Metastatic breast cancer to the gastrointestinal tract: A case series and review of the literature

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INTRODUCTION

Breast cancer is the most common neoplasm in women, accounting for approximately 32% of cancers in women, with a lifetime risk of 1 in 10\(^1\). Prognosis is related to the presence of hormonal receptors, the size and grade of the primary tumour, the presence of regional lymphadenopathy, and metastatic disease\(^2\). Metastatic breast cancer typically involves the lungs, bones, brain and liver, but occasionally can affect the gastrointestinal tract\(^3\). We report 6 patients with a variety of presentations involving the gastrointestinal tract, all of which were eventually found to be due to metastatic breast cancer. These examples highlight the importance of considering metastatic breast cancer as a potential cause of radiological abnormalities affecting any part of the gastrointestinal tract of women, especially those with a previous history of breast cancer.

CASE REPORTS

Case 1

A 51-year old female presented with a 3-mo history of progressive solid food dysphagia. Initial barium swallow and endoscopy were normal. Esophageal manometry showed impaired relaxation of the lower esophageal sphincter, but no other abnormality. A decision was made to follow the patient and re-investigate her in 6 mo. The patient returned after 5 mo with worsening dysphagia and 20-pound weight loss. Barium swallow demonstrated retained secretions, esophageal dilatation and tapered narrowing in the region of the lower esophageal sphincter (Figure 1). Repeat manometry demonstrated changes consistent with achalasia. Repeat endoscopy showed a dilated esophagus and a narrowed gastroesophageal junction with no intrinsic mucosal abnormality. Pneumatic dilatation with a Rigiflex 35 mm balloon was unsuccessful and the patient was referred for thoracoscopic myotomy. At the time of surgery, the left lower lobe of the lung was found to be fixed to the gastroesophageal junction by tumor that extended to involve the distal esophagus and pericardium. Biopsies showed infiltrating lobular breast carcinoma. The patient had a right mastectomy 15 years previously. The patient recovered from surgery and was treated with tamoxifen with gradual normalization of her swallowing function. She declined repeat manometric or radiological assessment.

Case 2

A 58-year old female with a previous history of Paget's disease...
of the bone involving the cervical spine, multinodular goitre and neck trauma secondary to a motor vehicle accident presented with oropharyngeal dysphagia and mild dysarthria. Barium swallow demonstrated poor bolus formation, decreased laryngeal elevation, incomplete oropharyngeal clearance, and aspiration of barium. Electromyography was suspicious of a motor neuron disease, demonstrating paralysis of the left vocal cord, tongue fasciculations, and denervation of the left sternocleidomastoid. The patient underwent magnetic resonance imaging (MRI) which demonstrated a soft tissue density at the C2 level, as well as marrow replacement in several vertebrae (Figure 2A and 2B). Open biopsy of the soft tissue showed adenocarcinoma consistent with metastatic breast cancer. The patient had a modified left radical mastectomy for ductal adenocarcinoma followed by radiation therapy 20 years previously.

**Case 3**
A 66-year old female presented with solid food dysphagia for several months. Barium swallow demonstrated a mid-esophageal stricture that was suspicious of neoplastic disease (Figure 3). Endoscopy and biopsy confirmed metastatic infiltration of the esophagus by lobular breast carcinoma. Unfortunately, attempted palliative dilatation resulted in perforation of the esophagus. The subsequent course of events resulted in prolonged hospitalization with multiple surgical procedures, complications and eventually death. The patient had a modified right mastectomy and radiotherapy 13 years previously for node negative malignancy. The patient had known metastatic disease to the left hilum, proven by biopsy, 6 years prior to the presentation of dysphagia.

