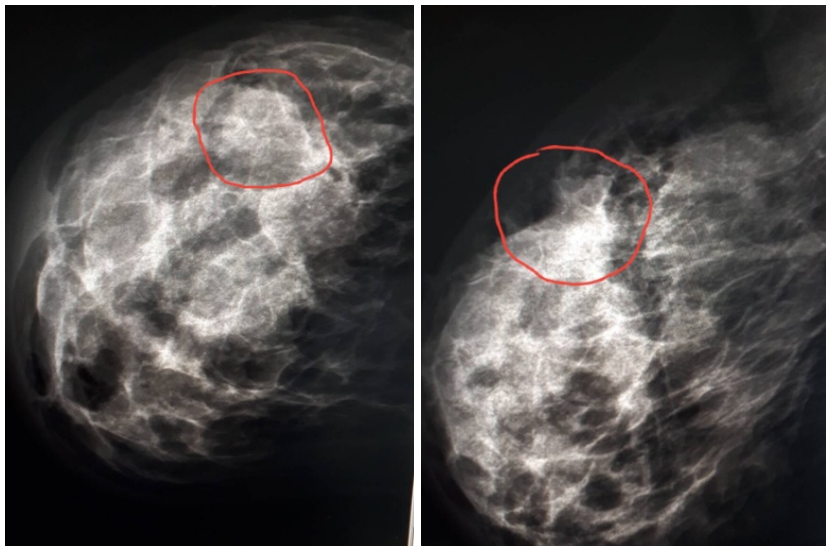


Figure 1: Mammography

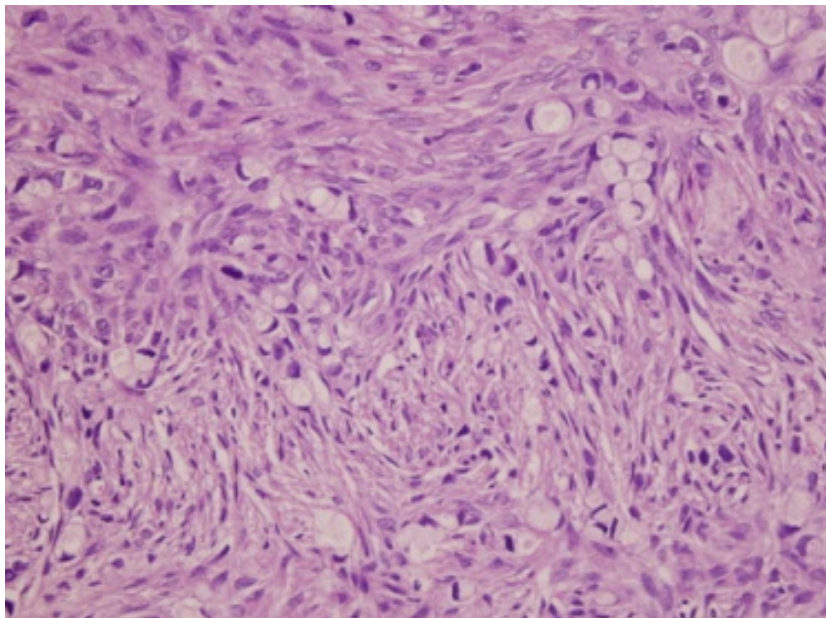


Figure 2: Breast tissue histology

CASE PRESENTATION

A 32-year-old married lactating woman, mother of 3 children presented to breast clinic with a rapid painless diffuse swelling of right breast over few weeks, not associated with redness, she had also mild diffuse abdominal pain but good appetite no vomiting no weight loss or change in bowel habit. Her review of systems was otherwise negative, no family history of cancer.

At breast clinic ultrasound and mammography of breast was taken the ultrasound of right breast revealed large size, hard, moderately heterogeneous tissue texture, multiple well defined hypo-echoic cystic lesions, largest one is 14*9mm at 10 o'clock with multiple duct dilatation and periductal thickening. In right axilla inflammatory lymph node of 13*5mm was detected, cortex of 3mm, echogenic hilum was detected, normal left breast and left axilla.

Mammography CC and MLO view was taken, breast composition ACR 4, a single superficial well defined dense lesion at superior-lateral aspect was seen, normal left breast, clear both axillae (**Figure 1**). Core biopsy from the mass was taken, histopathology reported metastatic mucin secreting adenocarcinoma (**Figure 2**). IHC was as follow (ER negative, PR negative, HER2 negative, KI 67: 60%, E-cadherin positive, CA125 negative, WT1 negative, mammaglobin negative, CDX2 positive, moderate nuclear staining (**Figure 3**).

