CLINCAL CASE

CUTANEOUS METASTASES UNVEILING BREST CANCER – THERAPEUTIC AND DIAGNOSTIC CONSIDERATIONS

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Abstract

Metastatic cutaneous lesions are seen more commonly in breast cancer than in any other malignancy in women. Secondary breast cancer happens when cancer cells spread from the breast to other parts of the body. Sometimes breast cancer cells can spread to the skin. This can happen through the blood or lymphatic system. The presence of skin metastases signifies widespread systemic disease and a poor prognosis. The chest wall, the abdomen, the back, and the upper extremities are common sites. We present the case of a 69-year-old woman presented to our Dermatology Department in June 2019, for the appearance of multiple subcutaneous painless, hardened, skin-colored nodules spread to the cervical region, anterior chest walls and upper limbs. Anatomopathological examination of the skin biopsy, performed on the anterior face of the left arm, showed dermal fragment with neoplastic, suggestive for lobular breast carcinoma (stage IV). The patient was referred to the oncological surgery department where our patient underwent a left total mastectomy and sentinel lymph node biopsy. The technique of mastectomy was the Madden technique. The surgery has no healing character, being more a necessity intervention that seeks to avoid the complications of the local evolution of the disease, such as ulceration, hemorrhage or suppuration, the possibility of applying the other forms of treatment (radiotherapy and / or polychemotherapy), elimination of a source of permanent metastatic sowing thus leading to more efficient treatment.

Keywords: cutaneous metastases, breast cancer, Madden technique, total mastectomy, sentinel lymph node biopsy

Introduction

Metastasis is defined as a neoplastic lesion originating from another primary tumor, with which it is no longer in contact. Cutaneous metastases occur in 0.7 to 10.4% of all patients that are diagnosed with cancer, although they represent only 2% of all types of skin tumors [1]. The cutaneous metastases can represent the first sign of a clinically silent neoplasm or they can even an indication of tumoral relapse [2].

Metastatic cutaneous lesions are seen more commonly in breast cancer than in any other malignancy in women, exceeding 20% of all cutaneous metastases [3]. About a fifth of people with secondary breast cancer will develop skin metastases. Secondary breast cancer happens when cancer cells spread from the breast to other parts of the body. Sometimes breast cancer cells

can spread to the skin. This can happen through the blood or lymphatic system. The presence of skin metastases signifies widespread systemic disease and a poor prognosis [4]. Patients present with a variety of symptoms ranging from nonpainful, single or multiple, firm, hard, indurated skin to tiny seed-like solid papules and large eggsized lesions, with sometimes an edema of the skin of the breast, known as the orange peel sign, without any specific clinical diagnostic criteria. The chest wall, the abdomen, the back, and the upper extremities are common sites, but the most common sites affected are the areas near where the original breast cancer was – for example the skin of the chest wall or around the surgical scar. Less commonly, skin metastases can occur on other areas of skin, such as on the scalp, neck, and upper limbs [5].

Case presentation

We present the case of a 69-year-old woman from the urban area, with grade II HTA, non-smoking, presented to our Dermatology Department in June 2019, for the appearance of multiple subcutaneous painless, hardened, skincolored nodules spread to the cervical region, anterior chest walls and upper limbs, 6 months prior to the consultation, associated to persistent dry cough and loss of 4 kg in this period. Our patient was postmenopausal and had given birth to two children whom she had breastfed for 6 months each. From hereditary background, we noted the colon cancer of the father.

On dermatologic examination the patient presented asymptomatic irregularly distributed subcutaneous skin-colored nodules of various sizes (measuring 2-3 cm in average) with a large indurated skin on. Dermatoscopic firm, examination of the nodules revealed a pinkorange background, yellow central areas, linear irregular and polymorphic vessels, whitish bright lines, whitish structureless areas, and linear irregular fissure-like depressions was confirmed with skin biopsies, and the patients were referred oncology department for to the further investigations and appropriate management.

