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REVIEW ARTICLE

BREAST METASTASES FROM COLORECTAL CANCER: CASE REPORT AND REVIEW OF LITERATURE

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ABSTRACT

Colorectal cancer most commonly metastasizes to the liver, lung and distant lymph nodes. Breast metastases are extremely rare and account for 0.5-6% of all breast malignancies. The most common cancers that metastasize to the breast are the contralateral breast tumor followed by metastasis from hematological malignancies, malignant melanoma, sarcoma, lung, prostate, ovary, kidney, stomach and carcinoid. Despite its rarity, when present, they are associated with a poor prognosis due to disease dissemination. Metastatic disease to the breast is an important diagnostic issue because its treatment differs greatly from that of primary cancer. The median overall survival is estimated to be less than one year after diagnosis of breast metastases. In some cases a palliative excision can be considered just for local control if is present pain, ulceration or in case of response to treatment and unique disease site. So it is important to differentiate breast metastases from primary breast carcinoma to avoid unnecessary surgical treatment.

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INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer in men and the second among women. Regional lymph nodes metastases are found, at diagnosis, in around 40 and 70% of patients. Typically, the most common sites of metastases are liver, lung and distant lymph nodes. Breast metastases (BM) are very rare and in literature, there are less than 20 cases (Shackelford, 2011). The tumors that more frequently metastatize to the breast are malignant melanoma, lymphoma, lung, gastric and contralateral breast cancer. The prognosis is poor due to the dissemination of the disease (Del Prete, 2009). Because of their rarity, BM are often confused with a primary breast cancer (Cabibi, 2011).

Case Presentation

In February 2015 a 53 years old woman presented to our Oncology Unit with severe recurrent lower abdominal pain associated with nausea. Computerized tomography (CT) scan showed multiple liver lesions and a descending colon heteroplasia.

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Patient underwent total laparotomy colectomy plus locoregional lymphadenectomy and the histopathological report confirmed a poorly differentiated adenocarcinoma. The stage of tumor was pT3pN0M1, G3. Three months after surgery, a breast ultrasonography showed a 20 mm sized nodule in the lower outer quadrant (LOQ) of the right breast and solid mass of 45mm in contralateral axilla (confirmed by mammography); subsequent 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET)/CT confirmed a solid mass of 40x48mm in left axilla (Fig. 1a) with 12.3 SUV (Fig. 1b) and a nodule of 26x17mm in the LOQ of right breast (Fig. 2a) with SUV 10.3 (Fig. 2b). Ultrasonography guided core needle biopsy of the right breast and left axilla showed a morphologically invasive ductal carcinoma. The immunohistochemical (IHC) analysis was performed with the streptavidin – biotin – peroxidase complex method after appropriate antigen retrieval. In IHC (Fig. 3a), estrogen receptor (ER), progesterone receptor (PgR), HER2, CK7 and GATA-3 overexpression were negative. Therefore, based on the positive history of recent colorectal cancer diagnosis, an additional IHC exams was performed showing positive for CK20 (Fig. 3b) and CDX2 (Fig. 3c), compatible with colic origin of tumor tissue. The molecular assessment of the primary CRC and breast metastases (BM) showed a wild-type RAS (KRAS and NRAS) status. She started in May 2015 a chemotherapy regimen with 5-fluorouracil, oxaliplatin

Fig. 1a.

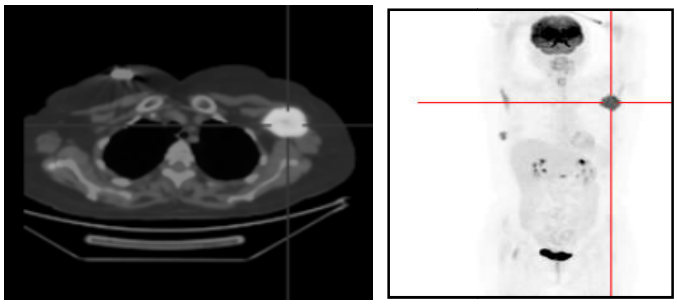

Fig. 1b.

