Lobular breast carcinoma with colonic metastases: A synchronous diagnosis in a 4-day period

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ABSTRACT

Lobular breast carcinoma involving the colon is a rare condition. In most cases reported in the literature, metastases are detected after a 20-year latency period after the initial diagnosis. Here we describe a case in which metastatic lobular breast carcinoma and colonic metastasis were simultaneously diagnosed—with only 4 days between the two diagnoses. A 55-year-old woman underwent mammography and colonoscopy in the setting of the National Cancer Screening Program. A malignant nodule in the left breast was detected, and core-biopsy revealed an invasive lobular carcinoma. Simultaneously, numerous intestinal micropolyps were sampled. Histological examination of the latter showed tumor cells growing in cords and presenting signet-ring appearance, thereby confirming metastatic breast carcinoma. In cases such as the one described here, pathological diagnosis can be extremely difficult and deep biopsies are required. Metastatic breast cancer involving the colon can be considerably underestimated because of the unspecificity of the clinical manifestations, the long latency period, and diverse radiological findings that can lead to misdiagnosis. We conclude that clinicians should rule out intestinal metastasis in patients diagnosed with breast cancer, especially the lobular type, and presenting non-specific abdominal symptoms.

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1. Introduction

Breast cancer is the most common malignancy among women, with approximately 12% of all women developing this disease in their lifetimes (based on 2010–2012 data from the National Cancer Institute). Although the survival rate has increased considerably as a result of early detection and improved treatment guidelines, breast cancer continues to cause high morbidity and mortality. However, more than 30% of patients will develop metastatic disease even after treatment [1,2]. Classic ductal carcinoma of the breast usually metastasizes to the lung, liver, and brain. In contrast, lobular carcinoma (LC) of the breast, which accounts for between 10 and 15% of breast neoplasms, metastasizes more frequently in gynecological organs, peritoneum, retroperitoneum, and extraperitoneal gastrointestinal tract. Nevertheless, involvement of the latter is rare [3,4].

The diagnosis of LC metastasis to colon years after initial diagnosis has been widely reported. However, in only a few cases is the diagnosis of the involvement of the two sites simultaneous. Herein, we report an exceptional presentation of metastatic LC.

2. Case report

2.1. Clinical presentation

In the setting of the breast and colorectal National Cancer Screening Program, a 55-year-old woman was referred to our hospital because of detection of unilateral nipple retraction during self-examination and a positive fecal occult blood test. Past medical history was unremarkable, prior mammograms revealed no alterations, and no prior lower endoscopies had been performed.

The mammograms showed left nipple retraction and a distorted area measuring 68 × 65 mm, affecting the upper-external quadrant of the left breast (Fig. 1). A core biopsy of the lesion was performed, revealing an invasive classic-type lobular breast carcinoma (LC) (Fig. 2a). Immunohistochemical staining demonstrated that tumor cells showed staining for cytokeratins (CAM5.2, Ventana, Roche, Tucson, Arizona, USA) (Fig. 2b) as well as strong nuclear positivity for estrogen receptor...
immunohistochemistry was 0, and the Ki-67 proliferative index was around 1% (Ventana, Roche, Tucson, Arizona, USA).

Simultaneously, a colonoscopy was performed. We detected the presence of more than 100 plaque-shaped whitish micropolyps with a diameter between 1 and 2 mm along the right and left large intestine but not in the rectum (Fig. 3). Biopsies confirmed metastatic LC, consisting of a population of monomorphous and discohesive medium-sized cells with vacuolated cytoplasm, invading the lamina propria. Nuclei ranged from round to slightly irregular, with fine chromatin and inconspicuous nucleoli. Intracytoplasmic lumens were also observed (Fig. 4a–b). An immunohistochemical study was performed in order to make a differential diagnosis with other malignant tumors with a similar appearance, such as intestinal ‘signet ring carcinoma’, and also with other benign growths, such as intramucosal xanthomas. Tumoral cells showed strong cytoplasmic staining for cytokeratin AE1/AE3 (Diagnostic Biosystems, Palex Medical, Pleasanton, California, USA), and cytokeratin 7 (Ventana, Roche, Tucson, Arizona, USA). Nuclear ER immunostaining was positive (98%), although PR was detected in only a few scattered cells. E-cadherin staining was negative (Fig. 4c–d). Immunohistochemical expression was not detected for cytokeratin 20 or for CDX-2 (Ventana, Roche, Tucson, Arizona, USA), thereby ruling out an intestinal origin. Tumoral cells were also negative for histiocytic markers (CD68). The breast and colon pathological reports were only 4 days apart.

