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CLINICAL CASE

Gastrointestinal tract metastasis as first presentation of breast cancer

G. Savanis[1], G. Simatos[1], O. Tzaida[2], C. Tsikkinis[1], S. Ammari[1], A. Mylonas[1], E. Kafasis[1], A. Nisiotis[1]

[1]3rd Department of Surgery; [2]Department of Pathology, "Metaxa" Cancer Hospital, Piraeus, Greece

Summary

Gastrointestinal metastases of breast cancer are a rare occurrence. It is even rarer to be the first manifestation of an unknown breast cancer. We present 2 cases of metastatic breast cancer of the lobular type to the stomach and large bowel in 2 women, initially considered as primary disease. The establishment of diagnosis required experienced histopathologic and immunohistochemical examination. The management follows the principles of the primary disease. Surgery is spared for complications. Mean survival is one year. Prognosis is better for patients with positive hormonal receptors.

Key words: breast cancer, metastases, gastrointestinal tract

Introduction

Breast cancer is the most common cause of death from malignant disease in women. One of the most uncommon metastatic sites for breast cancer is the gastrointestinal tract. It is even rarer for the gastrointestinal metastasis to be the first manifestation of an unknown breast cancer. We present 2 cases of metastatic breast cancer to the stomach and large bowel in 2 women, initially considered as primary disease.

Case presentation

Case 1

A 75-year-old lady presented in July 2001 with large bowel obstruction. She underwent an emergency laparotomy. At operation a mass obstructing the descending colon was found. The patient underwent a left hemicolectomy. The histologic examination indicated a poorly differentiated adenocarcinoma with architectural and morphological features (subepithelial localization with total muscular infiltration by linear strands of non-cohesive neoplastic cells) as well as immunohistochemical characteristics compatible with metastatic carcinoma (Figures 1-3). A breast origin, probably of lobular type cancer, was suggested. Postoperative investigations revealed a 2 cm mass of the right breast. The patient underwent partial mastectomy and received postoperatively different chemotherapy regimens (epirubicin/paclitaxel, mitoxantrone/paclitaxel, cisplatin, gemcitabine/vinorelbine, and capecitabine). The histology report revealed an infiltrating lobular carcinoma, grade II-III, with abundant lobular *in situ* carcinoma foci and particular histology similar to the intestinal tumor.

The immunohistochemical and hormonal prognostic factors were as follows: estrogen receptors (ER) positive in 10-20%, progesterone receptors (PgR) negative, Ps2 negative, p53 negative, c-erb-B2 negative, MIB1 positive in 10%.

The patient died of generalized disease in September 2005.

Case 2

A 76-year-old lady presented in April 2003 with a 12-month history of epigastric pain, anorexia,

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Author and address for correspondence:

George Savanis, MD
65, Varnali street
142 31 N. Ionia
Greece
Tel: +30 210 2778815
E-mail: gasim@otenet.gr

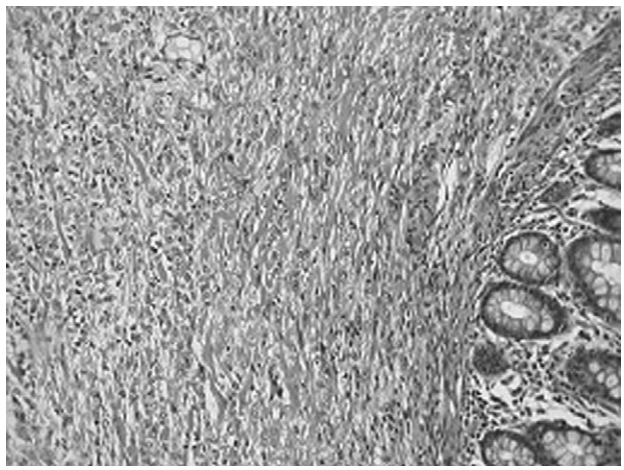

Figure 1. Submucosal diffuse infiltration of the intestinal wall by carcinoma cells (H&E ×100).