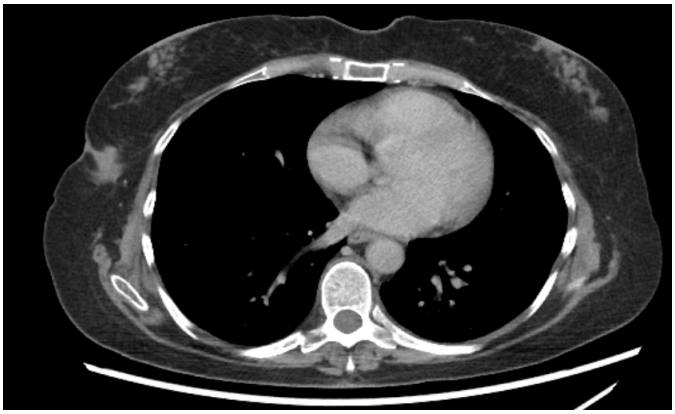

Fig. 2a.

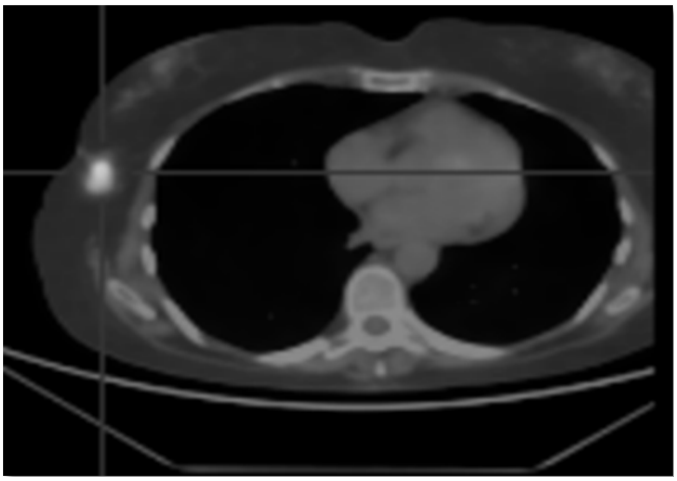

Fig. 2b.

(FOLFOX-4) plus cetuximab at standard dose for 8 cycles, with a stable disease (SD) as best response (RECIST 1.1 criteria). In September 2015 a CT scan showed a disease progression (PD) in breast and liver sites, so she started a new chemotherapy regimen with 5-fluorouracil, irinotecan (FOLFIRI) plus aflibercept for eight cycles, then for further disease progression she started in July 2016 treatment with REGORAFENIB, still ongoing to date.

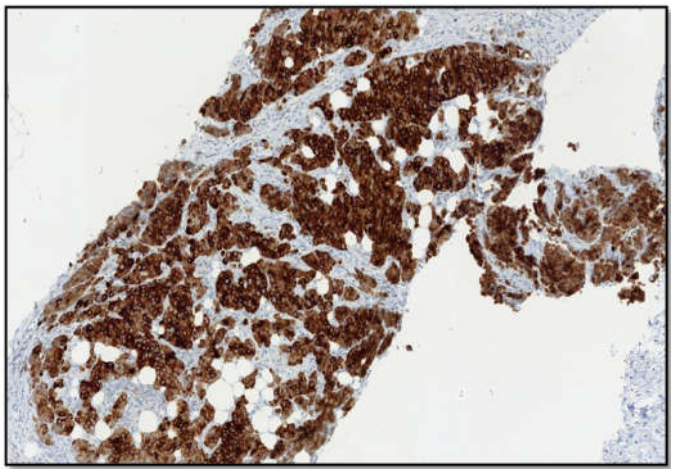

Fig. 3a.

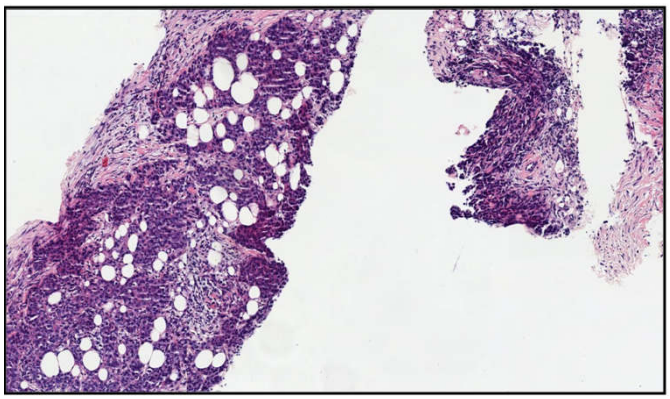

Fig. 3b.

