



Pyloric Metastases from Primary Breast Cancer- A Case Report and Literature Review

Authors

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Abstract

One in eight women is affected by breast cancer during their life time. The typical metastatic sites from a primary breast cancer are lung, bone, liver and brain. Breast cancer metastases to the bowel are rare. However, it is important to recognize patients who have been affected by breast cancer in the past, and now present with gastroenterological symptoms, such as nausea, vomiting, abdominal pain, bleeding or diarrhoea. A delay in reaching the proper diagnosis may result in inappropriate management or late treatment. This paper reports a case of breast cancer metastases to the pylorus and reviews relevant literature surrounding this topic.

Keyword: Breast Cancer; Lobular; Metastasis.

Introduction

Breast cancer is considered the most common cancer worldwide, and regarded as the main cause of cancer mortality in the UK. Distant metastatic sites are most commonly the lungs, liver, bones, brain and skin. Rarer sites include the bowel,

spleen, gallbladder, pancreas, genital organs, urinary bladder, and eyes^[1]. Regarding breast carcinoma metastasis to the gut, extrahepatic sites are rare. Breast cancer metastasis to the stomach may mimic primary gastric cancer. Proper clinical assessment and appropriate histopathological

analysis, including immunohistochemistry, is therefore vital to reach an accurate diagnosis. This will help to avoid unnecessary management and guides the physician towards the correct treatment options. In general, invasive lobular carcinoma has a higher tendency to metastasise to the stomach than invasive ductal carcinoma.

In this paper, we report a rare case of invasive lobular breast cancer (ILC) metastasising to the pylorus, and presenting as non-resolving dyspepsia.

Case Report

A 66-year old female presented with progressive dyspepsia, on a background of high BMI, hypertension, underactive thyroid and osteoarthritis. Three years earlier she had been diagnosed with invasive lobular breast cancer and staging sentinel lymph node biopsy had shown metastatic disease in the axilla. This was treated with primary chemotherapy, as a large area of the breast was affected (Figures 1&2).

The Intra-operative histology showed metastatic disease in the axilla. Post-chemotherapy imaging revealed partial radiological response. She subsequently underwent a mastectomy and axillary clearance. The post-operative histology indicated Grade II mixed (80mm lobular and 25mm ductal) carcinoma, with lymphovascular invasion. 18 out of 29 nodes were oestrogen receptor (ER) strongly positive (8/8), progesterone receptor (PR) strongly positive (8/8) and Her 2 negative. The histology reported a poor post-chemotherapy response in the lobular carcinoma but a moderate response in the ductal carcinoma. Tumour staging was T3N3M0 and Nottingham Prognostic Index (NPI) was 6.6, placing her in a poor prognostic group.

The preoperative staging CT scan showed incidental right ovarian cysts and mature cystic teratoma. CA 125, AFP and CEA were within normal range. During the breast surgery, she also underwent bilateral oophorectomy which revealed benign mucinous cystadenoma and mature teratoma of the right ovary. Following surgery, the breast MDT recommended radiotherapy to the

chest wall and supra-clavicular region, and the use of letrozole. She was placed under annual clinical and mammogram surveillance with the breast unit. This lady then presented 3 years later with dyspepsia. Clinically there was no evidence of loco-regional disease recurrence. However, CT abdomen revealed mural thickening within the region of the gastric pylorus with enlarged gastrohepatic and para-aortic lymph nodes, as well as evidence of small bowel pneumatosis and intra-abdominal free gas (figure 3&4). No definite site of perforation was identified. Clinical assessment of the patient ruled out an acute abdomen and no intervention was necessary. Gastroscopy showed a tight pylorus with duodenitis. Biopsies were consistent with chronic inflammation only. The patient was already on a PPI and symptoms did not resolve. Two months later, a repeat CT showed stable appearances of the pyloric thickening and associated lymphadenopathy. The small bowel pneumatosis remained unchanged, and there was no evidence of small bowel obstruction or perforation. A repeat gastroscopy showed inflamed pyloric and pre-pyloric regions, with thickened mucosa. The pylorus was narrowed and the endoscope was unable to be passed beyond the pylorus. These features raised a suspicion of "linitus plastica". The biopsy showed areas of uniform malignant cells arranged in cords, with small acini and nests (Figure 5). Immunohistochemistry staining showed positive expression for CAM 5.2 (Figure 6) and ER (8/8) (Figure 7). It also showed patchy positivity for GCDFP-15 (Figure 8) and CEA. The staining for Her-2 and E-cadherin (Figure 9) was negative and the Ki67 proliferation index was low (5%) (Figure 10). This staining profile supported the diagnosis of lobular adenocarcinoma of a breast primary and a palliative laparoscopic gastrojejunostomy was performed. During her operation, a piece of omentum was obtained and sent for biopsy. This showed extensive infiltration by adenocarcinoma cells (Figure 11). The ascites fluid was sent for cytology and the cells were positive for EP4, suggesting infiltration by carcinoma. Additionally,