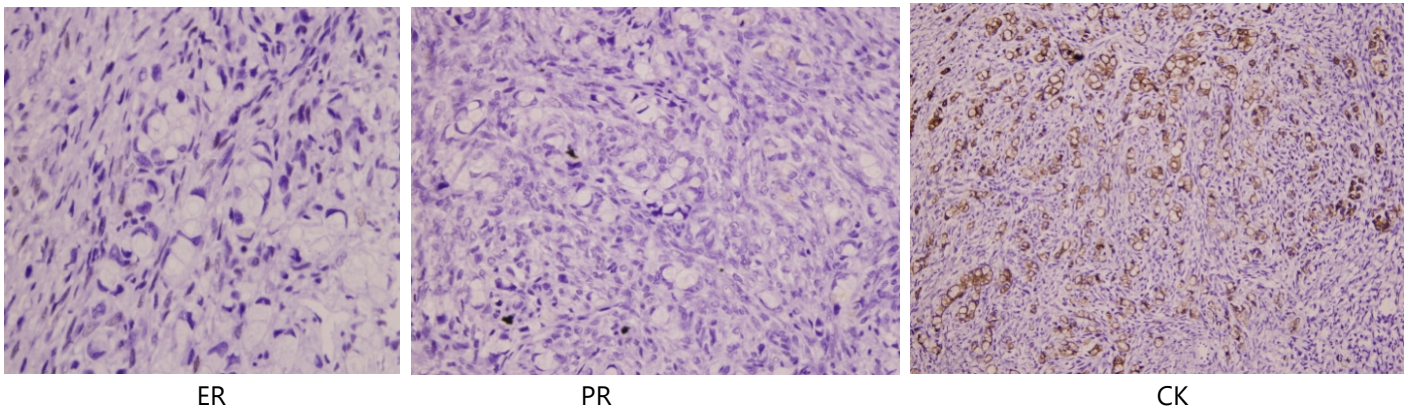


Figure 3: Breast tissue histology



Figure 4: Gastric endoscopy

Abdominal and pelvis ascites, diffuse infiltration of the peritoneum with omental cake as well as stranding of pelvic fat, enlarged and enhanced right and left ovary, diffuse gastric wall thickening were visualized on Dynamic staging computed tomography (CT) scan of chest, abdomen and pelvis.

Tumor markers were as follows CEA: 1.2 ng/ml, AFP: 2.23 lu/ml, CA 19.9: 0.62 u/ml, CA 125: 62.6 u/ml, CA 15.3: 19.7 u/ml.

Gastroenteroscopy was performed, easily bleeding ulcers were seen over great curvature from mid body till antrum (**Figure 4**), histopathology of gastric lesion reported poorly differentiated adenocarcinoma diffuse signet ring type (**Figure 5**), IHC results were positive for AE1/AE3 and negative HER2 status.

With collaboration of our oncologist, pathologist, radiologist we diagnosed and managed our case as signet ring cell gastric cancer, and she was started on EOX (Epirubicin 50mg/m², Oxaliplatin 130mg/m², Capecitabine 625mg/m²), on fifth cycle there was progression on image study, and unfortunately we lost her after 2 weeks.

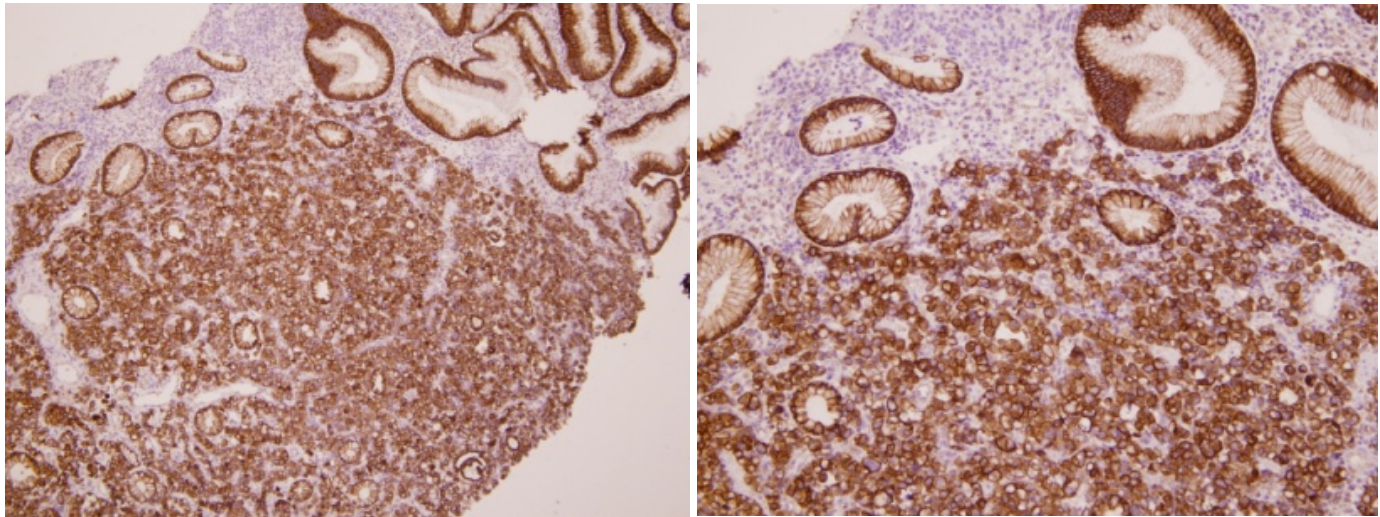


Figure 5: Histopathology of gastric tissue sample

DISCUSSION

Breast cancer accounts for the most common malignancies, but metastasis to breast from extra mammary malignancies is a rare condition and comprising around 3% of breast malignancies, the majority are from contralateral breast, less than 0.5% resulted from extra mammary sites (14). In 25% of cases breast involvement is bilateral (15).