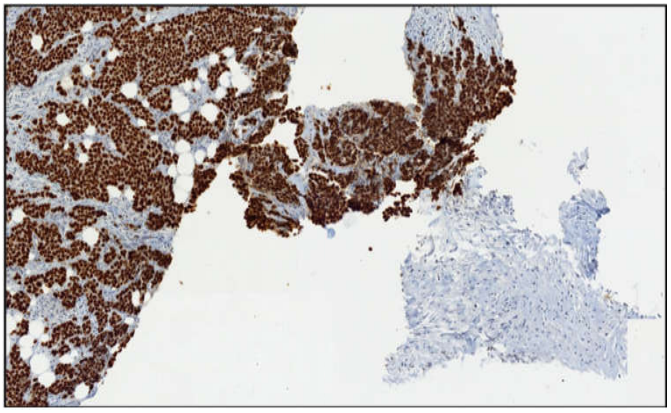

Fig. 3c.

DISCUSSION

McIntosh described the first case of breast metastases from colon cancer (CRC) in 1974 (McIntosh, 1676). The most common cancers that metastasize to the breast are the contralateral breast tumor followed by metastases from hematological malignancies, malignant melanoma, sarcoma, lung, prostate, ovary, kidney, stomach and carcinoid (Kinkor, 2010; Zhou, 2014; Georgiannos, 2001; Kothadia, 2015; Siegel, 2014; Ahmad, 2014 and Sanchez, 2008). The detection of breast metastases is extremely rare, about 0,43% of all malignancies of the breast (Georgiannos, 2001). On average

breast metastases occur approximately 21 months after the diagnosis of metastatic colorectal cancer (mCRC), in a range from 0 to 7 years, with only 15% of cases in which the breast metastases represent the first site of disease or it is synchronous with the initial diagnosis of mCRC (Shackelford, 2011). The median age of breast metastases is 54 years old and they are more common in women than in men (Georgiannos, 2001). As for the primary breast tumor, the axillary lymph nodes are often involved (Zhou, 2014). Mammography can be useful for a differential diagnosis with a primary tumor of the breast. In fact breast metastases appear radiologically as circular lesions, well-circumscribed without spicules or micro calcifications or skin involvement (Kothadia, 2015; Vakili, 2014 and Wood, 2008). The upper-outer quadrant (UOQ) is more frequently affected (Shackelford, 2011; Lee, 2007; de Bobadilla, 2004), with a predominance of the left site (Shackelford, 2011; de Bobadilla, 2004; Chaignaud, 1994). The majority of metastases are clinically described rapidly growing, determining histologically loss of elastosis (Sanchez, 2008), generally palpable masses, occasionally adhering to the skin confirmed by the presence of the tumor in subcutaneous tissues (Georgiannos, 2001; and Vergier, 1991), and rarely multiple or bilateral (Chaignaud, 1994), as in this case report. The diagnostic test is the breast biopsy (Vakili, 2014). Typically primary breast cancer is positive for CK7, ER, CK19, GCDP15 and Mammoglobin, while breast metastases from CRC are positive for CK20 and CDX2 and CEA, which are biomarkers indicative of a primary cancer of the colon (Shackelford, 2011; Kinkor, 2010; Chinyama, 1996 and Lagendijk, 1999). The prognosis of these patients is poor with median overall survival less than one year (Kinkor, 2010 and Zhou, 2014), due the dissemination of the disease and its chemoresistance. Probably the presence of breast metastases identifie a different subtype of CRC, more aggressive and with several molecular alterations, such as B-RAF mutation, shown in our patient too, which increase its resistance to chemotherapy. Local excision should be avoided in consideration of the low life expectancy (Lagendijk, 1999), and the risk of skin dissemination (Barthelmes, 2010). In some cases a palliative excision can be considered just for local control if is present pain, ulceration or in case of response to treatment and unique disease site (de Bobadilla, 2004).

Conclusion

Breast metastases from CRC have a rapid growth, respond poorly to chemotherapy or radiation therapy and have a poor prognosis. It is important to differentiate a metastatic breast lesion from CRC that requires a systemic treatment (chemotherapy), from a primary breast cancer, which need surgery with or without adjuvant chemotherapy.

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