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Advanced Metaplastic Breast Cancer: A Case Report

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Introduction

Metaplastic carcinomas of the breast are rare tumors of particular interest because of their clinical, radiological, anatomopathological and therapeutic differences from the usual form of breast cancer. The authors report a new case of metaplastic carcinoma of the breast, and through analysis of the data in the literature, review the various aspects of this type of breast carcinoma.

Patient and observation

Mrs MK, 38 years old, with no particular history, was admitted in June to the IBN ROCHD hospital in Casablanca with a tumour of the left breast discovered on autopalpation. Clinical examination revealed a large, neglected breast with foci of cutaneous necrosis measuring 20 cmx 20 cm, poorly limited, hard, fixed and painful, associated with inflammatory signs of erythematous placard and peau d'orange without nipple discharge (**Figure 1)**. Examination of the axillary and supra-clavicular lymph nodes revealed a homolateral axillary adenopathy measuring 1 cm, fixed and painless; the rest of the somatic examination was unremarkable.

Mammography found Density type C in the left breast, presence of a voluminous multinodular mass without a focus of microcalcifications throughout the breast, with muscle and skin invasion, measuring 27x22cm, Right breast: No palpable nodule (**Figure 2**). Voluminous tumour mass in the left breast *Absence of suspicious lesion in the right breast* with axillary ADP of 6.3 mm (**Figure 3**, **Figure 4**), vascularized on color Doppler. This ultrasound mammographic appearance is classified as ACR BI-RADS 4c. Microbipsies with tru-cut revealed a **metaplastic CMI, SBR III** IHC: **Triple negative** (RE:0%, RP:0%, Ki67:30% HER2:-

Figure 1 & **2:** Inflamed swelling of the left breast

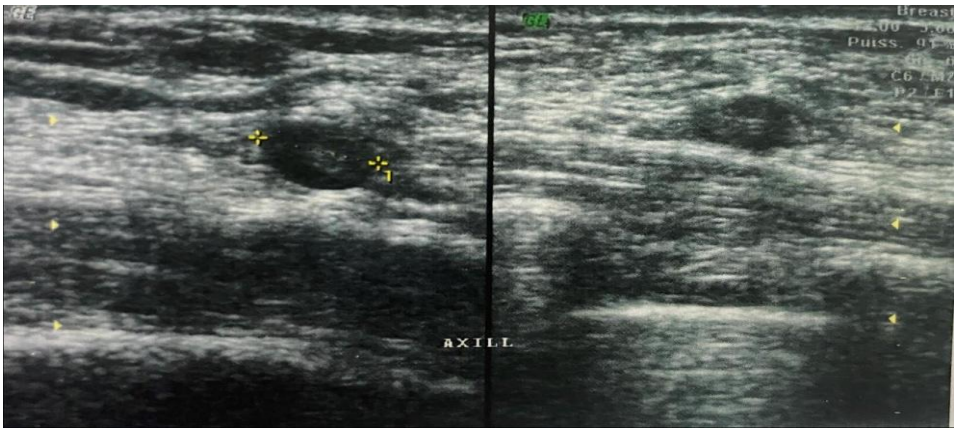

Figure 3 & 4: Ultrasound appearance of the tumor

The extension workup, including a **CT/PET scan**, revealed a voluminous left breast mass with satellite axillary adenopathies and no evidence of metastases of a left breast tumour mass, associated with homolateral axillary adenopathies, absence of any pathological metabolic abnormality, secondary distant visceral or bone neoplastic spread.