2.2. Follow-up

Breast magnetic resonance imaging (MRI) and a thoraco-abdominal computed tomography (CT) scan were performed one week later. The images pointed to the involvement of the ipsilateral axillary lymph
nodes and the presence of hepatic and peritoneal nodules. Fine-needle aspiration cytology and a liver biopsy confirmed that these structures had been compromised. The patient underwent treatment with paclitaxel-bevacizumab, achieving a partial response. However, this treatment was interrupted a year later because of gastrointestinal intolerance. She was then put on letrozole-bevacizumab. A cranial CT scan was performed 18 months post-diagnosis, revealing leptomeningeal progression, which required intrathecal administration of methotrexate. Subsequent CT scans of the brain, thorax, and abdomen were unremarkable, as were analytical parameters and serum tumor markers. These observations gave no evidence of malignant recurrence at the time of writing this report. The patient is now being treated with letrozole. She shows good tolerance and is subjected to routine monitoring.

3. Discussion

Breast cancer is one of the primary malignancies that most frequently spread to the extrahepatic gastrointestinal tract. However, in only a few cases breast carcinoma metastases to colon have been diagnosed simultaneously [2].

Washington et al. reported on the most common secondary tumors affecting the gastrointestinal tract in surgical specimens. According to their results, these were malignant melanoma, ovary, bladder, breast, and lung cancer, respectively [4]. The incidence of digestive system metastases from breast lobular carcinoma (LC) reported in autopsy studies varies from approximately 7% to 17%, [4–6].

The period of time between the diagnosis of LC and colon metastasis ranges from a synchronous diagnosis, as in the case we are presenting, to as long as 20–30 years, the latter being the most common presentation in most cases reported [2,7,8]. Stomach is the organ most affected by extrahepatic gastrointestinal metastasis, followed by the small bowel, colon, and rectum [9,10].

Clinical symptoms and signs of LC metastasis to the gastrointestinal tract are frequently non-specific, usually mimicking inflammatory
bowel disease, diverticulitis, or primary colon cancer [11–13]. Radiological and endoscopic features include mucosal nodularity and rigidity and thickening of intestinal wall, as well as lobulation and deformity caused by the presence of a mass [14]. The case that we present here is exceptional as the patient was asymptomatic and the endoscopy revealed multiple millimetric polyps mimicking a colonic polyposis.

Complicated cases with hemorrhage and/or stenotic lesions causing obstruction require palliative surgery.

Pathological diagnosis of metastatic breast LC to gastrointestinal tract can be quite difficult, especially when samples are superficial, reason why deep biopsies are needed in most cases [1,7,8]. Occasionally, a laparotomy may also be required to achieve histological confirmation. Metastatic LC has a typical pattern of invasion, with intramural infiltration throughout serosa, muscular propria and submucosa layers [1]. Tumor cells grow to form cords or small clusters and are medium-sized with monomorphic, round nuclei, inconspicuous nucleoli, and vacuolated cytoplasm. They commonly present a signet-ring appearance [2]. To distinguish the metastasis from a primary intestinal tumor, diagnosis is facilitated by the absence of dysplasia or nuclear atypia in the colonic epithelium and by the presence of infiltrating tumoral cells surrounding the preexistent glands. However, immunohistochemistry continues to be the best tool to achieve a precise diagnosis, especially in those cases with available information on the immunophenotype of the breast carcinoma (i.e. hormonal receptors and/or HER2 overexpression). Of note, metastatic LC can show isolated loss of ERs and PRs [15].

The incidence of metastatic LC may be underestimated because of the non-specificity of the clinical, endoscopic and radiologic manifestations, and also due to the long latency after initial diagnosis and patient death from metastatic disease [2,8]. Therefore, it is important to consider the contribution of metastatic breast neoplasm in women presenting abnormal radiological results involving the digestive system [12] and presenting microcytic anemia caused by fecal occult bleeding.

The case reported herein is exceptional due to the presentation of LC with a synchronous diagnosis of gastrointestinal metastases in an infrequent location, such as the colon.

4. Conclusions

LC metastasis to colon is a rare condition that can be extremely difficult to diagnose depending on the clinical manifestation. Given the increased survival rate with current therapeutic measures, more unusual disease presentations can occur. Hence, recognition of possible manifestations is meaningful and should be considered in order to achieve an accurate diagnosis and treatment.

Patients presenting vague abdominal symptoms and with a history of breast cancer, particularly the lobular type, should be subjected to an endoscopic examination in order to rule out metastases in this location, even in cases when the initial diagnosis of LC was decades earlier.

References