

Gastrointestinal Metastases of Breast Cancer: Report of Two Cases and Review of the Literature

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ABSTRACT

Breast cancer is the most common neoplasm in women. It often metastasizes to the bones, liver, lungs and brain. Nevertheless, gastrointestinal tract involvement is an exception. When it occurs, both clinical symptoms and endoscopic findings are nonspecific. Therefore it is essential to consider this clinical syndrome in patients with a history of breast cancer. We have performed an extensive search of the Cancer Registry of Príncipe de Asturias University Hospital between the years 2000 and 2016, both inclusive. We report on two patients with gastrointestinal metastases in different locations due to breast cancer.

Key words: Breast cancer; Gastrointestinal metastases; Small bowel obstruction

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INTRODUCTION

Breast cancer is the most common tumor in women; one in eight women will be affected in their lifetime^[1]. Metastatic breast cancer typically involves the lungs, liver, bones and brain whilst digestive tract metastases are unusual^[2,3]. The literature only collects autopsy series or case reports, mostly in patients with an advanced and widespread disease. We present two cases of different gastrointestinal involvement from breast cancer.

MATERIAL AND METHODS

We have conducted an exhaustive search of the Hospital-Based Cancer Registry (HBCR) of Príncipe de Asturias University Hospital which covers a population of approximately 250.000 people. We have found 617 codes “infiltrated by” or “metastasis from” coming from 569 biopsies, obtained from 438 patients. The search time spans the years from 2000 to 2016 both inclusive. The total number of women with breast cancer registered in the HBCR is 2417, of which 13 patients appears concurrently in the group of 438 patients with tumoral dissemination in digestive tract. After revising the histologic reports, only two patients had metastases from breast carcinoma in different locations of the gastrointestinal tract.

CASE REPORTS

The first case (patient 1) is about a 70-year-old woman who underwent a right radical mastectomy for infiltrating lobular carcinoma in 2009. In 2013 she had locoregional recurrence treated with surgery followed by radiation therapy and hormonotherapy. In

2015 she was admitted to the Gastroenterology Department because of nausea, persistent vomiting and constitutional symptoms. She did not have abdominal pain. Computed Tomography (CT) scan of the thorax and abdomen showed post-surgical changes related to right mastectomy, liver of normal size and morphology without space occupying lesions and no significant adenopathies were identified in the abdominal cavity. Gastroscopy revealed erythematous antrum mucosa and at duodenal bulb, there appeared a raised area which partially stenosed the lumen with rocky consistency when taking the biopsies. The histological examination of the samples revealed infiltration from breast adenocarcinoma with signet ring cells (figure 1a signet ring cells marked with arrows). Immunohistochemical techniques were strongly positive for cytokeratin 7 (Figure 1b), estrogens, mammaglobin and gross cystic disease fluid protein 15 (GCDPF15) and negative for cytokeratin 20. She underwent a palliative gastrojejunostomy and hormonal therapy. During the following months she had multiple complications including septic shock from bile ducts and finally died 7 months after the diagnosis of small bowel obstruction due to metastatic breast cancer.

The second case (patient 2) is a 60-year-old woman who was diagnosed with infiltrating ductal breast cancer in 2012. She had bone metastases shown in the CT-body without identifying other metastatic involvement. She received systemic chemotherapy. Four years later, she was referred to our Gastroenterology Department after finding in a follow-up CT a circumferential thickening of right and transverse colon. Furthermore, she had newly onset anemia. In May 2016 the patient underwent endoscopic studies including gastroscopy and colonoscopy. Gastroscopy showed gastric body mucosa with an edematous and infiltrative appearance (Figure 2). Several biopsies

were taken. Colonoscopy was performed until theoretical liver angle where there was found an edematous and erythematous mucosa with infiltrative appearance (Figure 2). This lesion did not allow for the passage of the endoscope through it. Numerous biopsies were taken. The histology study of both pathological areas confirmed metastatic involvement of gastrointestinal tract with immunophenotype consistent with breast origin (Figure 3). The patient received different chemotherapy treatments. Surgery was ruled out because of the widespread disease. Despite of chemotherapy lines used, she finally died.

