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# A 58-Year-Old Woman with Acute Gastric Perforation Due to Metastatic Ductal Carcinoma 18 Years Following Bilateral Mastectomy for Invasive Ductal Carcinoma of the Breast

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Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
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**Conflict of interest:** None declared

**Patient:** Female, 58-year-old  
**Final Diagnosis:** Gastric perforation  
**Symptoms:** Abdominal pain • peritonitis  
**Medication:** —  
**Clinical Procedure:** Jejunostomy tube placement • laparoscopic surgery • open surgery  
**Specialty:** Surgery

**Objective:** Unusual clinical course


**Background:** Invasive lobular carcinoma and ductal carcinoma of the breast can metastasize to all sites in the body, including the gastrointestinal tract. Late presentation of metastases of lobular carcinoma of the breast to the gastrointestinal tract have previously been reported, but late metastasis of ductal carcinoma of the breast to the gastric mucosa is rare. This report is of a 58-year-old Lebanese woman who presented with acute gastric perforation due to metastatic ductal carcinoma, 18 years following bilateral mastectomy for invasive ductal carcinoma of the breast.

**Case Report:** We present the case of a 58-year-old woman who underwent a right modified mastectomy for an invasive ductal carcinoma in 2002 combined with a contralateral prophylactic mastectomy for cosmetic purposes. She presented a secondary gastric lesion 18 years later. The clinical presentation resembled perforated ulcer. The choice of gastrectomy was denied due to retrogastric and pancreatic invasion by the tumor. A laparoscopic gastric closure failed to heal the perforation. A supraumbilical laparotomy incision was performed for the placement of a Pezzer tube in the gastric perforation and the installation of a feeding jejunostomy.

**Conclusions:** This report is of a rare presentation of metastatic ductal carcinoma of the breast to the gastric mucosa associated with gastric perforation that presented 18 years after bilateral mastectomy. This case highlights the importance of obtaining a full past medical history to identify previous primary malignancy, and also is a reminder that ductal carcinoma of the breast can present with metastatic involvement in the gastrointestinal tract several months, or even years, following mastectomy.

**Keywords:** Breast Neoplasms • Digestive System Diseases • Neoplasm Metastasis

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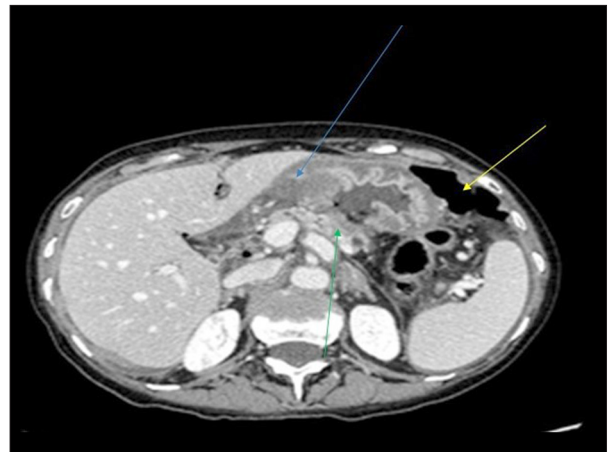
## Background

Breast cancer is the most common cancer in the world and represents the fifth most common cause of death among women. It accounted for 30% of all cancers in 2020 [1]. The lifetime risk of an American woman developing breast cancer is 12.5% [2].

About 12% of patients diagnosed with breast cancer will develop metastatic disease, mainly in the lungs, the liver, the bones, and the brain [3,4]. However, digestive tract metastasis of breast carcinoma is rare, with the stomach being the second most frequent gastrointestinal location after the colon [5]. The invasive lobular carcinoma (ILC) subtype is most commonly responsible of gastric metastasis [6], with a molecular pattern dominated by estrogen receptor positive (ER+) and human epidermal growth factor 2 (HER2) negative subtypes. In 2017, Mathew et al reported on the distinct patterns of metastases from invasive lobular carcinoma of the breast and showed that, when compared with invasive ductal carcinoma, patients with invasive lobular carcinoma were more likely to develop metastases to the ovary and gastrointestinal tract [7]. Differentiating gastric primary and secondary lesions is a crucial challenge, and relies on clinical, endoscopic, and pathological features with different therapeutic implications [8]. Gastrointestinal metastasis of breast cancer is rarely diagnosed, with most cases being either asymptomatic, or synchronous to other metastatic sites upon diagnosis, or even discovered on autopsies [5,9]. Recently, De Gruttola et al reported the case of a 61-year-old woman who presented with gastric perforation due to metastatic lobular carcinoma of the breast, 8 years following diagnosis and mastectomy [10]. The present report is of a 58-year-old Lebanese woman who presented with acute gastric perforation due to metastatic ductal carcinoma of the breast 18 years following bilateral mastectomy.