staining for calretinin was negative. The appearances were in keeping with the previous reports of metastatic lobular breast carcinoma. The MDT recommended chemotherapy, and she was started on Paclitaxel. However due to side effects, this was switched to Abraxane. After chemotherapy, hormonal manipulation with aromatase inhibitors (AI) was advised.

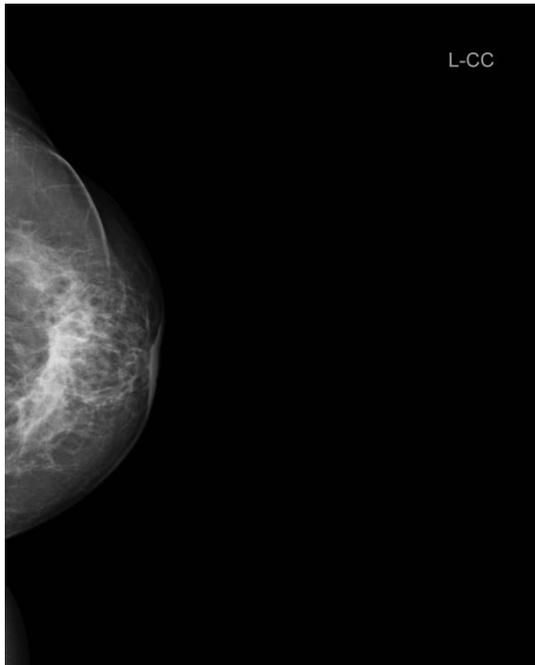


Fig 1: Left mammogram.



Fig 3: CT coronal view of the abdomen.

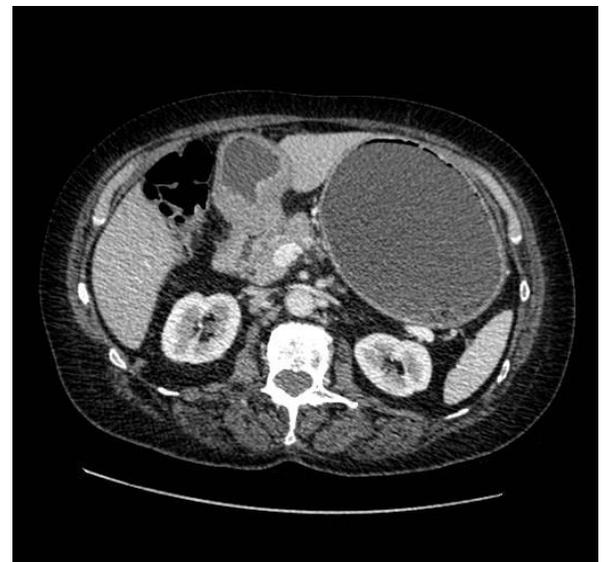


Fig 4: Axial CT view of the abdomen.

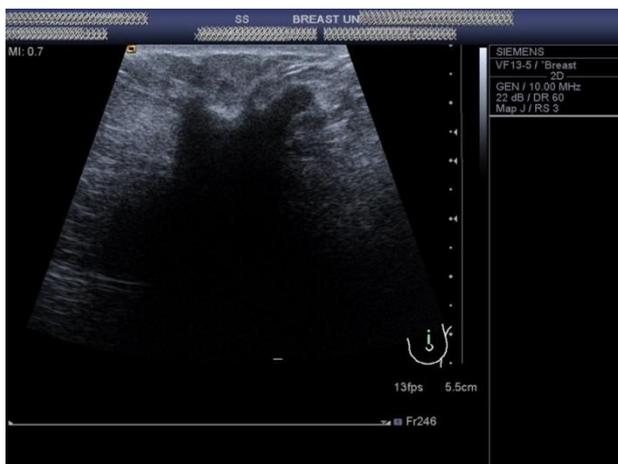


Fig 2: Left breast ultrasound.

