Introduction

Primary squamous cell carcinoma of the breast is a rare tumor which accounts for less than 1% of all invasive breast carcinomas. About 80 cases have been described in literature, affecting patients aged between 20 and 90 years (mean age: 53) (1). This tumor may appear as a palpable breast lump, that is sometimes bigger than 5 cm and may resemble a breast abscess (2). Upon X-ray investigation, it does not show the features of malignancy; lumps are normally regular, with well-defined margins and often without microcalcifications. The histological diagnosis of a primary squamous cell carcinoma of the breast must rule out a carcinoma deriving either from the overlying skin, the nipple or from distant metastases (3-6). Primary squamous cell carcinoma of the breast consists only of squamous cells that may be keratinizing or non-keratinizing, with a spindle and acantholytic aspect. These histological aspects may be concomitant or prevalent. The absence of elements mixed with ductal cancer is extremely important for the histological definition. As to the histogenesis, most authors claim that primary squamous cell carcinoma derives from epithelial or myoepithelial cells of glandular ducts with squamous metaplasia, generally as a consequence of inflammation. The tumor size is very important for prognosis, as it spreads to the axillary lymph nodes only in 10-15% of cases. The therapeutic approach is complicated by negative estrogen and progesterone receptors, as well as by HER2/neu negativity (triple negative breast cancer). A unanimous agreement among oncologists on standardized treatment of this carcinoma variant has not yet been reached (7, 8).

Primitive squamous cell carcinoma of the breast (SCCB): case report of an uncommon variant of metaplastic carcinoma

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SUMMARY: Primitive squamous cell carcinoma of the breast (SCCB): case report of an uncommon variant of metaplastic carcinoma.

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Introduction. Metaplastic carcinoma of the breast includes a heterogeneous group of neoplasms characterized by admixture of adenocarcinoma with areas of squamous, chondroid and osseous differentiation. If the tumor shows pure squamous differentiation, it is designated as squamous carcinoma. SCCB accounts for less than 1% of all invasive breast carcinoma. It can present as cystic lesions and simulate a breast abscess.

Case report. A 75-year old woman was visited at our General Surgery Unit for a palpable lump, about 5 cm in size, at the lower inner quadrant of right breast. Mammography revealed 3 cm oval opacity with micro calcifications and US appearance as isoechogenic lump with lesion solid-cystic appearance; cytology deposes for cystic inflammatory lesion (C2) to be monitored. A subsequent ultrasound check one year latter confirmed an increase of volume, so micro histology sampling was made with suspect malignancy (B4). After biopsy, the patient underwent excision of cyst. Final histological examination showed SCCB with diffuse positivity for Cytokeratin 34beta-E12 and p63; negative reactions to ER and PR; monoclonal antibody Ki67 > 40%; HER2/neu with score 2+ and FISH examination negative. Subsequently, the patient underwent radical Madden mastectomy which confirmed the histological diagnosis and the negativity of the lymph nodes.

Discussion. In literature, prognosis and therapy are still discussed; SCCB has shown very little responsiveness to common chemotherapy.

Conclusion. A quadrantectomy or a radical mastectomy with lymph node dissection must be considered the best treatment for this rare neoplasia.

KEY WORDS: Breast abscess - Breast primary squamous cell carcinoma.
Case report

A 75-year-old woman was visited at our General Surgery Unit for a palpable lump measuring 5 cm, at the lower inner quadrant of the right breast. The patient’s history recorded an oval opacity of about 3 cm at the right breast lower outer quadrant, with microcalcifications, observed during mammography (Figure 1B). Ultrasound scan showed a dyshomogeneous iso-echoic lump similar to a cyst (Figure 1A). Fine needle aspiration was performed and cytology indicated the presence of proteinaceous material including many inflammatory cells, macrophages and blood cells. The finding was compatible with an inflamed cystic lesion, to be monitored over time. Antibiotic therapy was recommended. Nine months later, the patient underwent a new ultrasound check associated to mammography, which confirmed the presence of a cyst-like lump, that had increased in size to 5 cm. Breast cyst aspiration was performed several times, yielding large quantities of serous fluid, which reformed after two or three days. Cytological examination of the aspirated fluid always revealed the presence of varying numbers of granulocytes, lymphocytes and macrophages. The decision was made to perform microhistological sampling on tru-cut.

