

## Late Gastric Metastasis from Breast Invasive Lobular Carcinoma: A Case Report and Literature Review

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### Abstract

Primary gastric carcinoma is the most common malignancy of the stomach, however, secondary cancers are also seen in the stomach. Invasive breast carcinoma is known to metastasize to the stomach and may cause the development of gastric outlet obstruction or perforation. This case presents the late recurrence of lobular breast carcinoma with metastasis to the stomach.

**Keywords:** Metastatic Breast Cancer; Invasive Lobular Cancer; Gastric Carcinoma

### Introduction

Breast cancer is regarded as the most frequent malignancy in women worldwide. It accounts for approximately 32% of all cancers [1,2] and is the cause of 19% of cancer deaths in females internationally [3]. Invasive breast cancer usually metastasizes to lymph nodes, lungs, liver, bone, and brain [4]. Other rarer sites of breast malignancy with distant metastasis include oesophagus [5], stomach [1,6], colon [7], thyroid [8], and urinary bladder [9]. The time interval between the diagnosis of the primary breast cancer and the presentation of gastrointestinal metastasis can vary widely ranging from initial presentation up to 30 years later. This paper presents a case of a late recurrence (after 23 years) of breast invasive lobular carcinoma in the form of gastric metastasis.

### Case Presentation

An 84-year-old female patient presented with a recent history of progressive dysphagia and weight loss. She had a mastectomy for invasive breast cancer twenty-three years ago. Additionally, she had a hysterectomy performed for uterine cancer and was also known to suffer from type 2 diabetes and Meniere's disease.

The patient underwent a gastroscopy which demonstrated mild oesophagitis and an abnormal area in the stomach with non-specific inflammatory changes. As a result, a biopsy was taken from this region. The histopathology results from the biopsy revealed gastric mucosa that was infiltrated by single cells of malignant neoplasm with atrophy of crypts (Figures 1 and 2). The malignant cells were further analysed with immunohistochemical staining and were found to be positive for Cam 5.2 (Figure 3), CK7 (Figure 4), oestrogen (Figure 5), and patchily for GCDFP-15 (Figure 6). The sample was found to be negative for CD45, CD3, CK20 (Figure 7), TTF-1 (Figure 8) and synaptophysin. Additionally, the proliferative index with Ki67 was determined to be 10%. As a result, the patho-

morphological features were found to be suggestive of a metastatic lobular adenocarcinoma of the breast.

**Figure 1:** Gastric mucosa infiltrated by single cells of malignant neoplasm with atrophy of crypts 10x.

**Figure 2:** Gastric mucosa infiltrated by single cells of malignant neoplasm with atrophy of crypts 20x.

**Figure 3:** Tumour cells are positive for CAM5.2.

**Figure 7:** Tumour cells are negative for CK20.

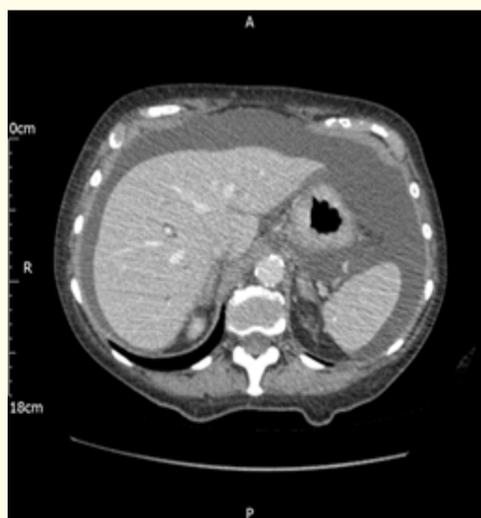
**Figure 4:** Tumour cells are positive for CK7.

**Figure 8:** Tumour cells are negative for TTF-1.

**Figure 5:** Tumour is strongly positive for oestrogen receptor.

The patient underwent further investigations and a CT of the chest, abdomen, and pelvis was performed. This imaging revealed massive ascites within the abdomen along with thickening in the gastro-oesophageal junction (Figure 9). There were also innumerable sclerotic and lytic lesions identified showing metastasis to the bony skeleton in addition to incidental gallstones (Figures 10 and 11).

**Figure 6:** Tumour cells show patchy positivity with GCDFP-15.



**Figure 9:** CT abdomen, axial plane: Massive ascites with thickened gastro-oesophageal junction.



**Figure 10:** CT abdomen and pelvis- coronal view: Ascites, multiple sclerotic and lytic metastasis in the bony skeleton.



**Figure 11:** CT abdomen and pelvis- sagittal plane: Ascites, multiple sclerotic and lytic metastasis in the bony skeleton.

## Discussion

In the United Kingdom, breast cancer is regarded as the most common malignancy in females and accounts for almost a third (31%) of all female cancers. It is followed by lung cancer (12%) and bowel cancer (11%) [10]. Worldwide, breast cancer is regarded as the most frequent malignancy in women. It accounts for approximately 32% of all cancers [1,2] and is the cause of 19% of cancer deaths in females internationally [3]. Lung cancer is the most common cause of cancer deaths in UK females (21%). Breast cancer is the second leading cause of death from cancer in women (15%), mainly due to metastatic spread, whereas bowel cancer is in the third place (10%) [10].

