Brief Communication
Communication abrégée

LINITIS PLASTICA AS THE FIRST INDICATION OF METASTATIC LOBULAR CARCINOMA OF THE BREAST: CASE REPORT AND LITERATURE REVIEW

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Breast cancer is the most common malignant tumour in women, accounting for 30% of newly diagnosed cancers.[1–3] Breast cancer may recur after a prolonged disease-free interval in local, regional or metastatic form. Metastases from breast cancer have been described to almost every organ; however, bone, lung, liver and brain harbour the majority of distant tumour foci.[4] Several reports cite extrahepatic gastrointestinal metastases from breast cancer.[5–8] Although early diagnosis of the primary malignant lesion is paramount, early detection of metastatic disease may also provide some benefit, as response to hormonal therapy or chemotherapy, or both, has been reported in the treatment of disseminated breast cancer.[5,9] We describe a woman who presented with linitis plastica of the stomach as the first and only indication of metastatic breast cancer.

CASE REPORT

A 79-year-old woman presented with early satiety, progressive dull epigastric pain, and 11.4-kg weight loss over several months. She had undergone a right segmental mastectomy with axillary node dissection 11 years earlier for an invasive lobular carcinoma. Pathologically, the margins of the operative specimen were negative for cancer, and lymph nodes were free of tumour. In accordance with National Surgical Adjuvant Breast Project protocol, the patient received adjuvant radiotherapy to the right breast, and she remained disease free until the current admission.

An extensive work-up of the gastrointestinal system was done. An initial gastroscopy indicated that the gastric wall was firm with prominent gastric folds but no mucosal lesion. Multiple random biopsies of the gastric wall were taken, all of which were negative for cancer cells. A subsequent barium contrast study of the stomach demonstrated normal mucosa and normal transit time. Multiple gastroscopies with biopsy of gastric mucosa were carried out because her symptoms persisted. Eventually infiltrating adenocarcinoma, initially thought to be primary in the stomach, was found.

Gastric wall thickening was noted on abdominal CT, but there was no evidence of intra-abdominal spread. Therefore, elective gastrectomy was scheduled, with the presumptive diagnosis being primary gastric cancer, linitis plastica type. At laparotomy, the tumour was found to involve the entire stomach and distal esophagus; the liver was free of metastases, but an omental implant was detected. Because of the extent of the disease, we felt that the patient would not benefit from an extensive resection, so the implant was excised and a feeding jejunostomy placed. The pathological features of the omental implant raised the suspicion that this tumour was a metastatic focus of a primary breast carcinoma. Results of the gastric mucosal biopsies were consistent with this diagnosis. In addition, both the omental and gastric biopsies were strongly estrogen- and progesterone-receptor positive, further supporting the diagnosis of metastatic breast cancer.

Postoperatively the patient recovered from the procedure and was discharged home on tamoxifen. Unfortunately she did not respond to the hormonal manipulation and was readmitted shortly thereafter with feeding intolerance and weight loss. Two courses of aggressive chemotherapy were attempted, but she died 14 weeks after the original procedure. The family refused to allow an autopsy.

Pathological findings

The first positive endoscopic biopsy of the stomach contained small tumour cells, many of which were signet-ring cells, in the lamina propria (Fig. 1). They were distributed individually and in loose clusters. The nuclei showed only subtle features of malignancy. Intracytoplasmic mucin was demonstrated by both periodic acid-Schiff and mucicarmine stains. The histologic picture was consistent with the clinical diagnosis of primary gastric cancer, linitis plastica type. The initial negative endoscopic biopsies were carefully reviewed and contained no tumour cells.

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Accepted for publication Feb. 9, 1999.

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A biopsy of an omental metastasis was obtained during exploratory laparotomy. A quick- frozen section revealed a metastatic deposit of small signet-ring cells in an inflammatory and fibrotic background, consistent with metastatic carcinoma from a gastric linitis plastica.

Permanent sections revealed a metastatic deposit of small cells with a prominent signet-ring cell population. The cells tended to arrange themselves in Indian-file trabeculae and to form target-like lesions (Fig. 2). At high power, the cells again showed only subtle malignant features, nuclear molding of adjacent cells and occasional cells with small intracytoplasmic lumina in addition to the more prominent signet–ring cells (Fig. 3). These architectural and cytologic features were reminiscent of a lobular carcinoma of the breast with prominent signet-ring cells, features well described in the literature.[10–12] In addition, the sections of both the omental metastases and the gastric biopsies were stained immunohistochemically for estrogen and progesterone receptors, and both were strongly positive.

Preoperatively, the nature of the patient's original breast surgery was not known. As a result of the histopathologic findings mentioned above and the possibility of breast cancer metastases to the stomach, we recalled the patient's files from the institution where the mastectomy had taken place. The records confirmed that the patient had undergone a segmental mastectomy for lobular carcinoma of the breast 11 years before. We retrieved the slides from this specimen and compared the two tumours. They were histologically identical. In addition, blocks from the original specimen were provided, and further histochemical tests for mucin, and immunohistochemical tests for estrogen and progesterone receptors showed appearances identical to the omental metastases. We concluded that the clinical picture was related to lobular carcinoma of the breast metastatic to the stomach and omentum.