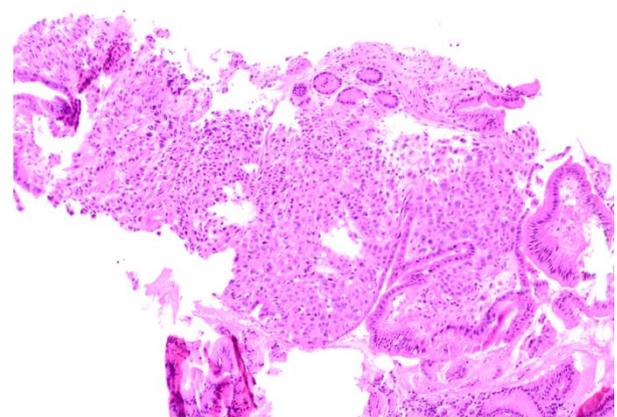


Fig 5: Gastric mucosa infiltrated by malignant neoplasm. The tumour consists of cells with nuclear pleomorphism, arranged into sheets, cords, small acini and nests.

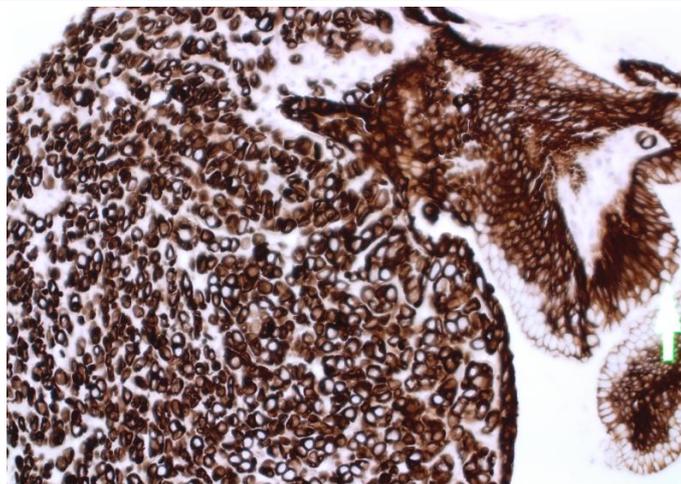


Fig 6: Gastric tumour strongly positive for CAM 5.2.

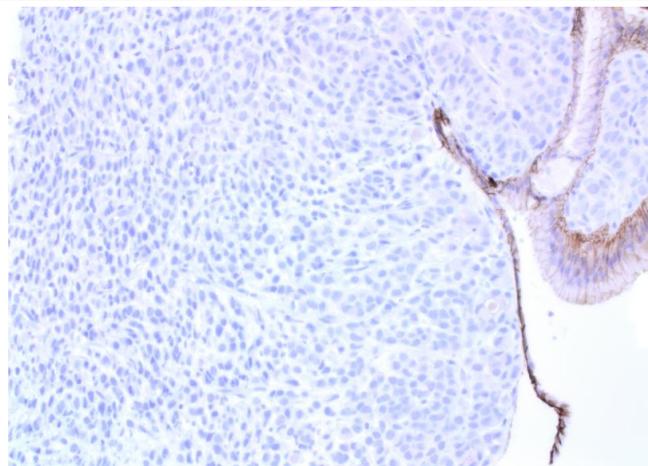


Fig 10: Gastric tumour negative for E-cadherin.