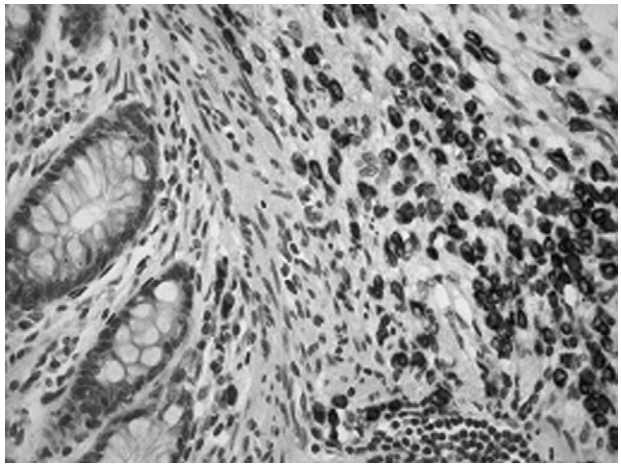

Figure 2. Cytokeratin 7 highlights the submucosal infiltrating carcinoma cells (×400).

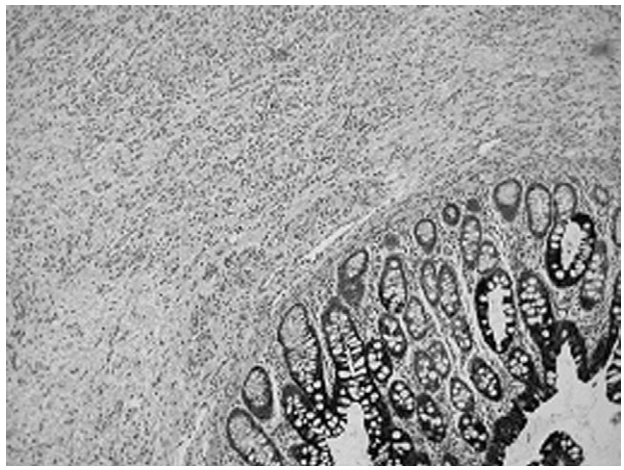

Figure 3. Cytokeratin 20 positive expression exclusively to the mucosa (carcinoma cells unstained) (×40).

vomiting and loss of weight. Upper gastrointestinal endoscopy showed oedema and mucosal ulcerations. The biopsy indicated a diffuse infiltration of the gastric mucosa and submucosa by poorly differentiated carcinoma cells without mention of their origin. Computed tomography of the abdomen and thorax showed pleural effusion, ascites and pelvic bone metastases. At clinical examination a lump was found in the right breast with collateral axillary lymph nodes. The breast lump was removed and the histologic examination revealed a grade III mixed carcinoma of the breast of both ductal and lobular type. New biopsies from the stomach were taken. The comparative morphological and immunohistochemical analysis of both gastric biopsies and the mammary tumor revealed that the stomach was, in reality, metastatically involved by the breast adenocarcinoma. The patient received chemotherapy (FEC) and she died one year later of generalized disease.

Discussion

Breast cancer is the most common malignant disease in women, followed by lung and large bowel cancer. Over the last years prognosis with appropriate management has improved a lot, even in the presence of metastases. The 5-year survival for stage IV is 13%. More common sites of metastases are the lymph nodes, bones, lungs, liver and the brain. The gastrointestinal tract is an uncommon site of metastasis for breast cancer, with stomach being the more frequently affected organ. Gastrointestinal metastases are found in 15% of autopsy specimens as part of widespread disease. 8-10% of them become clinically apparent during lifetime, while acute clinical manifestations such as haemorrhage, perforation and obstruction have been reported in less than 1% of all cases of breast cancer [1]. In contrast, up to 30% of hepatic and 65% of pulmonary and bone metastases become clinically apparent during lifetime. The most common form of extrahepatic abdominal metastases are peritoneal which are accompanied with metastases in other sites. Nevertheless, this form of metastases presents with long survival -especially if they have positive hormonal receptors- which justifies appropriate hormonal and chemotherapeutic manipulations [2]. Regarding metastases to the gastrointestinal tract, there are very few reports in the literature and most of them are for lobular carcinoma. It seems that infiltrating lobular carcinoma has a different metastatic behavior than ductal carcinoma with a predilection for the gastrointestinal tract and the retroperitoneal space, where, in about 7% of the cases, it causes obstruction of