Discussion

Metastases to the lung, liver, brain and bone account for the majority of breast cancer dissemination; however, extrahepatic gastrointestinal metastases have been well documented.[4] Several authors have commented on gastric involvement of metastatic breast cancer.[5–8] From an autopsy series, Abrams and associates[13] reported a rate of gastric metastases of 15%. Most researchers, however, have reported a lower rate.[14–16] Gastric metastases from invasive breast cancer may occur as discrete nodules or as linitis plastica with extensive diffuse infiltration of the submucosa and muscularis propria. In the case of linitis plastica the mode of dissemination is usually hematogenous, first affecting the submucosa and muscularis propria. This may hinder tissue diagnosis by endoscopic

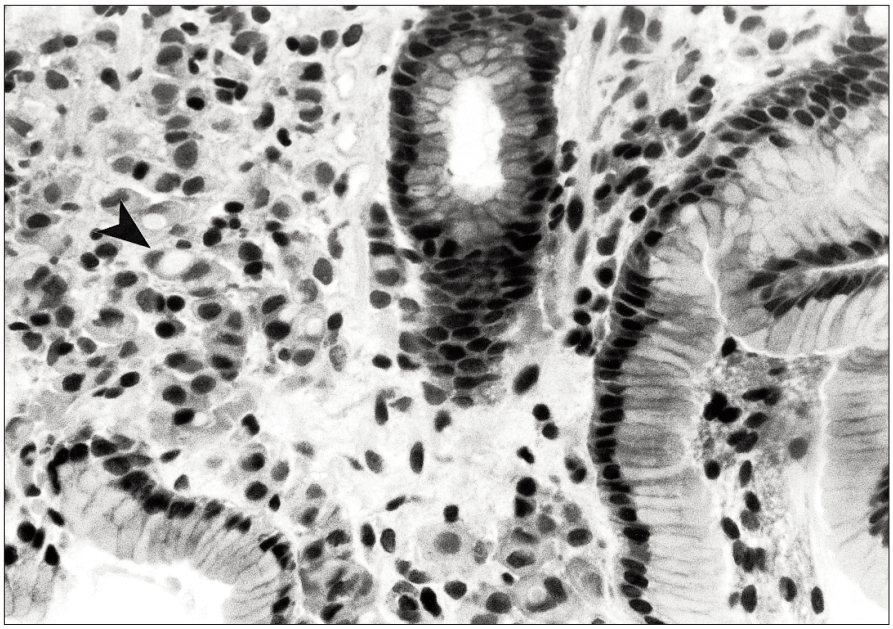

FIG. 1. Small cancer cells with several signet-ring cells (arrowhead) in the lamina propria of a gastric mucosal biopsy (hematoxylin–eosin, original magnification × 400).

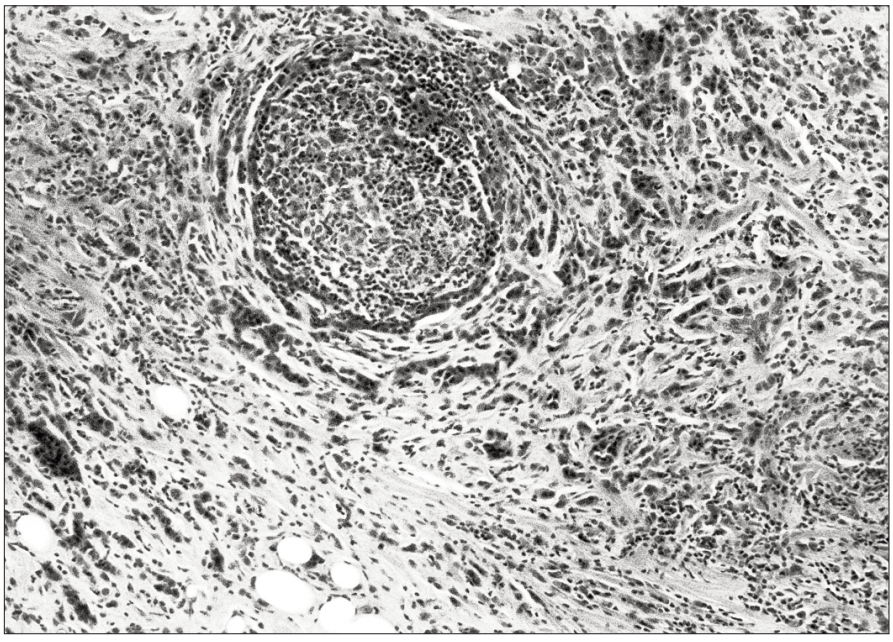

FIG. 2. Metastatic carcinoma in omentum, with targetoid and Indian-file patterns (hematoxylin–eosin, original magnification × 100).

biopsy because superficial biopsies may give false-negative results.[17] Therefore, when linitis plastica is suspected, deeper biopsies are warranted.

