A rare case of primary rectal adenocarcinoma metastatic to the breast

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ABSTRACT

إنّ ظاهرة سرطان الغدّية المستقيمية الأولية المنتقل إلى الثدي حالة نادرة جدًّا، و تدبيرها يختلف عن تدبير سرطان الثدي الأولي كما هو يتّضح من هذه الحالة، و التي قُدِّمت فيها حالة امرأة تبلغ من العمر 63 عاماً و التي كانت في ثديها كتلة لمدة 30 شهرا بعد استئصال المستقيم البطني العجاني بسبب السرطان في المرحلة الثالثة $T_3N_1M_0$. وبعد استئصال المستقيم خضعت المريضة إلى دورة من العلاج الكيمياوي مع أوكزِ البلاتين و 5 فلورويوراسيل، ثمّ تمّ إجراء تصوير الثدي شعاعياً وعن طريق الموجات فوق الصونية والأشعة المقطعية للبطن والخزعة الاستئصالية للكتلة في الثدي. وكشفت الخزعة الاستئصالية للكتلة في الثدي عن ملامح شكلية مماثلة لسرطان المستقيم الأصلي. وكانت نتائج المناعة النسيجية الكيمياوية سلبية لمستقبلات الأستروجين والبروجسترون و GCDFP–15 و موجبة جداً لخلايا المادة القرنية CK–20 و CEA. وانتقال السرطانة الغدّية المستقيمية إلى الثدي علامة حصول الانتشار الانتقالي مع التوقعات السيّئة. وقد توفي المريض بعد العلاج الكيميائي الملطف. أن استئصال النقائل و العلاج الكيميائي هو الأسلوب الأكثر شيوعاً لعلاج هؤلاء المرضى.

Primary rectal adenocarcinoma metastatic to the breast is an exceedingly rare event. Its management differs from that of primary breast cancer, as illustrated by this case. A 63-year-old woman presented with a breast lump 30 months after abdominoperineal resection for rectal adenocarcinoma, stage $T_3N_1M_0$ (stage III), followed by standard postoperative radiochemotherapy. The patient underwent a mammography and ultrasonography. A CT scan of the abdomen showed metastatic disease. An excisional biopsy of the breast lump was performed; morphological features were identical to the original rectal cancer. Immunohistochemical results were negative for estrogen and progesterone receptors and gross cystic disease fluid protein-15, and intensity positive for cytokeratin 20 and carcinoembryonic antigen. The patient died after treatment with palliative chemotherapy. Metastatic disease from rectal carcinoma to the breast is a marker for disseminated metastatic spread with poor prognosis.

The vast majority of breast metastases from extramammary primaries originates from lymphoma, melanoma, and bronchial carcinoma. Metastases from gastrointestinal malignancies are much less frequent.[1,2] Cancer of the colon and rectum most commonly spreads to the lymph nodes, liver, lungs, and bones in that order. It is very rare for rectal cancer to metastasize to the breast. In the literature, this way of diffusion have been described in only a small number of cases.[2-5] Prognosis of this patients is poor because it is usually indicative of a disseminated disease. It is important to distinguish metastatic disease from primary breast carcinoma, in order to better plan the appropriate treatment.[2,3,5] We describe here a case of a woman presenting with aggressive rectal carcinoma metastasizing to the breast, 3 years after abdominoperineal resection. Given that the metastasis of rectal cancer in the breast is very rare, it is important to distinguish them from the primary breast cancer because their treatment is different.

Case Report. A 63-year-old woman, presented to the clinic with complaints of a breast mass that had

increased progressively in size since she discovered it incidentally 3 months earlier. She had no other breast symptoms, and her past medical history showed no risk factors for breast cancer. Thirty months earlier, she had undergone an abdominoperineal resection for rectal adenocarcinoma, stage $T_3N_1M_0$ (stage III). No distant metastasis was detected. After resection, the patient received standard post-operative radiochemotherapy (5-fluorouracil [5-FU] with leucovorin and oxaliplatin [FOLFOX]).

