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METAPLASTIC BREAST CARCINOMA: A CASE REPORT

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Abstract

Metaplastic breast carcinoma is defined as a heterogeneous group of invasive breast cancer characterized by differentiation of the neoplastic epithelium into squamous or mesenchymal cells with differentiation into spindle, chondroid, bone or other cells. It is a rare malignant tumor that represents less than 1% of breast cancers. It is an aggressive tumor, with a poor prognosis and resistant to chemotherapy.

We report a case of metaplastic breast carcinoma, in order to discuss the epidemiological, clinical and histopathological particularities with a review of the literature. This case concerned a 52-year-old woman with a nodule in the upper outer quadrant of the right breast, with a history of excision of a cystic papilloma on the same site, classified ACR4 on mammography. Histological and immunohistochemical examination had concluded a metaplastic carcinoma.

Keywords: *breast cancer, immunochemestry, metaplastic carcinoma, Madagascar*

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INTRODUCTION

Metaplastic breast carcinomas are rare malignant tumors, representing less than 1% of invasive breast carcinomas [1], characterized by a differentiation of glandular epithelial cells into other completely different cell varieties, squamous and/or mesenchymal [2].

We report a case of metaplastic breast carcinoma diagnosed on a lumpectomy specimen in order to highlight the epidemiological, clinical and histological features of this tumour.

Observation

This was a 52-year-old woman presenting in 2018 a history of a right breast UOQ nodule. She was undergone excision of the nodule and the histological diagnosis was a cystic papilloma, which was completely removed. A recurrence of the nodule was observed on the same site since December 2019. Mammography and CT scan, performed 6 months later, showed a mass of calcium density, measuring 28.9 x 23.4 mm, classified ACR4. An excisional biopsy was performed. On gross examination, the specimens consisted of multiple, beige-yellowish, firm, non-reconstitutable fragments, measuring in clusters 5 x 4 x 2.7 cm. Histological examination showed a biphasic tumor. This lesion was composed by proliferation of carcinomatous cells with sometimes granular cytoplasm and moderate cyto-nuclear atypia, organized in solid masses, without particular differentiation. It was associated with atypical spindle-shaped cells, organized in short bundles with numerous osteoclast-like giant cells. There were 16 mitosis figures, sometimes atypical, on 10 HPF. On immunohistochemical examination, the tumorwas triple negative (RO-, RP-, HER2-) with negativity of Pan Cytokeratin and positivity of AML, CD68 and Vimentin. The diagnosis was metaplastic spindle cell carcinoma associated with osteoclast-like giant cells (Fig 1). The patient was lost to follow-up and we were unable to follow her further management and the evolution of her disease.

Discussion

Breast cancer is currently a major public health problem. There are several histological types. Some are more frequent and others rarer such as metaplastic carcinomas. It is a very rare pathological entity which is classified histologically according to the presence of different types of tissues, glandular and non-glandular, which compose them. The term metaplasia defines the non-glandular change of cancer cells by dedifferentiation of pluripotent stem cells [3].

These tumors usually occur in postmenopausal women over 55 years of age [4], as in our patient's case. However, the age of onset of the tumor may vary from country to country. In a study carried out in California on 43 patients, Giatri Dave et al reported a mean age of 53.6 years (26 to 83 years) [4]. In their series of 5 patients in Morocco, Chraibi M et al [1] found a younger age of onset (35 to 54 years), with an average age of 44.5 years.

The diagnosis is based on pathological examination. Macroscopically, it is usually a firm tumor, well-bounded or sometimes with a blurred boundary, irregular tumor with a tumor sizeranging from 1 to 18 cm, and a mean diameter of 3.9 cm [1, 2]. In our patient, the macroscopic evaluation was difficult because the specimen was multi-fragmented. However, on mammography, the nodule measured 28.9 cm and was poorly circumscribed.

Histologically, metaplastic carcinomas present characteristic morphological aspects. Their glandular component may be partially or totally replaced by one or more non-glandular components. The histological variants depend on the characteristics of the metaplastic component(s) and determine the histological classification of these tumors. They are morphologically heterogeneous and are classified into low- and high-grade tumors [5], which can be monophasic (with a single metaplastic component) or biphasic (with two or more components). Both components may be metaplastic with squamous cells and/or spindle cells and a mesenchymal component, or consisting of a metaplastic component and an adenocarcinoma [2, 6].