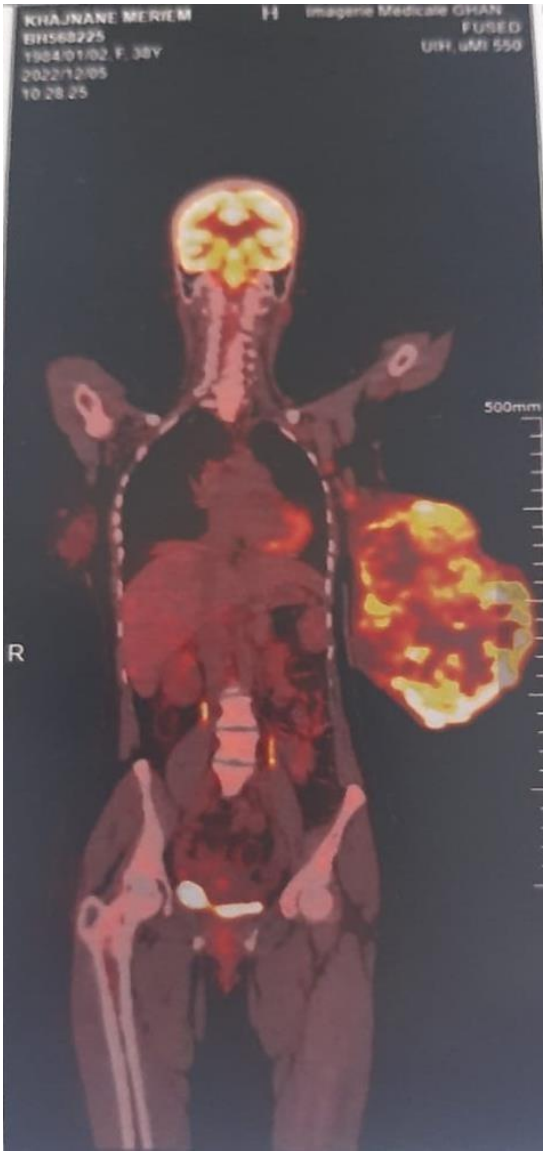

Figure 5: PET SCAN

Stage T3N1M0. Radical surgical treatment with Patey-type axillary lymph node dissection was performed. Macroscopic examination of the mastectomy specimen revealed a large, fairly well-bounded, hard, whitish tumour measuring 8 cm in long axis. The smears showed a high-grade malignant process. Histopathological study reveals a partially necrotic carcinomatous proliferation made up of cords, clusters of small masses with rare tubes (score3). The cells have an enlarged, anisokaryotic, hyperchromatic and nucleolated nucleus (score2).The cytoplasm is eosinophilic. The mitotic index is 15 mitoses per 10 fields at high magnification (score3).the cells show signs of squamous differentiation, with signs of dyskeratosis.

Pathological examination concluded in a Scarff Bloom Richardson grade II squamous cell carcinoma. There was no evidence of carcinoma in situ, vascular emboli or perivenous sheathing. Boundaries are healthy and there is no lymph node involvement, hormone receptors and herceptest are negative. The patient was referred to the oncology department for chemotherapy, with no recurrence or metastasis.

Discussion

Metaplastic carcinoma of the breast is a rare but growing primary malignancy **[1, 2]**, accounting for 0.2 to 5% of all breast cancers. An increase in the number of cases reported annually has been noted and can be explained by an increase in the incidence of the disease and the attention given to its diagnosis **[1, 2]**. The 2003 World Health Organization classification distinguishes between purely epithelial carcinomas, including squamous cell carcinomas, adenocarcinomas with fusiform differentiation, adenosquamous carcinomas and mixed carcinomas with a dual epithelial and mesenchymal component **[3]**.

These tumors occur in postmenopausal women with an average age of 53 **[4]**, which does not correspond to our patient's age. Clinical symptoms are non-specific. The tumor usually appears as a mass comparable to a benign tumor, but usually progresses rapidly. Mastodynia, inflammatory signs, nipple discharge, nipple retraction, skin ulceration and sometimes breast abscess are often reported. Node involvement is rare **[5,6]**. In our patient, the rapid evolution of the tumour, the abscessed appearance and the inflammation are more consistent with malignancy. The radiographic appearance is also non-specific. However, signs such as hyperdensity of the mass and absence of micro-calcifications may be suggestive on mammography **[5]**. Mammary ultrasound may reveal foci of haemorrhagic, necrotic or cystic changes, which are common **[7]**. These tumours may escape detection, as they usually progress rapidly **[4]**. In our patient, ultrasound revealed a rounded, irregular, heterogeneous, solid and cystic mass. The macroscopic appearance was non-specific, and the tumour was generally firm and well- limited, with a significant tumour size ranging from 0.5 to 18 cm **[4,6]**. In our patient, the tumour was large, measuring 6 cm long. Histologically, squamous cell carcinomas are easy to diagnose, and are characterized by a proliferation of polygonal squamous cells linked by visible desmosomes, with or without foci of dyskeratosis. Adenocarcinoma with spindle cell metaplasia is a glandular carcinoma with extensive epithelial spindle cell foci. Adenosquamous carcinomas are made up of two malignant epithelial contingents, glandular and epidermoid. Mixed metaplastic carcinomas are characterized by the association of an infiltrating carcinoma and heterologous mesenchymal elements represented by zones of cartilage, bone or muscle differentiation... When the mesenchymal contingent is malignant, the tumor is called carcinosarcoma **[8]**.