the ureters. It is not unusual invasion of the retroperitoneal space to be considered as retroperitoneal fibrosis, resulting in delay in the diagnosis. It has been hypothesized that the route of metastatic spread in these cases is via the lymphatics [3]. In contrast with ductal carcinoma, lobular carcinoma which accounts for 8-14% of all breast cancers, has no characteristic mammographic findings and can escape early detection. In these cases metastases can be the first manifestation of the disease. Symptoms vary according to the site of metastasis and the kind of complication. These can be haemorrhage, obstruction and less often perforation, particularly if the metastasis is located in the small bowel.

Complications from the gastrointestinal tract as primary manifestation of breast cancer are very rare. Usually the gastrointestinal manifestations present 4-5 years after the initial diagnosis and management of the primary disease. There have been reports of gastrointestinal manifestations as late as 13 years after the initial presentation.

Several authors describe acute appendicitis from metastatic breast cancer that obstructs the lumen of the appendix. The possibility of perforation in these cases is high and the mortality significant. For this reason it has been advocated that appendicectomy should be performed in women with breast cancer that undergo laparotomy for another reason (i.e. cholecystectomy, oophorectomy etc) [4,5].

If the large bowel is the site of metastasis the differential diagnosis includes diverticulitis, inflammatory bowel disease and ischaemic colitis [6].

If the primary breast disease is not known, the diagnosis is difficult and the metastatic abdominal tumor can be considered as primary adenocarcinoma of the stomach or the bowel [7,8]. The role of the pathologist is fundamental. Metastatic lobular breast carcinoma grows infiltrating the muscular layer of the gastrointestinal tract. The cells are arranged in a linear fashion that is described as “Indian file”. It takes the appearance of schirrous carcinoma in the large bowel and that of linitis plastica in the stomach which is considered as characteristic of the lobular carcinoma. The mucosa can be normal, making diagnosis difficult. In the large bowel the infiltration of the muscular layer produces a circumferential stenosis and obstruction of the lumen. The metastatic infiltration of the bowel can produce a situation similar to the primary schirrous carcinoma which is very rare. The absence of dysplastic features of the gastrointestinal epithelium and the characteristic architectural pattern are rather suggestive of a metastatic tumor than a primary one. The immunohistochemical study with positivity to appropriate markers such as keratin 7, ER and PgR in contrast to negativity to CEA and keratin 20 leads to correct diagnosis.

The management of the gastrointestinal and peritoneal metastases of breast cancer follows the guidelines for the primary disease. The response to hormonal therapy and/or chemotherapy varies between 30-80%. The best response is seen in metastases with positive hormone receptors and is the same for both lobular and ductal carcinomas.

Surgery is spared for acute complications such as obstruction and perforation.

Prognosis varies with a mean survival of one year. Survival is longer in patients with positive hormone receptors who respond to tamoxifen. Amongst all metastatic carcinomas of the gastrointestinal tract, this group of patients together with the patients with solitary metastasis of melanoma to the small bowel have the best prognosis.

In conclusion, gastrointestinal metastases of breast cancer are a rare occurrence. Even rarer they can be the first manifestation of an undiagnosed breast cancer, most often of the lobular type. Treatment follows the principles of management of primary breast cancer. Surgery is applied only for complications. The mean survival is one year. Prognosis is better for tumors with positive hormone receptors. A high degree of clinical suspicion and experienced pathologic investigation are necessary in order to establish the correct diagnosis.

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