Depending on the morphological appearance, the tumor can also be classified according to the current World Health Organization (WHO) classification into purely epithelial tumors (low grade or high grade adenosquamous carcinoma, squamous cell carcinoma) or pure sarcomatoid carcinoma (spindle cell or matrix-producing carcinoma) or mixed epithelial and mesenchymal carcinoma (mesenchymal differentiation carcinoma) [7]. Carcinoma with mesenchymal differentiation is an aggressive tumor composed of a mixture of differentiated mesenchymal components, including chondroid, bone, rhabdomyoid and rarely neuroglial elements [2]. Most often, it is a mixture of cartilage and bone differentiation. Although uncommon, some tumors may present with osteoclast-like giant cells [2, 8]. In our case, it was a biphasic tumor with a poorly differentiated epithelial component and a spindle-shaped cell sarcomatous component with osteoclast-like giant cells whose morphological appearance was inconclusive and required immunohistochemical examination to determine the exact nature ofthe tumor cells.

Immunohistochemistry is integral to the diagnosis of metaplastic carcinoma. All variants of metaplastic carcinoma are nearly negative for estrogen and progesterone receptors, and do not show overexpression for HER2/neu [9]. This was found four our patient, the tumor cells were RO-, RP- and HER2-. Importantantly, metaplastic carcinomas are positive for high molecular weight cytokeratins/basal cytokeratin, including CK5/6. Another useful marker in the diagnosis of these tumors is p63, with high sensitivity and specificity [5]. Some authors have found that spindle cells of metaplastic carcinoma express myoepithelial markers (like AML). Other studies have reported higher expression of AE1/AE3,

ranging from 63% to 100%. Thus, AE1/AE3 remain the most used and sensitive markers, along with vimentin, to identify spindle cells in metaplastic carcinoma, particularly for the monophasic subtype [8]. In our case, the tumor cells showed Pan Cytokeratin negativity and AML, CD68 and Vimentin positivity.

Based on the morphological and immunohistochemical aspects, our case was diagnosed as metaplastic spindle cell carcinoma. This is an aggressive variant of metaplastic carcinoma, characterized by spindle-shaped cells with marked cytonuclear atypia, presenting areas of necrosis and frequent and obvious mitotic figures. According to the literature, other architectural organizations can be observed, but generally the cells are arranged in wavy, intertwined and superimposed bundles [10]. Focal squamous differentiation can be observed.

Two differential diagnoses should be considered: phyllodes tumors and mammary sarcoma, primary or metastatic. When present, a carcinomatous component is an argument in favor of metaplastic carcinoma and is extremely useful in the differential diagnosis [10].

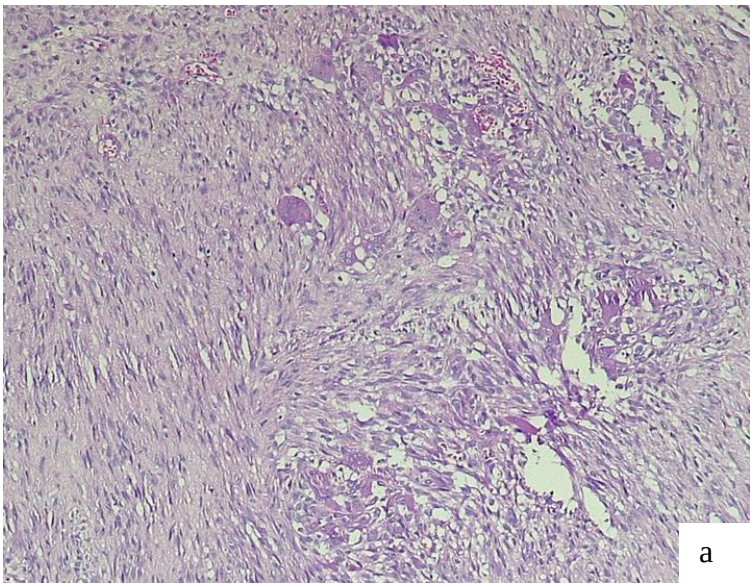
Regarding the pathophysiological mechanism, genetic studies support a monoclonal origin of the heterogeneous components of metaplastic carcinomas, and some authors advance the concept of a late change in tumor dedifferentiation rather than an origin from a basal stem cell [2]. However, the somatic mutations causing the differentiation of the different subtypes are not yet elucidated, and no specific pathognomonic mutations for metaplastic carcinomas have yet been identified. Frequently mutated genes include rp53 and PIK3CA. Overexpression and mutation of the EGFR gene, positive immunostaining for p63 is found in metaplastic carcinoma with squamous cell and spindle cell differentiation [7]. Regarding metaplastic spindle cell carcinoma, some authors hypothesize that this particular variant may arise from myoepithelial cells, since spindle cell carcinomas are frequently positive for at least one myoepithelial marker such as p63, smooth muscle actin and CD10 [10]. In our case, we could not perform a molecular study due to a lack of financial means.