**Case 4**
An 80-year old female presented with a history of early satiety and vomiting. Double contrast upper gastrointestinal barium examination was consistent with linitis plastica (Figure 4A). Endoscopy with biopsy of the gastric body and antrum confirmed metastatic infiltrating lobular carcinoma of breast origin. Subsequent computed tomography (CT) scanning demonstrated changes in the stomach and duodenum (Figure 4B). The patient received palliative care, but her symptoms were progressed after 14 mo. Plain films of the abdomen demonstrated a small bowel obstruction, suspected to be due to intra-abdominal spread of the disease. The patient underwent modified left radical mastectomy 2 years previously and had node positive disease.

**Case 5**
A 60-year old female presented with a history of diarrhea,
abdominal cramps and vomiting. Crohn’s disease was suspected and she was initially treated with prednisone with clinical improvement. Several months later she experienced an exacerbation of her symptoms and presented with a partial small bowel obstruction. Small bowel enteroclysis demonstrated multiple abnormalities, including persistent narrowing of the gastric body and antrum (Figure 5), prominent irregular gastric rugae with diffuse mucosal serration, as well as 3 separate strictures of the ileum. The findings were compatible with the diagnosis of Crohn’s disease, but upper gastrointestinal endoscopy showed gross findings suspicious of malignancy. Biopsy demonstrated adenocarcinoma of breast origin. CT examination demonstrated ascites and mesenteric involvement, subsequently confirmed at laparotomy. The patient had a modified radical mastectomy 10 years previously.

**Case 6**

A 51-year-old female had a 3-year history of increasing abdominal pain. CT examination demonstrated a dilated small bowel as well as ascites (Figure 6A). Subsequent laparotomy demonstrated that the patient had a small bowel obstruction secondary to carcinomatosis consistent with metastatic breast cancer. After surgical and hormonal therapy, the patient improved clinically. One year later, she presented with diarrhea. A double contrast barium enema demonstrated lesions in the ascending, distal transverse and sigmoid regions of the colon (Figure 6B). The appearance of the lesions was consistent with synchronous colonic cancers, but proved to be metastatic breast adenocarcinoma on pathology. The patient was diagnosed with breast cancer 4 years prior to the presentation with small bowel obstruction.

**DISCUSSION**

Breast cancer accounts for 19% of cancer deaths in women[9]. Current therapies have had a significant impact on the mortality and survival rates of breast cancer[10]. Prognosis is related to several factors including the presence of metastases with tumor histology being one of the predictors of metastatic spread. For example, tubular and mucinous carcinomas have a lower incidence of metastases and a better prognosis[11]. Lobular carcinoma, though less common and by mechanisms that are not clear, is more likely to metastasize to the gastrointestinal tract[12]. Although the gastrointestinal tract is a less common site for metastatic involvement by breast cancer, recognizing the range of possible presentations is important for early and accurate diagnosis and treatment. The cases we described in this report highlight these features. Also, our patients presented with gastrointestinal manifestations after an average of 9.5 years and as long as 20 years of initial diagnosis. A 30-year interval between the original diagnosis and the presentation of metastatic disease has been reported in the literature[13]. Given the increased survival of breast cancer patients with current therapeutic regimes, more unusual presentations of metastatic disease, including involvement of the gastrointestinal tract can be anticipated[14,15], and hence this diagnosis should be considered in any woman with a previous history of the disease presenting with new gastrointestinal complaints.

Previous case reports and small series that have documented gastrointestinal involvement by metastatic breast cancer, together with the cases presented here, are summarized in Table 1. Any region of the gastrointestinal tract can be involved. However, oropharyngeal and esophageal involvement presenting as dysphagia is unusual[15]. Our series is unique in that it includes three examples of this: case 1 with pseudoachalasia, case 2 with oropharyngeal dysphagia secondary to nerve involvement, and case 3 with malignant esophageal stricture. In our review of the literature, this is only the third reported case of pseudoachalasia secondary to metastatic breast cancer[15]. As well, this is the first reported case of oropharyngeal dysphagia resembling case 2. There is a previous report of one case of metastases to the tongue[16]. Esophageal involvement most commonly presents as a short-segment of extrinsic obstruction in the mid-esophagus and has been reported to occur up to 22 years following the initial diagnosis of breast cancer[17]. Mediastinal and hilar lymphadenopathy may be present[15,18], and endoscopic biopsy may not provide the diagnosis.
if the obstruction is extrinsic and does not involve the mucosa. Long segment involvement of the esophagus, up to 20 cm, has been described\[13\]. Symptoms as well as radiographic findings may mimic radiation-induced or peptic stricture\[12\].