DISCUSSION

According to the data given by the Spanish Association Against Cancer, breast cancer constitutes the leading cause of cancer death in Spanish women. This implies 16.7% of all cancer deaths in the female sex. The prognosis is determined by several factors such as tumor size, presence of hormonal receptors, histologic type or the existence of regional lymph nodes and metastatic disease^[4]. Due to improved imaging techniques and screening protocols, only 10% of patients have metastases at diagnosis^[2]. Gastrointestinal metastases are rare. Borst J *et al*^[5] published a long series with more than 2500 cases of breast cancer with metastatic disease during an

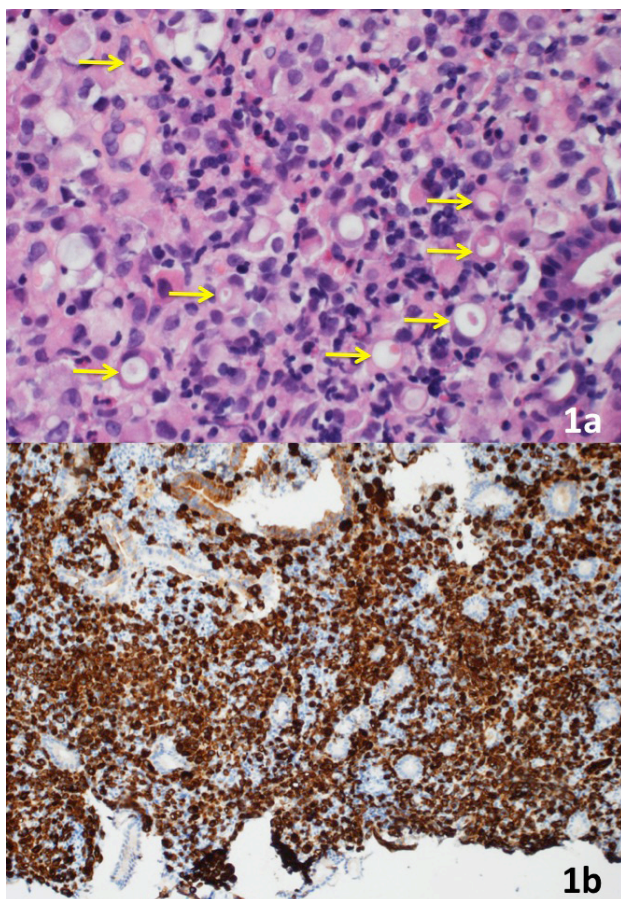


Figure 1 Patient 1's gastroscopy specimen.

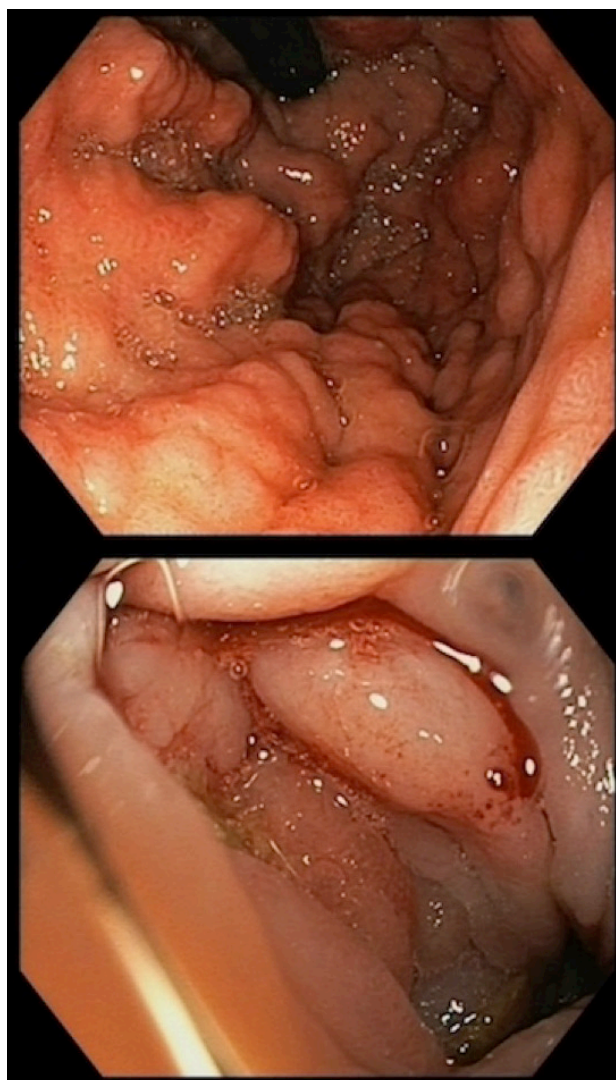


Figure 2 Images of the gastroscopy (at the top) and colonoscopy (at the bottom) showing the mucosa with infiltrative appearance.

