Matrix-Producing Carcinoma of the Breast: A Case Report

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Key Words

Breast · Metaplastic carcinoma · Monoclonal origin · Mammotome

Abstract

Matrix-producing breast cancer (MPC) is a subtype of metaplastic carcinoma of the breast. It is a very rare tumor, which constitutes less than 1% of all malignant mammary tumors. The origin of this tumor is still unclear: there are molecular studies that suggest an origin from myoepithelial cells, whereas other studies underline the neoplastic transformation of a multipotent stem cell. Even the differential diagnosis of MPC and other breast neoplasms (phyllodes tumors and real sarcomas of the breast) is not always easy. In the literature, a certain chemoresistance has been demonstrated, and a standard treatment of this tumor does not exist at this time. We report the case of a 44-year-old, premenopausal, female patient with a 6-cm breast lump. Neither imaging nor fine needle aspiration biopsy was crucial in achieving a diagnosis. The patient underwent a simple mastectomy. In consideration of the negative lymph node status, the patient was not subjected to radiotherapy or adjuvant chemotherapy. Moreover, since the receptor status was negative, hormone therapy was not necessary. The patient has been disease free for 4 years now.

Introduction

The medical literature [1] considers metaplastic carcinoma of the breast to be a rare neoplasia, constituting less than 1% of all breast cancers, with a poor prognosis and a high incidence of recurrence. Matrix-producing metaplastic carcinoma of the breast (MPC) is characterized by nonaggressive behavior and occurs more frequently in older age (postmenopausal, i.e. age 60 years), as a large, painless, palpable mass.

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Metaplastic carcinoma of the breast can be split up into several different subgroups based on histology, biology and prognosis. The MPC subgroup is characterized by ductal and mesenchymal elements, such as bone, cartilage, fibrous tissue and smooth muscle or striatum, immersed in an abundant extracellular matrix. Infiltration of lymph nodes is less common than in nonmetaplastic histotypes, and the expression of hormone receptors is often negative. The role of radiotherapy and chemotherapy is not yet fully understood, and, often, surgical treatment is the only choice.

Case Report

We present the case of a 44-year-old premenopausal woman, without a family history of breast cancer and no significant medical history, who was referred to our Tumor Prevention Center after detection by self-palpation of a mass in the upper inner quadrant of the left breast, with a maximum diameter of about 6 cm. Consistency of the mass was only slightly increased, and there was no skin or nipple retraction or adhesion to the skin. Moreover, clinical examination did not reveal axillary lymphadenopathy. On mammography, there was a radiopaque lump, with a maximum diameter of 5.5 cm. There were no calcifications inside and no well-defined regular margins. It was classified as BI-RADS category 4.

On ultrasound (fig. 1, fig. 2), the lesion appeared as a nodular formation, oval, hypoechoic and inhomogeneous due to the presence of numerous anechoic internal areas, without ultrasonic attenuation. The lump had a maximum diameter of 5.5 × 5 cm, occupying almost the entire gland. Near the lump, another hypoechoic nodule (max. diameter 2 × 2 cm) with multilobulated margins was observed. Results of a fine needle aspiration biopsy (FNAB) stained with Papanicolaou staining showed amorphous material and a bloody background with some foam cells (cytology reporting category C1). Next, a core needle biopsy was performed with a mammotome and an 11-gauge probe; histological examinations carried out on the sample showed necrotic material and, in a few fragments, vital tissue with proliferation of cellular elements with chondroid structures, immersed in a variously differentiated chondroid matrix. The cells showed noticeable pleomorphism and frequent atypical figures. These findings led to the diagnosis of chondrosarcoma, and histological confirmation was postponed until the excisional biopsy.

The patient underwent surgery for a simple mastectomy with removal of skin and the nipple as well as axillary lymph node dissection. The extemporaneous histological examination showed macroscopically a 10 × 7-cm lesion with well-demarcated boundaries; it was whitish, with a hard consistency and had foci of cystic and hemorrhagic degeneration. Histologically, the lesion appeared as a proliferative process of mesenchyme, with spindle-shaped and chondroid cells but without an epithelial component. The sentinel lymph node appeared normal. The definitive histological examination confirmed the presence of a malignant tumor with high mitotic activity and marked polymorphism.