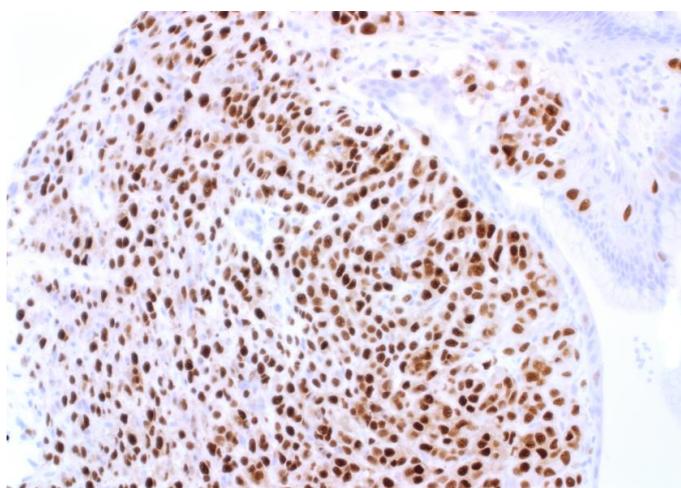
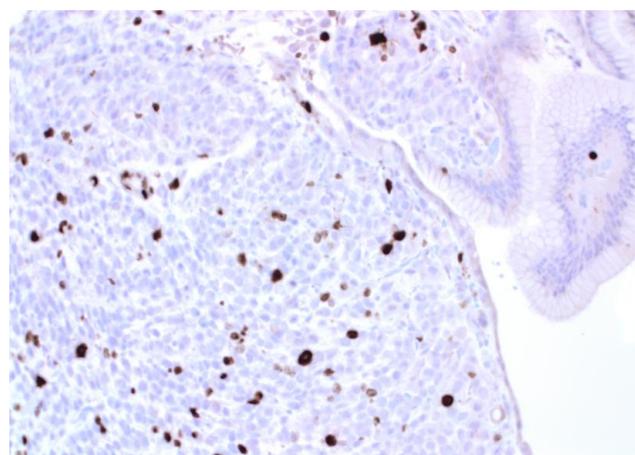


Fig 7: Moderate to strong expression of ER.



Low Ki-67 proliferative index (approx.5%)

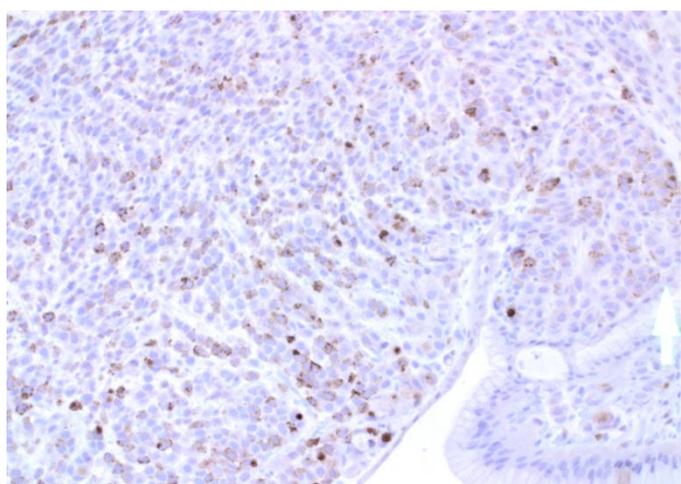


Fig 8: Gastric tumour weakly positive for GCDFP-15.

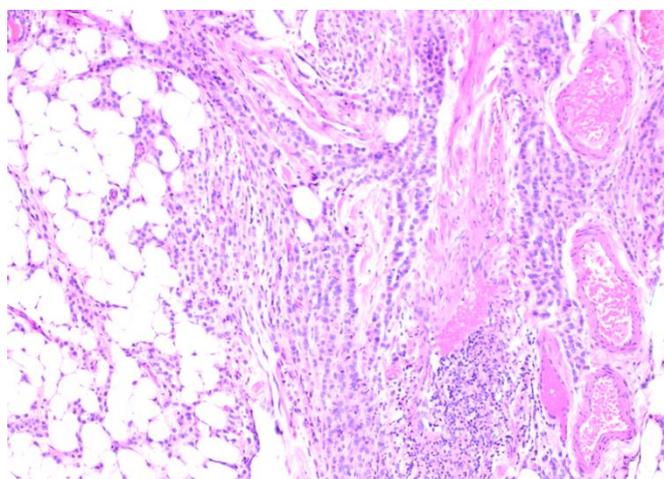


Fig 11: Breast lobular carcinoma metastasis to omentum.

Discussion

Breast cancer is regarded as the most frequent malignancy in women worldwide, accounting for approximately 32% of all cancers^[1] and 19% of cancer deaths in females^[2]. In the United States, it

is the second most common malignancy in women after skin cancer^[3]. Metastatic disease is seen in 30% of patients despite treatment involving surgery, chemotherapy, radiotherapy and hormonal manipulation. The recognised sites for distant metastases from breast cancer are bone, lung, liver, brain and vulva^[4].

The most common primary site for gastrointestinal tract (GIT) metastasis and carcinomatosis peritonei is malignant melanoma (MM). Although primary breast cancer metastasis to the GIT is rare, it is regarded as the second most common primary malignancy to metastasise to the GIT after MM^[5]. In 2005, McLemore *et al.* reported that cases of gastrointestinal metastasis from primary breast cancer accounted for 0.6% of breast cancer cases (73/12,001 cases)^[6,7].