18 year period. Out of these, only 17 patients (< 1%) had digestive involvement. In our review the incidence of gastrointestinal metastases from breast cancer is 0.08% which is close to the data collected in the literature. Ductal breast cancer is the prevalent type, whereas lobular subtype appears in approximately 35%, being more frequent bilateral and multicentric^[6]. Both subtypes seem to have a different metastatic pattern. Infiltrating lobular carcinoma is more likely to spread to the gastrointestinal tract, gynecologic organs, peritoneal and the retroperitoneal tissue^[5]. Taal *et al* presented two case series of patients with gastrointestinal metastases^[7,8]: the first one included 27 patients with gastric involvement and the second one had 17 patients with spread to colorectal tissue. In both articles they found that infiltrating lobular carcinoma was more common than the ductal subtype. These data were corroborated by Lamovec *et al*^[9] who reported an autopsy series in which they noticed a statistically significant higher percentage of gastric metastases in patients with lobular carcinoma with regard to those with ductal carcinoma (20% vs 3.6% $p < 0.004$). In the same way, patients with lobular carcinoma had intestinal metastases more frequently than those with ductal subtype (40% vs 2% $p < 0.00001$). In our cases, one of the patients presented with synchronous spread to the stomach and colon due to infiltrating ductal breast cancer; the other patient presented with small bowel obstruction secondary to infiltrating lobular breast cancer.

The clinical symptoms are usually nonspecific (nausea, vomiting, abdominal pain...) mimicking other disorders such as Crohn's disease or bowel obstruction. These data are supported in the present report. One of our patients presented with symptoms which simulated a small bowel obstruction; in the other case a newly onset anemia was responsible for initiating the diagnostic study. In addition, other factors complicate the diagnosis: long disease-free interval, presence of widespread disease as it has been reported in many cases in the literature^[7,8] and the histologic pattern which can imitate other entities too. In both our patients, the disease did not show other distant involvement except for gastrointestinal tract. In 2016 Buka *et al*^[10] reported a case of a patient initially diagnosed with gastric carcinoma with signet ring cells. Two years later, she presented diarrhea and weight loss. Because of these new symptoms a colonoscopy was performed and biopsies were taken throughout the colon. The histology revealed adenocarcinoma with signet ring morphology, positive for estrogen and progesterone receptors supporting the diagnosis of metastatic lobular carcinoma. Based on this new information they reviewed the gastric samples

and modified the original description of primary gastric carcinoma to gastric metastases from lobular breast cancer. Everything commented on above emphasises the relevance of a high index level of suspicion in making a correct diagnosis and appropriate prognosis approach. Our first patient had a breast cancer recurrence in the form of small bowel obstruction without presenting other distant involvement.

Endoscopic findings vary widely and may range from small ulcers, friable mucosa, linitis plastica-like inflammation, stenosis to obstructing mass, mimicking primary gastric or colorectal cancer^[4].

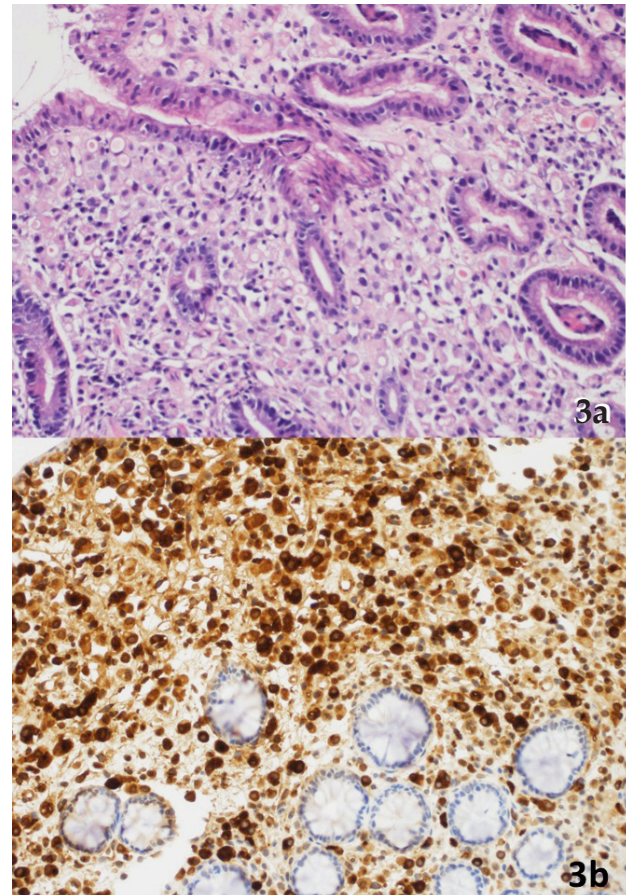


Figure 3 a: patient 2's gastric sample, H&E stain; b: colon sample positive with mammaglobin stain.