## Case Report

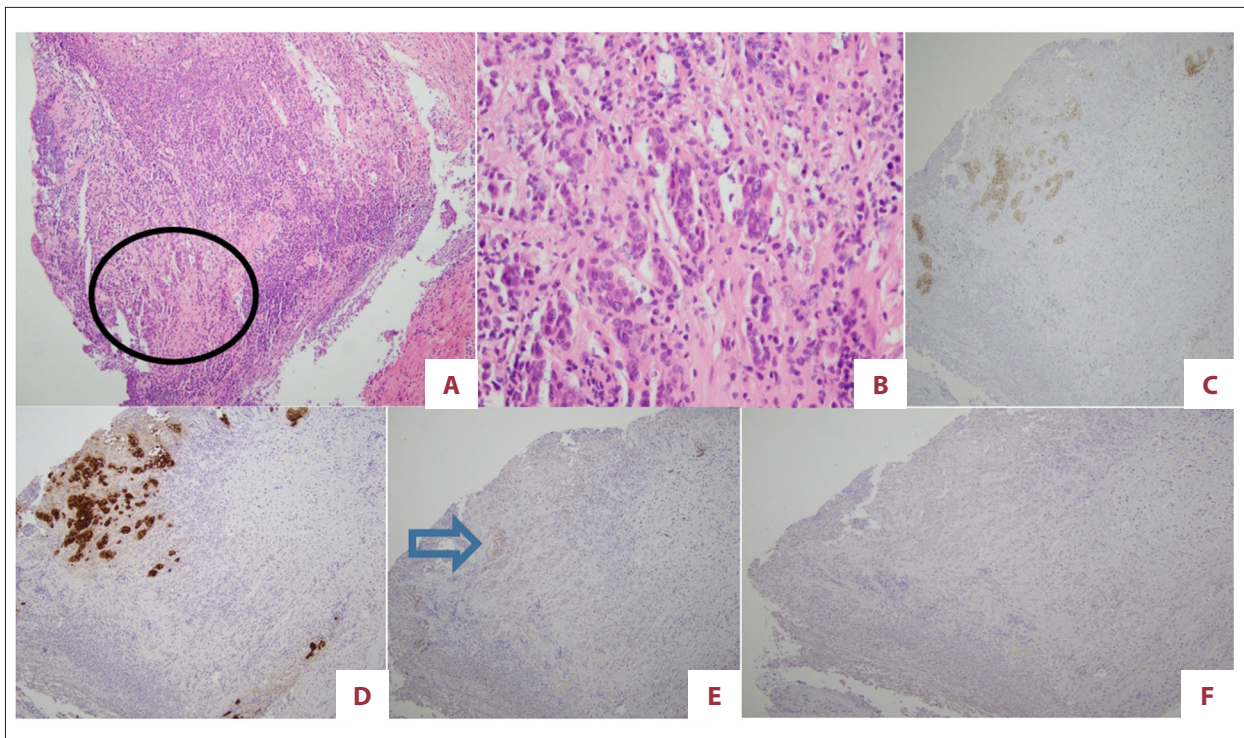
A 58-year-old woman presented to the emergency department with severe acute abdominal pain of 4 hours' duration with tachycardia and fever. On physical examination, she had diffuse abdominal tenderness with abdominal guarding in the epigastric area. The pain was not relieved by morphine injections. The medical history revealed dyspepsia, mild gastroesophageal reflux during the previous 6 months, with no hematemesis, nor melena, nor hematochezia. The patient was not taking any regular medication. Surgical history included a right modified mastectomy for an invasive ductal carcinoma (IDC), 18 years previously, combined with contralateral mastectomy for cosmetic purposes. Laboratory tests identified a white blood count of 9400 with 80% neutrophils and elevated C-reactive protein without any other abnormalities. Patient serum albumin level was 3.2 g/L and the patient had significant



**Figure 1.** Axial image from an abdominal computed tomography (CT) scan in a 58-year-old Lebanese woman who presented with acute gastric perforation due to metastatic ductal carcinoma 18 years following bilateral mastectomy. The yellow arrow shows pneumoperitoneum. The green arrow shows tumor in the pancreas. The blue arrow shows an area of fluid associated with gastric perforation.