Anatomopathological examination of the skin biopsy, performed on the anterior face of the left arm, showed dermal fragment with neoplastic proliferation developed at the level of the reticular dermis, composed of cells of smallmedium size with pale eosinophilic cytoplasm and minimal nuclear atypia, with interstitial arrangement in the form of an Indian strand between the dermal fibers of collagen. The lesion is a highly metastatic skin metastasis suggestive of lobular breast carcinoma. Results were consistent with moderately differentiated adenocarcinoma and the sample was sent for immunohistochemical examination. Immunohistochemistry positive was for cytokeratin 7, carcinoembryonic antigen (CEA), estrogen receptor (ER) and GCDFP-15; and negative for cytokeratin 20, thyroid-lung transcription (TTF-1), intestinal factor transcription factor (CDX2), S100 protein and mammaglobin, indicating the breast as the primary site of neoplasm.

Laboratory exams evidenced leukocytosis, severe anemia with Hb = 6.2 g / dl, severe thrombocytopenia, severe hepatic cytolysis syndrome, hyposodemia, LDH = 1363 U / L, the urine summary showed a high density with significant proteinuria and hematuria.



Figure 1 – Macroscopic image of the skin metastases. Multiple subcutaneous hardened, skin-colored nodules spread to the cervical region, anterior chest walls and upper limbs



Figure 2 – Dermatoscopic image of the skin metastases. Linear, irregular, arborizing and polymorphic vessels (*blue circle*), structureless yellow or yellow-orange areas (*red star*), white lines (*orange arrow*), white structureless areas or around yellow structures (*violet star*), linear skin depressions as fissure-like structures (*green arrow*), and pink structureless areas (*blue arrow*)



Figure 3 – Histopathological image of the skin metastases

Computerized tomography (CT scan) of head, chest, abdomen and pelvis did not reveal secondary determinations in the brain or liver. In contrast, a nonspecific pulmonary micronodule was located in the posterior segment of the right upper lobe, with fluid at the level of moderate bilateral pleura. At the level of the superoexternal quadrant of the left breast, an iodophilic area was compared with the rest of the breast glandular tissue. Also, diffuse densification in the bands with the micronodule and iodophilic nodules of the subcutaneous soft tissues and macronodular iodophilic lesion located in the subcutaneous fatty tissue of the right scapular region were highlighted. The left breast ultrasound showed an imprecisely delimited formation, with an infiltrating character with a large posterior attenuation, intensely vascularized peritumoral, located in the superoexternal quadrant, and adenopathic blocks with a left axillary tumor aspect.

The patient was referred to the oncological surgery department where our patient underwent a left total mastectomy and sentinel lymph node biopsy. The technique of mastectomy was the Madden technique under total anesthesia, with Stwart-Olivier type incision. Four sentinel nodes were retrieved using both the blue dye and the radioisotope methods. The surgical margins were free of tumor, and the four sentinel lymph nodes were negative. Our patient was diagnosed with invasive lobular breast cancer (stage IV), and was referred to the oncology department for further investigations and appropriate subsequently management. She received adjuvant chemotherapy with four cycles of cisplatin 80 mg/m2 on day 1 and etoposide 100 mg/m2 for 3 days, followed by four cycles of 5fluorouracil (5FU) 500 mg/m2, epirubicin 75 mg/m2, and cyclophosphamide 500 mg/m2 (FEC). Our patient has received adjuvant hormonal treatment with tamoxifen for 3 months so far. She is on regular follow-up in the cancer center.

Discussions

of cutaneous metastatic Assessment disease can be perplexing because the clinical presentation appears similar to other skin diseases such as cellulitis or lymphedema [6]. Although dermoscopy may provide a useful method for the differentiation between the diagnosis of metastasis to the skin and nonneoplastic dermatological diseases or other malignancies, the dermoscopic patterns of breast cancer metastases have not been well described [7]. To date, only a limited number of dermoscopic images of cutaneous metastatic solid tumors, especially breast cancer, have been published. Skin metastases are secondary breast cancers that form on or just below the skin [8].