Physical examination revealed a hard, mobile mass in the upper outer quadrant of the right breast, roughly 3×2 cm in size, with no associated lymphadenopathy. Mammography showed a single mass lesion in the right breast without axillary lymphadenopathy (**Figure 1**). Ultrasound of both breasts was then performed, and demonstrated one ill-defined hypoechoic lesion in the right breast, corresponding to the soft-tissue lesions found on the mammogram. These measured up to 2.5 cm, and caused posterior acoustic shadowing.

Open excisional breast biopsy was performed after mammography and ultrasound examination. A histopathological study confirmed metastasis to the breast from a rectal adenocarcinoma. On direct comparison with slides of the previous rectal cancer, the cell morphology was identical to that of the primary rectal cancer (**Figures 2A-2C**). Immunohistochemical results were negative for estrogen and progesterone receptors and gross cystic disease fluid glucoprotein-15 (GCDFP-15), and intensity positive for cytokeratin
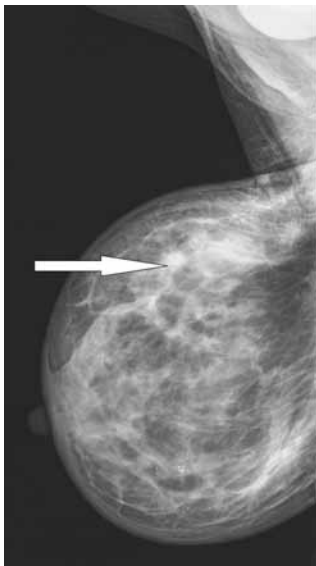

Figure 1 - A mammogram of the patient showing one mass in the upper outer quadrant of the right breast (arrow).
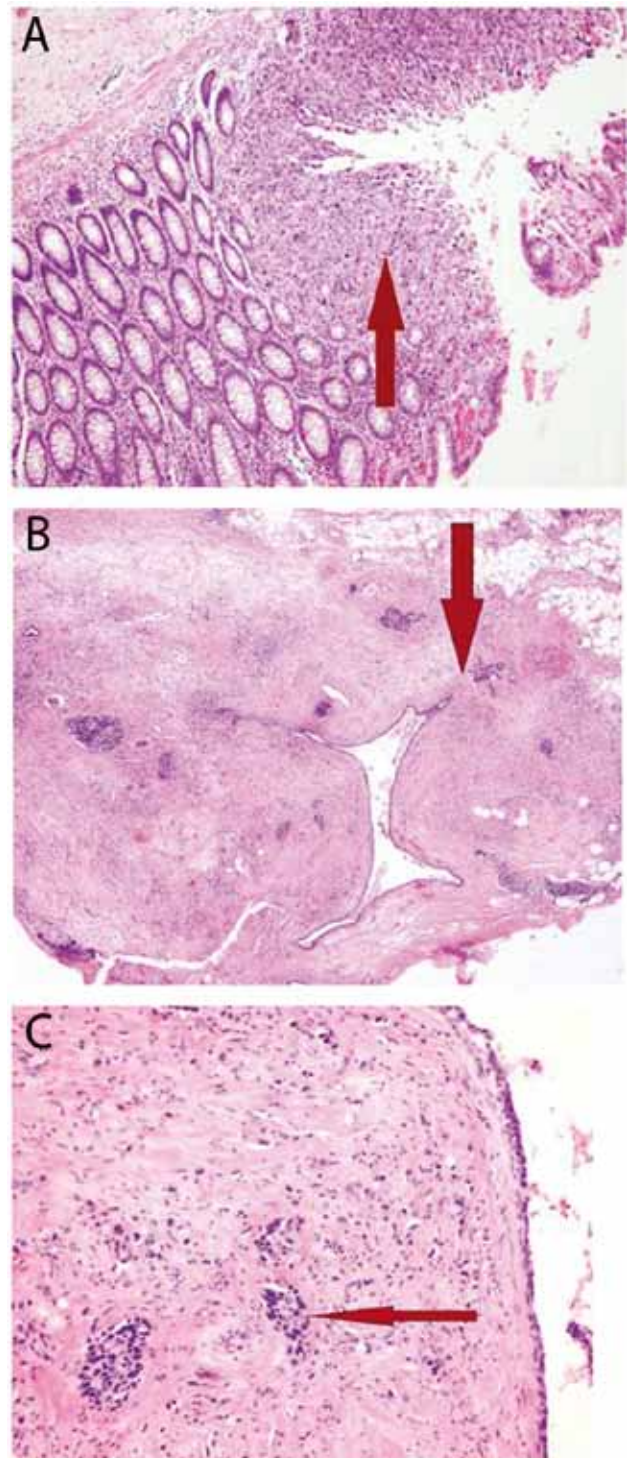