**Figure 2.** Coronal image from an abdominal computed tomography (CT) scan in a 58-year-old Lebanese woman who presented with acute gastric perforation due to metastatic ductal carcinoma 18 years following bilateral mastectomy. The arrow shows the site of gastric perforation.



**Figure 3.** Photomicrographs showing histopathology and immunohistochemistry of the surgical resection specimen from a 58-year-old Lebanese woman who presented with acute gastric perforation due to metastatic ductal carcinoma 18 years following bilateral mastectomy. (A) Low-power image showing a cellular tumor replacing normal gastric mucosa and gastric wall. Hematoxylin and eosin (H&E); magnification  $\times 10$ . (B) High-power image showing small cells with dark pink cytoplasm, arranged in small groups, consistent with the diagnosis of ductal carcinoma of the breast. H&E, magnification  $\times 40$ . (C) Immunohistochemistry for human epidermal growth factor receptor 2 (HER2) showing that the tumor cells are HER2-negative. Magnification  $\times 10$ . (D) Immunohistochemistry showing that the tumor cells are positive for cytokeratin 7 (CK7) (brown). Magnification  $\times 10$ . (E) Immunohistochemistry showing that the tumor cells are positive for GATA3 (brown arrow). Magnification  $\times 10$ . (F) Immunohistochemistry showing that the tumor cells are HER2-negative. Magnification  $\times 10$ .

weight loss during the previous 2 months. Computed tomography scan with intravenous injection showed a gastric perforation with diffuse pneumoperitoneum. It also revealed a tumor invading the posterior stomach wall, the celiac trunk, the splenic vein, and the left pancreas. A dilated Wirsung canal was also noted. An infiltrative gastric or pancreatic tumor was suspected (Figures 1, 2).

Laparoscopic exploration of the abdominal cavity showed diffuse peritonitis. A perforation of 2 cm diameter was identified in the anterior wall of the stomach at the level of the incisura angularis. The gastric wall surrounding the perforation area was thick and friable. The tumor bulk had invaded the lesser sac and the pancreas. An initial peritoneal lavage with normal saline solution followed by a biopsy of the perforation margins was performed. We then performed a laparoscopic simple interrupted suture of the perforation with absorbable synthetic 3-0 filament. Two large drains were placed along the sutures. The patient was given parenteral nutrition for 10 days and received 40 mg of omeprazole twice daily. An ingested computed tomography (CT) scan showed no gastric leakage on day

10. The patient was discharged after tolerating an enteral liquid diet on postoperative day 15. Histopathology of the tumor from the site of gastric perforation showed infiltrating malignant cells with histological characteristics of ductal carcinoma, which was supported by positive immunostaining for cytokeratin 7 (CK7) and GATA3, and negative immunostaining for estrogen receptor (ER) and HER2 (Figure 3). This result is compatible with the patient's breast primary IDC. A switch of the hormonal status was noted since the origin pathology was an ER+ tumor.

The initial breast surgery was a right modified mastectomy performed in March 2002. TNM staging was T2N1M0. The patient received adjuvant chemotherapy, which consisted of 4 cycles of taxotere and 4 cycles of endoxan followed by 5 years of prophylactic selective estrogen receptor modulators (SERMs). She stayed in full remission until the gastric perforation revealed gastric metastasis 214 months later.

One week after hospital discharge, the patient was readmitted for acute abdominal pain. CT scan revealed a gastric leak from the sutured perforation. A mini supraumbilical laparotomy

incision was performed for the placement of a Pezzer tube in the gastric perforation and the installation of a feeding jejunostomy. Exploration confirmed that the tumor was not resectable due to multiple-organ involvement. The patient was discharged on postoperative day 12 after tolerating enteral nutrition. The Pezzer tube was kept in place. Two months after her discharge, the patient was doing well, with a plan to start immunotherapy with pembrolizumab.