The stomach is the most common site of gastrointestinal involvement by metastatic breast cancer with an incidence of up to 15% at autopsy\[12,14\]. The usual presentation mimics linitis plastica and is typically due to lobular carcinoma\[4\], as illustrated by case 4. Findings include gastric wall thickening, rigidity and decreased peristalsis. Cases in which the linitis plastic-like presentation precedes the diagnosis of breast cancer have been documented\[16\]. In one series of 22 patients, endoscopy and biopsy could provide the correct diagnosis in only 13, most likely because tumor infiltration is deep to the mucosa\[10\]. Metastatic involvement of the stomach can mimic primary gastric neoplasms and inflammatory conditions such as peptic ulcer or gastritis\[14\]. Bleeding and perforation have also been reported\[17-19\].

Malignant neoplasms of the small intestine are uncommon and are usually primary adenocarcinomas\[20\]. Metastatic involvement of the small bowel can be due to malignant melanoma, or cancer of the colon, cervix, ovary or rarely esophagus\[12,20\]. Metastatic involvement of the small intestine is recognized at autopsy\[21,22\], but clinical presentation is uncommon. Patients can present with abdominal pain and diarrhea\[20\], similar to case 5, intussusception\[15\] or even appendicitis\[7\]. The terminal ileum is involved more often than the proximal small bowel, possibly due to the tracking of peritoneal fluid along the mesentery into the right lower quadrant. The clinical and radiological presentation can mimic Crohn's disease, as illustrated by case 5. Metastatic disease to the duodenum has also been described\[23\].

Colonic metastases are common with some series showing colonic metastases in up to 12% of patients with breast cancer\[22,24\]. Carcinoma of the breast is the most frequent source of hematogenous metastases to the large bowel\[25\], but involvement via peritoneal and lymphatic spread also occurs\[12\]. As in the stomach, the lobular form of breast cancer is more likely to metastasise to the colon\[5,4\]. The presentation can be similar to primary neoplasia of the colon or can mimic Crohn's disease, both clinically and radiologically\[12,14,15,18\]. Air contrast barium enema or CT may demonstrate diffuse or multifocal involvement\[16\]. Mucosal nodularity, stenosis, decreased distensibility, angulation and tethering are also characteristic findings\[26\]. Solitary apple-core lesions are less common\[25\]. Similar to the upper gastrointestinal tract, endoscopy and biopsy provide only a moderate diagnostic yield: 6 of 10 patients in one series\[23\]. Deep biopsy or laparotomy may be required for diagnosis\[24,27\]. Rectal involvement has also been described, including rectal stenosis secondary to metastatic breast cancer\[25,28\].

Other intra-abdominal sites of metastatic breast cancer that do not involve the gastrointestinal tract per se have been reported. Ascites, secondary to peritoneal carcinomatosis, is a common abnormality demonstrated by abdominal CT\[27\]. Metastatic spread to the hepatobiliary tract is well described\[19,28\]. Metastases to the diaphragm, the genitourinary tract, the retroperitoneum, the mesenteric lymph nodes, the abdominal wall and subcutaneous tissues have been reported\[11,12,27\]. Spread to the ovaries is identified histologically, but is not usually clinically evident or demonstrated with CT in the absence of other evidence for metastatic disease\[20\].

Metastatic breast cancer involving the gastrointestinal tract can produce a wide range of clinical and radiological presentations, often mimicking other gastrointestinal disorders. Given the high prevalence of this disease, breast cancer needs to be considered in any women presenting with new gastrointestinal complaints, especially those with a history of breast cancer, even if the initial diagnosis was made many years previously.

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