Regarding therapeutic management, due to its rarity and heterogeneity, there is no "standard" treatment for all patients with metaplastic carcinoma. In general, the therapeutic options recommended in their treatment follow the therapeutic principles of invasive breast cancer. In the majority of reported cases, mastectomy with or without axillary lymph node dissection was performed, followed by postoperative chemotherapy and radiotherapy. Hormone therapy is ineffective. [11-13]

In the literature, the prognosis is related to some extent with the type of metaplasia present. With the exception of low-grade adenosquamous and fibromatosis-like variants, metaplastic carcinomas are generally aggressive, drug-resistant, and highly metastatic. The 5-year survival for metaplastic carcinoma composed mainly of epithelial components and sarcomatous components is approximately 65% and 40%, respectively [4]. In our case, it should be a tumor with a poor prognosis because the tumor component consisted essentiallyof spindle cells with giant cells of the osteoclastic type.

Conclusion

Metaplastic carcinomas are rare. However, we were able to identify the key points to know about these tumors in our study. Histopathological and immunohistochemical examinations suggested that our case has a basal and triple-negative pattern. The diagnosis is sometimes difficult. There are some morphological elements to look for in order to eliminate differential diagnoses, especially with the spindle cell variant, such as the presence of a carcinomatous component. Their management is difficult but can be similar to that of other invasive carcinomas, the prognosis is poor.



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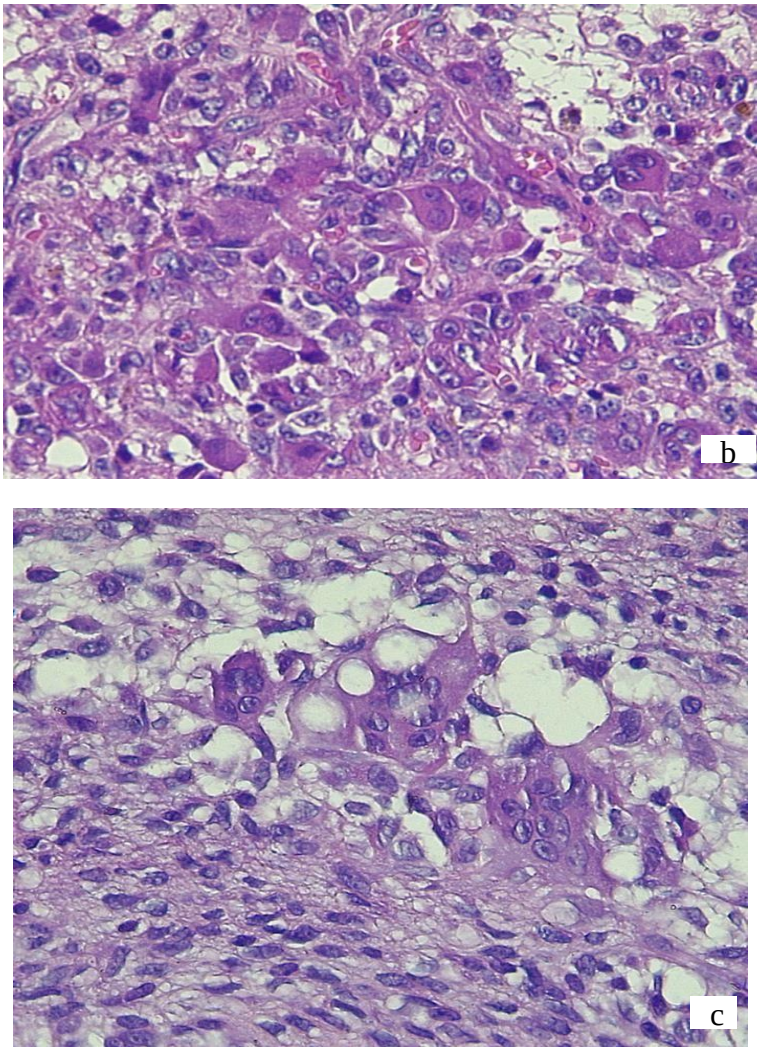

Figure 1: Metaplastic spindle cell carcinoma associated with osteoclast-like giant cells, HE x100 (a), HE x 400 (b, c).
Source: Department of Pathology, Joseph Ravoahangy Andrianavalona University Hospital,Antananarivo, Madagascar.

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