## Discussion

Asch et al provided the first description of metastasis of breast cancer to the gastrointestinal tract from autopsies in 1968; such metastasis was found in 25% of the 52 reported cases [11]. The largest retrospective series studying the spectrum of gastrointestinal metastasis of breast carcinoma reported an incidence of 0.3% for gastric metastasis [6]. **Table 1** summarizes the findings from previously reported cases of metastatic ductal and lobular breast carcinoma involving the stomach [8,10,12-33].

Our patient's clinical presentation, which mimicked a perforated ulcer, is a very rare clinical presentation of the disease, found only in 4 cases in the literature [10,28,31,32].

The primary breast cancer histological subtype in our patient was IDC, which represents only 20% of breast carcinomas responsible for gastric metastasis; ILC represents the remaining 80% [9].

The ability of primary tumors to spread and form secondary lesions differs between ILC and IDC tumors. The loss of expression of E-cadherin, a cell-to-cell adhesion molecule characteristic of ILC tumors, is found in 90% of metastatic cases [34] and may be responsible for the aggressive spread of ILC [35,36]. Other authors have signaled that gastrointestinal tract metastasis mechanisms are more complicated and are still poorly understood for both subtypes [37].

The diagnosis of gastric breast cancer metastasis is always difficult, both clinically and histologically. Clinical symptoms like anorexia, weight loss, epigastric pain, nausea, and vomiting are unspecific. This could cause an underestimation of the prevalence of this condition and a delay in its diagnosis [8]. Histological differentiation between breast cancer gastric metastasis and diffuse gastric primary carcinoma, also called signet cell carcinoma, is difficult [37]. Furthermore, the metastatic lesions are often misdiagnosed as signet cell carcinoma on biopsies. Increased expression of estrogen receptor on immunohistochemistry can differentiate between the two. Other useful markers include gross cystic breast disease fluid protein (GCDFP-15) and cytokeratin (CK) 5/6, especially when the tumor is ER negative [38]. In our case, confirmation

of the secondary origin of the gastric biopsy was challenging due to the switch in ER status from positive in the primary breast cancer to negative in the secondary gastric biopsy. This switch is frequently noted in gastric breast cancer metastasis [39]. Our patient's primary tumor was HER2 positive but positivity for the HER2 receptor cannot confirm a breast origin because 17.9% of gastric adenocarcinomas express this receptor [40]. The HER2 positivity rate in ILC cases, according to Almubarak et al [8], is 9%, and in our review, we found a very similar rate of 8.8%. The connection between HER2 and ER status, and metastasis of breast cancer to the gastrointestinal tract in the IDC subtype, has not been properly studied, and needs further investigation. In our case, CK7 positivity confirmed the tumor's adenocarcinoma nature [41], while the GATA3 positive state confirmed its mammary origin; this is more accurate than GCDFP-15 [42].

The mean interval between primary breast cancer and gastrointestinal metastasis diagnosis is around 7 years or 84 months [5]. As shown in **Table 1**, the longest reported interval is 230 months after breast cancer diagnosis [8]. Our patient presents the second longest interval between a primary breast cancer diagnosis and the discovery of a secondary gastric lesion, and the longest interval for an IDC subtype tumor. The interval was 214 months. The relapse after many years following primary diagnosis and adequate initial therapy can be explained by latent micro-metastases resistant to anti-ER therapy, such as the 5 years of treatment with SERM undergone by our patient. Some authors suggest that a delay in disease recurrence may be due to the addition of anti-aromatase medication for another 5 years without clearing the risk of metastatic clones. These hypotheses may explain the long time interval between initial diagnosis and the onset of gastric disease [43,44].