Table 1 Involvement locations of gastrointestinal metastases from breast cancer.

Author/Reference	Involvement Location				
	Esophagus	Stomach	Small Bowel	Colon/Rectum	Others (oropharynx, pancreas, bile duct)
Nazareno J <i>et al</i> 2006 † (n = 6)	33.3%; 100% Lob.	50%; 33% Lob.; 66% NA	33.3%; 33% Lob.; 66% NA	16.60%	16.6%; 100% Ductal
McLemore EC <i>et al</i> 2005 † (n = 53)	8%; 100% Lob.	28%; 66% Lob.; 33% Ductal	19%; 60% Lob.; 40% Ductal	45%; 58% Lob.; 33% Ductal	NA
Borst J <i>et al</i> 1993 † (n = 21)	9.5%; 50% Lob.; 50% Ductal	19%; 75% Lob.; 25% Ductal	47%; 80% Lob.; 20% Ductal	14%; 100% Lob.	9.5%; 50% Lob.; 50% Ductal
Taal BG <i>et al</i> 1992 ¶ (n = 364)		7.4%; 74% Lob.; 14% Ductal; 11% NA		4.6%; 88% Lob.; 5.8% Ductal; 5.8% NA	
Lamovec J <i>et al</i> 1991 ¶ (n = 220)		5.4%; 41% Lob.; 58% Ductal		6.3%; 71% Lobular; 28.5% Ductal	

† n: number of patients with gastrointestinal metastases; ¶ n: number of patients with metastases at any location. Lob.: Lobular; NA: not available.

This is the reason why endoscopy with deep biopsy is necessary for accurate diagnosis. Commonly, the lesion has desmoplastic reaction with formation of connective fibrous tissue and infiltrates all layers (serosal, muscular and submucosal), similar to linitis plastica^[3,4]. Immunohistochemical tests are useful to identify primary origin neoplasm. These techniques are positive with cytokeratin 7 and 19, mamoglobin, estrogen and progesterone receptors, e-cadherin (which moreover guide the pathologist to discern between ductal vs. lobular subtype), GCDFP15...

Obtaining the correct diagnosis of gastrointestinal metastases from breast cancer can be challenging because of several reasons mentioned above. Because of this, there are some authors which propose that, in women with a history of breast cancer and a newly gastrointestinal tumour, a histologic comparison (including immunohistochemistry) should be carried out^[11].

There is no consensus concerning the optimal management of this entity. It can be only systemic (hormonal or chemotherapy) or combined with surgery. McLemore *et al*^[2] submit that chemotherapy and hormonotherapy are favorable prognostic features with $p = 0.004$ and $p = 0.003$ respectively. On the other hand, age and the presence of gastric metastases are responsible for poor prognosis. Surgical treatment has not been shown to improve survival. In the majority of cases, it has a palliative role in order to ameliorate the clinical symptoms. The decision on a surgical approach has to be taken according to clinical presentation, access to chemotherapy and the patients' quality of life. One of the patients reported in this study underwent palliative surgical treatment in order to improve obstructive symptoms. Nevertheless, the disease progressed and she died months after diagnosis of breast cancer metastases. The other patient received chemotherapy and she is already on treatment.

In conclusion, gastrointestinal metastases from breast cancer are really uncommon. The lobular subtype of breast cancer is more likely to metastasize to the digestive tissues. In most cases, gastrointestinal metastases are part of widespread disease. The clinical symptoms and endoscopic findings are variable. Therefore, it is important for gastroenterologists to consider the diagnosis of gastrointestinal metastases in those patients with a history of breast cancer who develop digestive complaints, regardless of the time that has elapsed. Histologic evaluation of samples obtained from endoscopy are useful to establish the accurate diagnosis. Once the diagnosis is made, the appropriate treatment can be selected.

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