The main histological subtypes of invasive breast cancer are the invasive ductal carcinoma (IDC) and invasive lobular carcinoma (ILC), which account for 5-15% of invasive breast cancer^[3]. The invasive ductal carcinoma (IDC) has been shown to metastasise to lymphnodes, liver, lung, brain and bones, whereas invasive lobular carcinoma tends to metastasise to GIT, with an incidence of 2% to 18%^[9-11]. ILC also has a tendency for peritoneal cavity gynaecological tract metastasis^[5,6]. The tubular and mucinous carcinomas have a lower incidence of metastases and a better prognosis than invasive lobular and invasive tubular carcinomas^[7].

The clinical presentation of metastatic breast carcinoma to the gastrointestinal tract is usually similar to that of any primary GI cancer, however it may only be diagnosed following resection of the metastatic lesion^[12]. The signs of GIT metastases in breast cancer depend on the pattern of lumen involvement; localized or circumferential. A localized pattern usually causes a segmental thickening of the lumen, whilst circumferential infiltration causes lumen narrowing and presents as obstruction.

The most common variant of stomach involvement is a "linitis plastica" appearance, affecting muscle layer and submucosae; this is found in 73% of

cases^[13]. There is diffuse intramural infiltration of the gastric wall by the tumor; this results in narrowing of the stomach lumen, rigidity, and diminished peristalsis^[14].

The average presentation time between the initial breast cancer diagnosis and the gastrointestinal metastatic disease presentation is 6-9 years^[15,16]. However, a 30-year interval has also been reported in literature^[17]. If the interval between the primary breast cancer and occurrence of gastrointestinal lesions is lengthy, essential elements of the history may be missed.

Complete immunohistochemistry analysis is essential at the time of diagnosis, to distinguish between primary and metastatic disease. The immunohistochemistry panel included markers that have traditionally been detected in breast carcinomas: oestrogen receptor protein (ER), progesterone receptor protein (PR), GCDFP-15, and CAM 5.2^[13].

CAM 5.2 is an immune-stain used to detect Cytokeratin 7 (CK7), which is commonly low molecular keratin. It is found in breast, lung, ovary and urothelium, but usually not in the GIT or stratified squamous epithelium^[18]. It was positive in our case.

Gross cystic disease fluid protein 15 (GCDFP-15), is a marker of value in differentiation of breast tissue; its expression is higher in tumours with favourable prognostic features^[19]. GCDFP-15 was weakly positive in our case.

E- Cadherin is a calcium dependent transmembrane epithelial protein that promotes intercellular adhesion. It shows no expression in breast lobular carcinoma and LCIS (lobular carcinoma in situ)^[20]. This was negative in our case.

EP4 is an antibody to cell membrane glycoproteins expressed on healthy epithelia and in various carcinomas, also known as epithelial cell adhesion molecule. It is sensitive and specific for lung adenocarcinoma (positive) compared to mesothelioma (negative). Immuno-expression may predict poor survival in breast carcinoma^[21,22].

Calretinin is a calcium binding protein structurally related to S100 and inhibin. It is useful to differentiate between reactive mesothelial cells (positive) and carcinomas (negative) in effusion cytology of ascites fluid ⁽²³⁻²⁵⁾.

The typical management of primary breast cancer with gut metastases is systemic chemotherapy. However, surgery plays a key role in the initial treatment of a primary GI malignancy.

Linitis plastica, secondary to breast lobular carcinoma, has a good response to hormonal manipulation or/and chemotherapy, particularly when metastatic foci are ER and PR positive. However, the overall prognosis is poor, with an average survival rate of two years following the diagnosis of the metastatic gastric lesions ^[26].

Conclusion

This paper highlights the importance of considering breast cancer metastasis as a possible cause of abnormal radiological findings affecting the gut, especially in the presence of a previous history of breast cancer.

One of the challenges facing the physician is the delay between the primary breast cancer diagnosis and the metastatic relapse. Furthermore, lobular carcinoma of the breast metastasising to the stomach lumen presents endoscopically and radiologically as linitis plastica. Therefore, eliciting a proper past medical history is a key step towards reaching the correct diagnosis. A complete relevant immunohistochemistry panel is also essential in this situation.

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