Histological examination described laminar fragments of fibrous connective tissue covered by stratified squamous epithelial cells featuring clear cells, atypia and with numerous mitoses. Five months after the biopsy, the patient underwent a wide excision of the tumor. During surgery, the tumor appeared as a huge mass, 5.5 cm in size, with a solid wall, centrally excavated and containing necrotic and purulent material. The surgical specimen was extensively sampled and routinely processed. The final histological examination diagnosed a cancer consisting of squamous cells with wide keratinization within an atrophic parenchyma (Figure 2 A-B). No area of ductal differentiation was observed. Results of immunohistochemistry showed a strong and diffuse immuno-reactivity for 34β–E12 cytokeratins (Novocastra, Newcastle-upon-Tyne, UK) and p63 (DakoCytomation, Glostrup, Denmark) was expressed in more than 90% of neoplastic cells (Figure 2 C-D.), and negative staining for estrogen (Novocastra) and progesterone (Novocastra) receptors. HER2 (Novocastra) yielded a score of 2+, so, FISH (fluorescence in situ hybridization) examination was performed, which showed no gene amplification (Figure 3). The proliferation rate, measured by MIB1/Ki67-antigen (DakoCytomation) labelling, exceeded 40%. The skin and nipple were normal. Once the cancer had been diagnosed, in the absence of guidelines, the decision was made to complete the treatment with Madden radical mastectomy and complete axillary lymph node dissection. A later histological examination showed no tumor in the remaining parenchyma or lymph nodes. The patient refused chemotherapy and 12 months after surgery she was disease-free.

Discussion

SCCB is an extremely rare type of breast cancer, accounting for only 0.04 to 0.016% of cases. The histopathogenesis and treatment are still controversial. Some authors consider that it derives from a metaplasia occurring in the course of a benign breast disease. Mitra et al. (9) and Toikkanen et al. (1) claim that it is linked to the neoplastic transformation of dermoid or epidermal elements, independent of the overlying skin and of the nipple-areola complex. Breast cancer is defined as a...
primitive SCCB if the following criteria are met: i) no other breast cancer components are observed; ii) the cancer is independent of the overlying structures; iii) the patient does not suffer from SCC in other sites such as the esophagus, bronchi, bladder, renal pelvis, ovary, cervix (3).

This cancer can be observed in women aged between 29 and 90, and is often characterized by a fast growth over the course of a few weeks only. According to Cappellani et al. (2), in two thirds of cases, it presents as a cystic component with central necrosis simulating an abscess formation, as observed in our patient. Lymph node metastases are uncommon (5); in our patient axillary lymph node were negative. Mammography is often not diagnostic for malignancies, especially in the absence of microcalcifications, and only ultrasound scan can raise the suspicion of malignancy, due to the solid hypoechochic appearance with complex cyst elements inside an antibiotic-resistant, rapidly growing lump. The negativity of the tumor to estrogen and progesterin receptors - as in our case - is in accordance with what was described by Behranwala et al. (7). As to the overexpression of HER2, Karamouzis et al. (8) have described the only case reported in literature. Metaplastic breast carcinoma has an aggressive behavior and a poorer prognosis in comparison with invasive ductal carcinoma, both in general and with specific reference to triple negative carcinoma (3). Our case was a triple negative (ER-, PR-, HER-) metaplastic breast cancer.

Conclusions
It is important to emphasize the importance of performing a microhistological examination, even in the presence of clinically and mammographically benign lumps, which are normally investigated cytologically, particularly if they contain fluid, when the histological characteristics can add further information to the clinical diagnosis. In cases of persistence of clinical manifestations, surgical excision may be recommended. It should also be noted that a breast cancer diagnosis should always be suspected and excluded. Squamous cell carcinoma is a rare, aggressive tumor often associated to local and distant lymph node metastases; it is an exceptional finding,
lacking in peculiar clinical and instrumental data. The surgical approach, in agreement with reports in literature, is the same as for other breast tumors of considerable size, namely a modified Madden radical mastectomy. The bleak prognosis is correlated with the tumor size and nodal status, as in other forms of breast cancer. Moreover, as regards the tumor histological features, the acantholytic variant of squamous cell carcinoma seems to have the worst prognosis, with a risk of lymph node metastases, and a 5-year survival of about 64% (10). SCC of the breast has shown very little responsiveness to chemotherapy with cyclophosphamide, methotrexate, 5-fluorouracil and doxorubicin. A future research frontier will certainly be the identification of biologically active drugs against molecular targets such as the EGFr (Epidermal Growth Factor-receptor), in order to develop appropriate tumor-specific therapy. Less than 100 cases of squamous cell carcinoma of the breast have been reported in the literature (PubMed/Medline). Our clinical case adds further information to the previous experience described by a single center. Histological sampling should always be performed even of apparently benign lesions that can, in some cases like the one we observed, result malignant. This is especially important in non-responders to antibiotic and anti-inflammatory treatment, or patients with no risk factors for the development of benign mastitis, like puerpera. Considering the possible large size of such tumors, ample quadrantectomy or radical mastectomy, in association with lymphadenectomy, seems to be the best treatment to date, since no chemotherapy protocols have yet been validated for this rare tumor variant and new guidelines have still to be issued (11).

Conflict of interest
No conflict of interest.

Ethical approval
No ethical approval has been applied for this case report study, only the written and oral consent by the patient.

Acknowledgement
The authors are grateful to Mary V. Pragnell, BA, for language assistance.

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