Figure 2 - A histopathological image of primary rectal cancer and its metastasis to the breast showing: **A)** Poor differentiated adenocarcinoma of the large intestine (H&E X10); **B)** Breast tissue with dilated duct in right side and nests of tumor cells in fibrous stroma (H&E X4); **C)** Nests and single tumor cells with pale eosinophilic vacuolated cytoplasm, pleomorphic nuclei and irregular nuclear membrane (H&E X20).
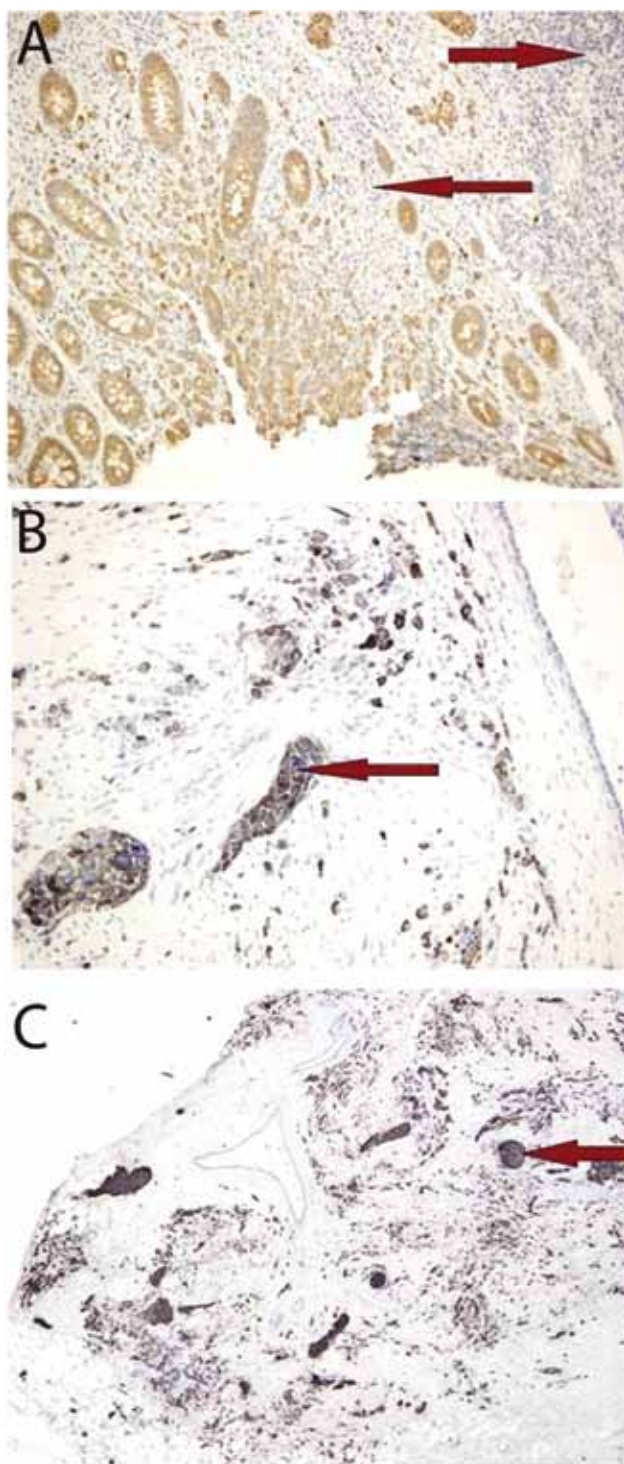
Figure 3 - Immunohistochemical staining for cytokeratin (CK)7, CK20 and carcinomebryonic antigen (CEA) showing: **A**) Intensive positive staining of tumor cells and normal intestinal gland in primary intestinal adenocarcinoma (CK 20x10); **B**) Intensive diffuse positive staining for CK20 in tumor cells in breast, and negative lining epithelium of duct (CK 20x20); **C**) Diffuse intensive positive staining for CEA in the tumor cells in breast, while the native duct epithelium is negative (CEA x4).