The role of radical resection is limited in treating breast cancer gastric metastasis, and palliative surgery has shown no effect on overall survival [5]. Synchronous extra-digestive metastases are frequently found at the time of gastrointestinal breast cancer metastasis diagnosis, and serve as supporting evidence of a large systemic dissemination of the disease. Systemic therapy such as chemotherapy or hormone therapy are considered in such cases rather than surgical resection [37]. In rare cases, aggressive surgical treatment has been recommended for a solitary gastric metastasis, followed by chemotherapy and systemic treatment; such courses of treatment have shown minor benefit to overall survival [45]. Less invasive techniques should be considered, such as embolization for gastric bleeding and endoscopic stent placement for obstruction [46,47]. In general, the median survival of patients with metastatic breast cancer ranges between 2 and 3 years [48]. In our review, rapid death was reported in 1 case [31], and the longest reported survival was 66 months [33]. Our patient is still alive at the

**Table 1.** Characteristics of gastric metastasis of breast cancer: Cases in the literature since 2005.

Authors	Year	Number of cases	Age [range] (years)	Histological type	ER	PR	HER2
Akali et al [11]	2005	1	50	IDL	NA	NA	NA
Kudo et al [12]	2005	1	59	NA	NA	NA	NA
Whitty et al [13]	2005	1	55	IDC	+	+	NA
Jones et al [14]	2007	2	51 61	ILC ILC	+ +	+ +	- NA
Dumoulin et al [15]	2009	1	60	ILC	+	+	-
Pectasides et al [16]	2009	8	44 52 63 67 58 61 75 49	ILC IDC ILC ILC IDC ILC ILC ILC	NA NA NA NA NA NA NA NA	NA NA NA NA NA NA NA NA	NA NA NA NA NA NA NA NA
Vennapusa et al [17]	2010	1	61	ILC	+	+	NA
Yamamoto et al [18]	2010	1	80	IDC	-	-	NA
Almubarak et al [8]	2011	35	55 [37-74]	34 ILC 1 IDC	19+ 2- 1+ 1-	19+ 2- 1+ 1-	19- 2- 1+ 1+
Koike et al [20]	2011	3	42 54 54	ILC ILC IDC	+ + +	+ + +	- - -
Abid et al [21]	2013	1	59	ILC	+	+	-
Loubna et al [22]	2013	2	70 50	IDC IDC	- -	- -	NA +
Hild et al [23]	2014	1	53	ILC	+	+	-
Eren et al [24]	2014	1	37	ILC	+	+	NA
Waseda et al [25]	2015	1	57	ILC	+	+	NA
Buka et al [26]	2016	1	58	ILC	+	+	-
El Hage et al [27]	2016	5	42 66 58 75 70	ILC ILC ILC ILC ILC	+ + + + +	+ - + + +	- - + - -
Wong et al [28]	2016	1	72	ILC	+	+	-
Rodrigues et al [29]	2016	12	[40-86]	5 ILC 7 IDC	+ 11/12	+ 6/9	+ 2/3
Yim et al [30]	2017	1	65	ILC	-	-	+
Barranco et al [31]	2017	1	48	IDC	+	-	NA
Gurzu et al [32]	2018	2	68 73	ILC IDC	+ -	- -	NA +
Woo et al [33]	2018	1	51	ILC	+	+	-
De Gruttola et al [10]	2019	1	61	ILC	+	+	-