Association with ductal cancer in situ is not uncommon (50% of cases) **[6]**. Immunohistochemically, hormone receptors are positive in less than 17% of cases **[2]**, HER2 overexpression is often absent and breast metaplastic carcinomas are triple-negative in 64% to 96% of cases **[1]**. Lymph node involvement is rare, ranging from 6% to 26% **[1]**. In our patient, the tumour showed squamous differentiation (**Figure 5**, **Figure 6**), with the presence of dyskeratotic cells with hormone receptors and a negative hercept test. On immunohistochemistry, cytokeratin 5 and 6 fixation was not sought, and the lymph nodes were all negative.

The histogenesis of carcinosarcoma has long been the subject of controversy. At present, the most likely hypothesis suggests the particular phenotypic transformation of epithelial cells into myoepithelial cells, then into sarcoma **[9]**. In terms of molecular biology, metaplastic carcinomas of the

breast have a basal-like transcriptomic profile and express one or more myoepithelial or basal-like markers (p63, 34'E12, cytokeratin5/6, CK14, S100 protein, actin and EGFR). Various studies have found overexpression of EGFR Human Epidermal Growth Factor Receptor-1(HER1), which may suggest a favourable response of these tumours to treatments targeting EGFR (HER1) **[10]**. Metaplastic carcinomas of the breast pose major problems of differential diagnosis, primarily with phyllodes and primary breast sarcomas. In the case of pure squamous cell metaplasia, carcinoma of cutaneous origin or metastasis must be ruled out.

The main differential diagnosis for spindle cell tumours is malignant phyllodes **[8]**. In the case of carcinoma with bone or chondroid metaplasia, fibroadenoma, osteosarcoma, chondrosarcoma and phyllodes should be ruled out. Many types of sarcoma can be found in the breast, the most common being angiosarcoma and liposarcoma **[10]**.

Treatment is based on surgery. It is often radical, but conservative surgical treatment is possible for small tumours **[1]**. Axillary lymph node dissection is recommended, despite their low lymphophilic nature **[1]**. The role of chemotherapy and radiotherapy is still debated **[7]**. Post-operative adjuvant radiotherapy is rarely indicated, as conservative surgical treatment is less frequent and lymph nodes are often negative **[1]**, but it appears to have an essential role in controlling local recurrence after conservative surgical treatment **[10]**. Standard chemotherapy is unsatisfactory, as chemoresistance is frequent **[7]**. L′hormonotherapy usually has no place, given the usual absence of hormone receptor expression. Herceptin cannot be introduced in most cases, as the′Herceptest is often negative. Overexpression of EGFR(HER1), could suggest a favorable response of these tumors to EGFR-targeted therapies (anti HER1). Other possible therapies include platinum salts and poly-ADP ribose polymerase (PARP) inhibitors **[10]**. The prognosis for squamous cell carcinoma remains poor, with the lung, liver, bone and brain the preferred sites for metastases within the first five years. Mean 5-year survival is estimated at 38% to 86%.

Conclusion

It is important to identify metaplastic carcinomas among the other types of breast cancer, as their therapeutic management is different and more cumbersome. Surgery remains the treatment of choice, but a new molecular approach could alter the low contribution of conventional systemic treatments.

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