20 (CK20) and carcinomebryonic antigen (CEA) (**Figures 3A-3C**). In view of the rising CEA level, the patient underwent a CT of the abdomen, which showed dissemination of cancer with liver metastases and peritoneal carcinosis. The patient restarted on palliative chemotherapy. She deteriorated rapidly and died 4 months after presenting the breast mass.

Discussion. The most common site of metastasis of rectal cancer is the liver, followed by the lungs, and bone. Metastasis to sites other than the liver and lung are uncommon, and if they occur, it is usually in the setting of extensive liver and lung metastases.[1,4] Primary colorectal adenocarcinoma (CRC) metastatic to the breast is extremely rare, with the medical literature having very few cases.[5] Typically CRC metastatic to the breast is indicative of a widely disseminated disease, and a poor prognosis with less than a 20% one-year survival.[4,6]

The breast is an unusual site for metastasis deposits. The correct diagnosis is crucial in these patients. These metastatic lesions must be differentiated from primary breast tumors on the basis of history, clinical and radiological features, morphology of the tumor, and immunohistochemistry findings.[4,6,7] Most metastases present as palpable breast masses, occasionally adherent to the skin. There is a slightly left breast predominance, and the most common site is the upper outer quadrant. Only rarely are they multiple or bilateral lesions.[1,2,6,8]

Differential diagnosis between primary and metastatic breast neoplasms is not always easy. Mammograms can help in setting up a doubt for metastatic breast cancer.[5,6] The classic mammographic finding is a rounded, well-circumscribed mass. Typically, there is no speculation, microcalcification, or thickening of the skin.[2,6,9] Excisional or incisional biopsy are the most commonly used procedure for the differential diagnosis of metastases and primary tumors of the breast.[3,7] In some cases, immunohistochemistry can help to make an accurate diagnosis. Testing for expression of CK7 and CK20 is considered to be the most beneficial. The great majority of primary breast cancers are CK7-positive and CK20-negative, while colorectal carcinomas are usually CK7-negative and CK20-positive. Our patient's breast tumor was CK20-positive, and consistent with her previous colorectal cancer.[2,3,6,7]

Hypothetical rectal cancer can metastasize to the breast in different ways. First, the tumor spread via lymphatic vessels, and the ductus thoracikus, and body

circulation. Second, metastasis through the branches of blood vessels between the portal vein and the intercostal vein. Third, the spread of metastases through the inferior hemorrhoidal veins and vein hypogastrica.

Surgical treatment of secondary breast cancer is usually palliative. Metastasectomy is usually sufficient in the surgical treatment of these patients. Mastectomy has no significant role, because it usually works on patients with rectal cancer dissemination to other organs. Systemic chemotherapy is necessary in these patients. Metastasectomy with effective systemic chemotherapy can prolong survival of these patients.[1,2,5-9]

In conclusion, primary rectal cancer metastatic to the breast is very rare. The real incidence is difficult to estimate and is probably much higher. Metastasis to the breast usually indicates disseminated disease, and the prognosis is poor. Radiologic studies of the breast may be misleading, but immunohistochemistry can help to make an accurate diagnosis. Metastasectomy is usually appropriate and provides adequate local control.

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