**Table 1 continued.** Characteristics of gastric metastasis of breast cancer: Cases in the literature since 2005.

Authors	pTNM	Interval to GM [range] (months)	Perforated	Treatment for gastric metastasis	Other metastasis	Survival (months)
Akcali et al [11]	T2N0M0	108	No	TG+ chemotherapy	No	Alive at 41
Kudo et al [12]	NA	48	No	Endoscopic resection	No	Alive at 24
Whitty et al [13]	T2N0M0	131	No	TG+ Total colectomy	No	NA
Jones et al [14]	T2 T3N1	36 168	No No	TG + D2 Chemotherapy	Bone Bone, brain	Palliative care NA
Dumoulin et al [15]	pT1cN1M0	120	No	Diagnostic laparoscopy	Peritoneal carcinosis	Palliative care
Pectasides et al [16]	NA NA NA NA NA NA NA NA	35 18 55 2 38 50 82 44	No No No No No No No No	Chemotherapy for all	Ovaries, bone Bone, lung No No Skin, lung, bone Peritoneum, bone Bone No	Dead after 11 Dead after 23 Alive at 9 Alive at 44 Dead after 4 Dead after 9 Dead after 1 Alive at 39
Vennapusa et al [17]	T2N1M1	0	No	Chemotherapy	Ribs, vertebrae, orbit	NA
Yamamoto et al [18]	pT2N2M0	6	No	Chemotherapy	Brain	Alive at 12
Almubarak et al [8]	9T1 15T2 8T3 3T4	57 [0-230]	No	4 TG 3 Bypass 26 Chemotherapy 2 Hormonotherapy	20: Bone, liver, peritoneum, skin, colorectal, esophagus	53% overall 24 months survival
Koike et al [20]	NA NA NA	NA NA NA	No No No	Chemotherapy Chemotherapy Chemotherapy	No Bone Bone	Alive at 56 Dead after 58 Dead after 27
Abid et al [21]	T1N1M1	0	No	Chemotherapy	Colon	NA
Loubna et al [22]	T4N2M0 pT1cN0M0	12 60	No No	Chemotherapy Surgery	No No	Dead after 3 Alive at 18
Hild et al [23]	T3N2	84	No	Chemotherapy	No	Alive at 30
Eren et al [24]	NA	72	No	Chemotherapy	NA	Dead after 3
Waseda et al [25]	NA	60	No	Chemotherapy	Liver	NA
Buka et al [26]	NA	-14	No	TG + D2	Colorectal	Dead after 86
El Hage et al [27]	T3N2M1 T1bN1M1 T2N2M0 T2NxM1 T2N3M1	0 68 40 2 18	No No No No No	Chemotherapy for all	No Yes Yes Yes Yes	NA Dead after 11 Dead after 13 Dead after 1 Dead after 19
Wong et al [28]	pT2N0M0	48	Yes	Laparotomy for perforated ulcer	No	Alive at 12
Rodrigues et al [29]	NA	[0-156]	No	8 chemotherapy 4 surgery: 3 TG +D2 1 STG +D2	10/12: 9 Bone 3 Lungs 1 Large bowel 1 liver 1 skin 2 esophagus 1 mediastinum	MS: 14.58 MS 4 surgical cases: 38
Yim et al [30]	pT2N3M0	48	No	Chemotherapy	Bone	NA
Barranco et al [31]	NA	0	Yes	None	NA	Instant death

**Table 1 continued.** Characteristics of gastric metastasis of breast cancer: Cases in the literature since 2005.

Authors	pTNM	Interval to GM [range] (months)	Perforated	Treatment for gastric metastasis	Other metastasis	Survival (months)
Gurzu et al [32]	NA	0	Yes	TG + D1	NA	Dead after 2
	NA	24	No	STG +D1	NA	Alive at 4
Woo et al [33]	pT3N3M1	12	No	STG with Bilroth II +D2	Bone, ovary, bone marrow, omentum	Alive at 66
De Gruttola et al [10]	T3N0M0	96	Yes	TG + Hormonotherapy	No	Alive at 6

D2 – D2 lymphadenectomy; ER – estrogen receptor; GM – gastric metastasis; HER2 – human epidermal growth factor receptor; IDC – invasive ductal carcinoma; ILC – invasive lobular carcinoma; MS – mean survival; NA – not available; PR – progesterone receptor; STG – subtotal gastrectomy; TG – total gastrectomy.

time of writing of this paper, 3 months after the discovery of her gastric metastasis.

In our case, the patient had gastric perforation with diffuse peritonitis. To our knowledge, we are the first team to attempt a laparoscopic primary closure of the perforation, taking a less invasive approach without knowing the initial diagnosis at the time of surgery. Prior surgical approaches include aggressive total gastrectomy (with no mention of patient survival benefit) [10], and a laparotomy for lavage and drainage [12]. Understanding the unresectable status of the tumor, our second intervention consisted of a mini supraumbilical incision for the placement of a Pezzer tube in the gastric perforation and the installation of a feeding jejunostomy. This approach was chosen to facilitate further systemic treatment and provide appropriate nutritional support, as mortality is associated with malnutrition in advanced metastatic disease [47,48].

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## Conclusions

This report is of a rare presentation of metastasis of ductal carcinoma of the breast to the gastric mucosa, associated with gastric perforation, presenting 18 years after bilateral mastectomy. This case highlights the importance of obtaining a full past medical history to identify previous primary malignancy, and also is a reminder that carcinoma of the breast can present with metastatic involvement of the gastrointestinal tract several months, or even years, following mastectomy.

## Conflict of Interest

None.

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