In histological sections, the following characteristics could be seen: several round and spindle-shaped cells, densely thronged, sometimes in sarcomatoid organization; a myxoid matrix containing medium to large cells with large and hyperchromatic cell nuclei, vacuolated cytoplasm, and an overall chondroid appearance; aggregates of giant multinucleated osteoclastic cells. The diagnosis of metaplastic carcinoma with squamous metaplasia, containing spindle-cell, chondroid (matrix-producing carcinoma) and osteoclastic components, was confirmed. Immunohistochemical analysis confirmed the origin of the histologically metaplastic breast lesion and its epithelial nature. Cytokeratins and S-100 protein showed immunopositivity; estrogen was also weakly immunopositive (<10%). The

neoplastic cells were negative for progesterone and HER-2; Ki-67 was 70%. The margins of resection, the skin and the nipple were not infiltrated. The sentinel node was negative. The staging was pT3 pN0 PMX, G3.

At present, there are few data on the best pharmacological treatment of this type of malignancy. In particular, the most recent data mostly show a certain chemoresistance [2]. In accordance with the negative lymph node status and the radical surgical treatment, the patient did not undergo radiotherapy or adjuvant chemotherapy.

To date, the patient is alive and in good health.

Discussion

MPC is a very uncommon type of breast cancer, with a frequency of less than 1% of all mammary gland cancers. The fundamental histopathological phenomenon in this subgroup of tumors is the epithelium-mesenchyme transition; histologically, MPC is characterized by the presence of ductal epithelial cell carcinoma with areas of cartilage and bone differentiation, either immersed in an abundant chondroid matrix or frankly osteoid, composed of acid mucopolysaccharides [3]. The observations made by electron microscopy and immunohistochemical study indicate the myoepithelial origin of MPC. In the literature, in most cases, the cancer cells are positive for vimentin, S-100 protein and cytokeratins (AE1/AE3, CK7, CK8 and CK19), whereas they are negative for α -SMA, p63, CK5/6 and GFAP [4]. However, to date, the cellular origin of MPC is not yet clear, but some studies suggest a neoplastic transformation of a totipotent stem cell.

In about half of the cases, diagnosis is not possible by means of FNAB [5] due to the wide variety of tumor presentation; in most cases, optical microscope observations showed plenty of extracellular matrix in which chondroid and epithelial cells with different degrees of atypia were immersed. The Papanicolaou staining in these cases is less appropriate than the indicated Giemsa staining. In addition, cytological examination is often not able to differentiate between MPC and true sarcoma of the breast with cartilaginous metaplasia or phyllodes tumors. A differential diagnosis is not easy from the imaging perspective, and physicians often have to resort to more invasive techniques such as core needle biopsy, which provides tissue for histological examination. In our case, the imaging modalities showed a patchy nodule with colliquative areas; however, based on morphology it was impossible to make a differential diagnosis. Even the FNAB with Papanicolaou staining was not decisive and further testing with a core needle biopsy was required. Histological examination of the excised tissue was unable distinguish between true chondrosarcoma of the breast and MPC in order to yield a differential diagnosis.

A simple mastectomy was performed on this patient, with removal of skin and the nipple as well as axillary lymph node dissection. Only the histological examination of the surgical specimen made it possible to make a diagnosis of MPC. The overall picture confirmed the diagnosis of metaplastic carcinoma with squamous metaplasia, containing spindle-cell, chondroid (matrix-producing carcinoma) and osteoclastic components. Immunohistochemical analysis confirmed the origin of the histologically metaplastic breast lesion and its epithelial nature. Cytokeratins and S-100 protein showed immunopositivity; estrogen was also weakly immunopositive (<10%). Progesterone and HER-2 were immunonegative; Ki-67 was 70%. The margins of resection, the skin and the nipple were not infiltrated.

MPC rarely metastasizes via the lymphatic system, preferring to metastasize via the blood. The sentinel node in our patient was disease free. In view of the surgical treatment

and negative nodal status, adjuvant radiotherapy was not considered. Radical surgery offers patients an average 5-year survival rate of 70% compared to 50% offered by local surgery [6].

Due to intratumoral heterogeneity, metaplastic carcinomas of the breast are chemo-resistant. In addition, many tumors in this subgroup are hormone receptor negative on immunohistochemical examination, thus making hormone therapy unnecessary. The data in the literature are few and inconsistent, and there is no standard treatment for this subgroup of breast cancer. Recent clinical trials have shown targeted gene therapy plays a role following genetic profiling.

Considering the receptor status of our patient and the chemoresistance reported in the literature, adjuvant chemotherapy was not proposed. Oncological radicality could only be guaranteed by radical surgery, with good disease-free survival results.

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Fig. 1. The lesion appears as an oval, hypoechoic and inhomogeneous lump (max. diameter 5.5 × 5 cm) due to the presence of numerous anechoic internal areas without ultrasonic attenuation.

Fig. 2. Near the lump we observed another hypoechoic nodule (max. diameter 2×2 cm) with multilobulated margins.