Usually, when the skin is affected by metastases, other organs have already been

involved marking the former as a sign of poor prognosis [9]. Generally, their color is similar to that of normal adjacent skin and they are asymptomatic. On occasion, lesions may erode and ulcerate secondary to the tumoral mass pressure on cutaneous surface. The anterior thoracic wall is the area most affected by cutaneous metastases secondary to breast cancer, as described in this report. Other clinical presentations include erysipeloid infiltration, sclerodermiform, inflammatory carcinoma, en cuirasse, telangiectatic, neoplastic alopecia and palpebral nodules. Cutaneous metastases result from lymphatic embolization, hematogenous or contiguous dissemination or also direct implantation during surgical procedures [9,10]. Breast carcinoma is the second most common cancer in women and the most common tumor leading to the appearance of skin metastasis [11]. In the largest case series already published, cutaneous involvement was observed in 23.9% of all patients [12].

Sometimes the symptoms of skin metastases, such as redness and inflammation, may look like an infection of the skin called cellulitis. Skin metastases can also cause lymphoedema, which is swelling of the arm, hand or breast area. Other possible symptoms include: pain, bleeding, infection, odor (smell) [13].

The age range with the highest incidence of cutaneous metastases is that between 50 years old and 70 years old. In patients with primary breast cancer, cutaneous metastases usually appear later than metastases in other organs [14], but in our case, the metastases revealed the existence of a primary breast tumor.

Usually, the histologic features of the metastases are similar to the primary tumor, although metastases may be more anaplastic and exhibit less differentiation. Cutaneous metastases are one of the most distressing presentations of breast cancer [15].

Besides cutaneous metastases, our patient's lung was also affected by metastases. The lung is often the first site metastases from a breast cancer. The most frequently seen pattern is that of pleural metastasis, follow by hilar and mediastinal lesions and pulmonary nodules, as observed in this case. It is estimated that 60-74% of patients that die of breast cancer, had also pulmonary metastases, with the lung as the sole site of metastases in 21% of cases [16].

While surgical resection and radiation therapy offer local control, treatment with antineoplastic therapy controls systemic disease. In stage V of breast neoplasm, as is the case discussed, the surgery has no healing character, being more a necessity intervention that seeks to avoid the complications of the local evolution of the disease, such as ulceration, hemorrhage or suppuration, the possibility of applying the other forms of treatment (radiotherapy and / or polychemotherapy), elimination of a source of permanent metastatic sowing thus leading to more efficient treatment. The operation Madden, the technique chosen in our patient's case, respects the principles of oncological surgery, because it aims to block the organ-headquarters of the neoplasm, the regional cell-lymph-fat tissue that may be interested, and the central lymph node, tributary (axillary lymph nodes) [17].

Conclusion

The skin does not appear to be a preferred target organ for the development of metastases. Usually, when the skin is affected by metastases is a sign of poor prognosis. Cutaneous metastases arising from breast cancer may present varied morphology. The most common presentation is in the form of nodules. These nodules vary in size from 1 to 3 cm and appear as hardened lesions, either single or multiple, located on dermis and subcutaneous tissue, as observed on the patient in question.

A biopsy of the skin helps in confirming a diagnosis of tumor. The pattern noted and the microscopic appearance often suggests the likely tissue of origin. Generally, the histologic features of the metastases are similar to the primary tumor. Effective treatment depends on treatment of the underlying tumor. In our case, the surgery no healing character and the has total mastectomy was chosen to avoid the complications of the local evolution of the disease and for the possibility of applying the other forms of treatment.

Cutaneous metastases can be the first clinical manifestation of an unknown intern malignant tumor or the first sign of metastasis

from a seemingly treated cancer, but in both cases, the appearance of these lesions indicates generalized metastatic disease, that came with a poor prognosis. Patients often survive for a short period of time, depending on the type of carcinoma. Therefore, although rare in dermatologists' clinical practice, cutaneous metastases are clinically important, because their immediate detection may contribute to reduce associated morbidities and mortality.

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