Prognosis is poor, according to reported cases overall survival ranged from 12 day to 18 month (16).

Around 400 cases have been reported to have breast metastasis from extra-mammary sides, their incidence ranged from 1.7%-6.6%, 1.2%-2%, 2.7% in (autopsy, clinical, and cytological reports) (17), and the most common source from highest to lowest rate were from melanoma, lung, ovary, prostate, kidney, stomach, ileum, thyroid, cervix, squamous cell carcinoma of the tongue and floor of the mouth, fibrosarcoma of the nasal septum and pancreatic adenocarcinoma.

With our case another 38 case have been reported so far to have metastatic disease from stomach, 22 of them had histological feature of signet ring cell carcinoma (16).

Unlike our case that had synchronous multiple metastasis at presentation, breast metastases appears on the average 1.9 - 2.0 years after discovery of the primary lesion (12,13,18), and usually signifies disseminated metastatic gastric tumor (15,19), while in some cases there may be no history of neoplasm (14). The age at diagnosis ranges from 22-70 years (mean 46 years; median 46.5 years) (16,20,21). Breast metastasis from gastric carcinoma mainly occurs in female (95%) than male (5%), Georgiannos et al. (14) attributed the reason behind this phenomena to differences in size and vascularity between two gender's breast, hormonal factors, endothelial cell adhesion molecule, angiogenic factors, immunologic determinants, hormone receptor, or other cellular components also may play a role since they are expressed differently in male and female breast.

Secondary involvement of breast occurs mainly in elderly patients while lung and gastric cancer particularly signet ring cell variant of stomach develop in younger age group and anticipate more aggressive nature (22,23).

Clinical manifestations are quite similar to primary breast cancer which make suspicion of elsewhere primaries unusual but essential to avoid; unnecessary radical operation and providing optimal treatment, reported cases in literatures had different presentation, from inflammatory breast cancer (18,24,25) to painful/painless lumps and often occur in upper outer quadrant with presence of axillary lymphadenopathy (12,13).

Radiological findings are not specific which makes the diagnosis quit difficult, they may present as a solitary or multiple lesions, well demarcated or poorly marginated masses, diffuse hypoechoic lesions, diffuse involvement of skin or parenchyma or both (12,20), and some time there is no any radiologic findings (26,27). Kawak et al. reported that for those with clinical feature suggesting inflammatory breast carcinoma after confirmation of signet ring cell breast carcinomas has been made, metastatic signet ring carcinomas should be considered if there is no micro-calcification or masses on radiographic findings (13,18). But metastasis from ovarian carcinoma may demonstrate microcalcification with psammoma bodies (28,29).

Pathologically it's hard to differentiate between primary breast cancer and metastasis, breast cancer can have ambiguous histological feature that can be easily mistaken for extra mammary cancers. (14) Some histologic feature may help in recognizing secondary from primary like absence of elastosis which is found in primary and indicating a slow

growth and rarely found in secondary tumors (30). A sharp transition at the border of the tumor may give clue for metastasis (31). Tumors in subcutaneous rather than parenchymal or breast tissue and absence of in situ component support extra mammary origin (14).

Tumor metastasize to breast by unexplained pathway, this intriguing situation have been attributed to estrogen and high blood supply of breast in premenopausal women (32,33).

Unlike our case in most of the reported cases breast metastasis from gastric cancer has happened in left breast although there is no consistent explanation but Lee et al, (19) reported that this laterality may suggest presence of a lymphatic pathway or higher incidence of breast invasion from stomach via left supraclavicular lymph node.

With our case another 5 cases have been reported to have breast and ovarian metastasis, it is uncommon to have invasion of hormonal –dependant organs especially in premenopausal women (26).

Immunohistochemistry of breast metastasis from stomach are usually positive for CK7, CEA, and GATA3 but negative for GCDFP-15(gross cystic disease fluid protein-15), ER, PR, and CK20. (34,35) What supported our case to have breast metastasis from gastric cancer was having positive CDX2, CK7 and negative CK20, ER, PR, CA125, WT1, Mammaglobin, HER2 status.

IHC can differentiate metastatic signet ring cell carcinoma from primary signet ring cell carcinoma of breast, the latter one is a variant of invasive lobular carcinoma of breast and account for 14% of breast cancer (36), its incidence is increasing among postmenopausal women and have aggressive nature with tendency for early metastasis to abdomen and GIT tract, on IHC they demonstrate positive ER, PR and GCDFP (34,37).

CONCLUSION

Breast metastasis from extra-mammary sites is uncommon with poor prognosis; clinical presentation might be quit misleading to primary breast cancer. Confirmation through clinical presentation, clinical history, histopathology, Immunohistochemistry and radiological examinations is crucial to ensure the appropriate therapy and avoiding unnecessary surgical treatment.

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