The most common sites for breast cancer metastasis are lymph nodes, lung, liver, brain, bones, and skin. The metastasis of breast cancer to the gastrointestinal tract (GIT) is known to be rare. However, it is the second most common malignancy to metastasize to the GI tract after malignant melanoma [11]. The gastrointestinal metastatic deposits may be found in the oropharynx [12], oesophagus [5], stomach [1,6], duodenum [13], jejunum [14,15], terminal

ileum [11], colon [16] and rectum [7]. The involvement of the gastrointestinal tract with breast cancer metastasis may involve more than one site. The involvement of the gastrointestinal metastasis may include multiple sites during presentation such as gastric and concurrent colonic involvement [17,18]. It may also occur with isolated metastases to the gastrointestinal tract without metastasis to other organs, however, this is quite rare [14]. The distribution of gastrointestinal metastasis secondary to breast invasive carcinoma has been reported by Ambroggi in 2012. The report found that metastasis to the stomach (60%) was the most common. Other areas that were found included the esophagus (12%), colon (11%), small bowel (8%), and rectum (7%). The prevalence of breast cancer metastasis in resected stomach specimens is 0.3% [19]. Usually the pathological subtype is invasive lobular carcinoma that is oestrogen receptor (ER) positive, progesterone receptor (PR) positive, and Human Epidermal Growth Factor-2 (Her-2) positive [20-22] in 83% of the cases [19]. However, a triple negative breast invasive cancer has also been found to metastasize to the gastrointestinal tract also [15].

Some reports mentioned that the most common primary malignancy with metastasis to the stomach is malignant melanoma (MM) [1,18]. However other literature claims that breast, lung, and renal cell carcinoma are the most frequent malignancies with metastasis to the stomach [23]. There have also been cases of ovarian cancer that have been reported with metastasis to the stomach [24].

In cases where a primary breast cancer initially presents with gastric metastasis, the presentation may be similar to a primary gastric cancer. Symptoms in these cases may include epigastric pain, dyspepsia, anorexia, vomiting, bleeding, and weight loss [24]. Other rarer presentations have also been reported and include an acute abdomen due to a gastric ulcer, stomach perforation [22], or gastric outlet obstruction [25].

Breast cancer metastasis can occur many years after diagnosis and subsequent management of the primary cancer. The time interval between the diagnosis of the primary breast cancer and the presentation of gastrointestinal metastasis can vary widely from initial presentation up to 30 years later [1,26,27]. The average time ranges from 4 to 10 years [19,28]. In our case, the presence of ascites and bony metastases suggests that blood born metastasis is the mode of spread. The rich gastric blood supply could be a possible reason for the stomach to be a target of metastatic disease.

The diagnostic pathway usually involves endoscopy, imaging and pathomorphology. Less pleomorphic tumor morphology and single file pattern are commonly seen in lobular carcinoma of the breast. Immunohistochemistry (IHC) should follow the histological evaluation.

It is recommended to include oestrogen receptor status in the IHC panel. Approximately 70% of invasive breast cancers express estrogen receptor (ER), and the majority of ER positive cancers also express progesterone receptor (PgR) [29]. Metastatic invasive lobular carcinoma will exhibit positivity for gross cystic disease

fluid protein-15 (GCDFP-15) [26], it has high specificity but low sensitivity [9]. Our case was GCDFP-15 positive.

Carcinomas that originate in the breast are usually positive for CK7 and are negative for CK20 (CK7+/CK20- pattern). In contrast, the primary tumours of the gastrointestinal tract are almost always CK20 positive [14]. CK20 may be positive in only 5% of metastatic lobular carcinomas [4]. Our case was CK7+/CK20-.

The marker GATA3 is sensitive and specific for breast cancer [25]. It is useful in metastatic and recurrent breast carcinomas that don't express the other specific markers of the breast. It is particularly useful in triple-negative and metaplastic carcinomas [14]. Another marker called mammaglobin is regarded as more sensitive than GCDFP-15 for breast origin but it is less specific [30]. Cluster of differentiation 3 (CD3) is a multimeric protein complex, known historically as the T3 complex and present in 95% of T-lymphocytes. It is useful in diagnosis of lymphoid malignancies [31]. CD45 (lymphocyte common antigen) is a receptor-linked protein tyrosine phosphatase that is expressed on all leucocytes. It is seen in human leukaemia/lymphoma cell lines [32]. In our case both CD3 and CD45 were negative in our patient.

The management of gastric metastasis from primary breast cancer usually is systemic palliative chemotherapy in combination with hormonal manipulation in ER/PR positive cancers [1]. There is a small window for surgical intervention as in obstruction or perforation [22]. Gastrectomy should be considered in the absence of other secondary foci and when the primary lesion has been treated [19].

## Conclusion

The presence of a malignant lesion in the stomach with a previous history of breast cancer should raise the possibility of metastatic disease recurrence. Differentiation of metastatic breast carcinoma from primary gastric adenocarcinoma is crucial and should be done using thorough histological examination. In addition, a detailed immunohistochemical study is a prerequisite to differentiate the two tumours.

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