Cormier and associates[5] reported 6 cases of linitis plastica of the stomach due to metastatic breast cancer and reviewed an additional 25 patients from the Mayo Clinic registry over 20 years. Although the majority of these patients presented with synchronous or early (within 5 years) gastric metastases, there may be an extended disease-free interval before symptoms develop. Less than 10% of patients in the Mayo Clinic series presented with symptoms related to gastric involvement more than 10 years after diagnosis of their primary disease. However, Benfiguig and associates[8] described a patient with linitis plastica metastatic from breast cancer arising 30 years after mastectomy. Symptoms encountered most often are weight loss, nausea and vomiting, epigastric pain and early satiety.[5]

The radiologic appearance of linitis plastica from breast cancer metastases is similar to that of primary gastric cancer. Barium swallow usually demonstrates mural rigidity, with thickening of the gastric wall.[18,19] CT findings of gastric metastases of breast cancer usually present as diffuse gastric wall thickening. Elliott and colleagues[20] suggested that CT criteria for linitis plastica type of gastric metastases from breast cancer include a gastric wall diffusely thickened by more than 1 cm in an adequately distended stomach.

The histologic subtype of invasive breast cancer appears to influence the site of metastasis.[21] All reported cases of linitis plastica of gastric metastases from breast cancer have arisen in patients with documented invasive lobular carcinoma. Lobular carcinoma of the breast can contain a high percentage of signet-ring cells,[11] which, when combined with a diffuse pattern of spread, can render the metastasis to the stomach almost indistinguishable from primary gastric linitis plastica.[6] Ductal carcinoma has been noted to metastasize to the stomach, but in a discrete nodular pattern.[5]

Hormone-receptor status of the primary tumour is of vital importance when considering the therapeutic options for patients with advanced breast cancer. Response to hormonal manipulation is well described in patients with metastatic estrogen- and progesterone-positive breast cancer.[9] With regard to gastric metastases of breast cancer in particular, survival of up to 4 years was reported in patients treated with various hormonal or chemotherapeutic regimens.[5] This is in contrast to the dismal prognosis and usually ineffective nonsurgical management options facing the patient with linitis plastica due to primary gastric cancer.

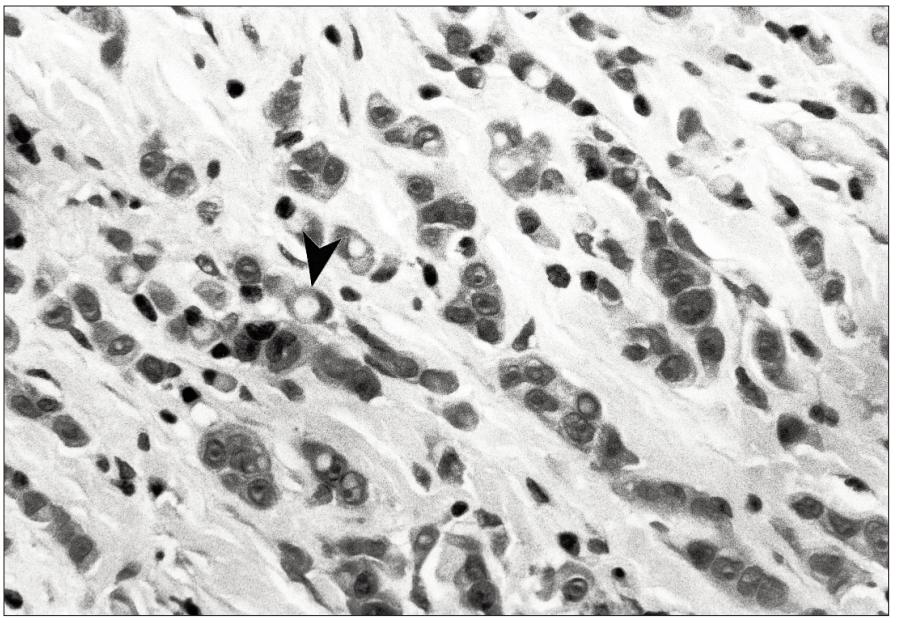

FIG. 3. Small cancer cells in omentum with prominent signet-ring cells (arrowhead) in Indian file (hematoxylin–eosin, original magnification × 400).

Our objective in reporting this case was to increase the awareness of surgeons to gastric metastases from primary breast cancer. Although not common, this is well documented in the literature. The onset of gastrointestinal symptoms in a patient with a history of invasive lobular carcinoma should prompt the treating surgeon to entertain the possibility of gastric metastases and organize the appropriate investigations. Gastric metastases and linitis plastica may arise much later than the primary disease, thus a prolonged disease-free period should not discount the possibility that the gastrointestinal symptoms may be due to breast cancer dissemination. We recommend that investigation of early satiety, weight loss and epigastric pain in patients previously treated for invasive lobular carcinoma should include gastroscopy and biopsy, with the understanding that a negative biopsy may represent an insufficiently deep sampling of the gastric wall and multiple bites of tissue may be required. Although the prognosis is still uncertain, patients with linitis plastica from breast cancer metastases have been noted to respond to hormonal therapy or chemotherapy, or both, particularly if the metastases are positive for estrogen or progesterone receptors. As more of these patients are identified and followed up, the treatment modalities and response may be better understood and defined.

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