



## METAPLASTIC BREAST CARCINOMA: ABOUT 13 CASES

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**ABSTRACT** The breast carcinosarcoma, often referred to as metaplastic breast carcinoma, is a rare malignant tumor composed of two distinct cell lines and is described as ductal breast cancer with a sarcoma-like component. It accounts for less than 1% of all malignant breast tumors. This is a retrospective study spread over one year, thirteen cases of breast carcinosarcomas were collected at the Moulay Ismail military hospital in Morocco during the year 2014. The median age was 53.46 years, all the tumors were high grade. The proposed treatment was based on breast surgery followed by radiotherapy and chemotherapy for adjuvant cases, lymph node involvement was noted in two cases, estrogen receptors were negative, while progesterone receptors were positive in 3 cases, the expression of Her2 was absent in all cases. Metaplastic breast cancer is a rare subtype of breast cancer that has a particular and aggressive profile; it often has a triple negative character. There is a need to develop other researchs pathways such as targeting the HER1 / EGFR Receptor.

**KEYWORDS :** Metaplastic breast carcinoma, chemotherapy, EGFR

#### Introduction:

Mammary metaplastic carcinomas are rare tumors, representing less than 1% of invasive breast carcinomas [1].

It is a heterogeneous group of tumors, characterized by the association of an adenocarcinoma component, more or less differentiated with an epidermoid or sarcomatoid component. Are also included in this group: pure squamous cell carcinomas, with the exception of tumors developed from the skin lining; carcinomas with osteoid or chondroid matrix, in the absence of fusiform or giant cells; tumors containing only sarcomatoid elements, but whose the pathological or immunohistochemical characteristics are in favor of an epithelial origin (intricacy with intraductal carcinoma, expression of cytokeratins) [2]

Metaplastic carcinoma belongs to the group of "triple-negative" breast cancers, which means without expression of hormone receptor or HER2 amplification. The Epidermal Growth Factor receiving Protein HER-1 / EGFR is expressed in the majority of metaplastic carcinomas and can potentially serve as a therapeutic target for the inhibitors of EGFR such as gefitinib and cetuximab.

Recent studies suggest that metaplastic carcinoma is a basal tumor, because of its immunohistochemical and genomic characteristics [2, 3,4]

The prognosis is dark and the evolution is marked by local recurrences and distant metastases

Through this series of 13 cases, we describe the aggressive nature, the anatomo-clinical aspects, the pathogenesis and the evolution of this rare entity.

#### Patients and methods:

Thirteen cases of primary metaplastic breast cancers were retrospectively collected at the moulay Ismail military hospital-Meknes during 2014-2015, all the patients received an echo-mammography and an extension assessment, namely: pulmonary X-rays, abdominal ultrasound, bone scintigraphy and a dosage of CA 15-3. The diagnosis was made by biopsy with immunohistochemical study for estrogen

and progesterone receptors, HER2 / neu protein, p63 antigen, cytokeratin and vimentin.

#### Results:

Thirteen cases of metaplastic breast carcinoma were collected at the medical oncology department at the Moulay Ismail military hospital - Meknes during year 2014. The average age of the patients is 53.46 years (41 - 75) the left breast is affected in 5 cases and the right breast is affected in 8 cases, there is no bilaterality, a mastectomy with lymph node dissection were performed in 10 cases, a conservative treatment was opted in one case, two cases have not benefit from surgery because of the secondary locations (lung, bone), lymph node involvement was noted in two patients, median height was 4.6 cm (1.2-9 cm), resection was R0 in all patients, all the tumors were high grade, the double epithelial and mesenchymal component was found in four patients (carcinosarcoma) and the pure epithelial component in nine patients (figure 1,2), only three cases expressed the progesterone receptors, no patient expressed estrogen receptors, HER2 / neu expression was not observed, ten patients received adjuvant chemotherapy with anthracycline and taxanes, one patient received neo-adjuvant chemotherapy and two patients received palliative chemotherapy, eleven patients received adjuvant radiotherapy: 50 gy on the chest wall, the axillary area and the internal mammary chain.

#### Discussion:

The association with the adenocarcinoma component, an epidermoid, sarcomatoid, chondroitoid or osteoid component also, defines metaplastic carcinoma [5].

Described by Huvos et al. in 1973 [6]. The World Health Organization recognized metaplastic breast carcinoma in 2000 as a full histological form. These tumors are rare (0.25 to 1% of breast cancers), very aggressive, similar to the prognosis of triple negatives [7, 8].

Pricolo et al. [9] require the absence of any other ductal or mesenchymal neoplastic component to be able to speak about primitive metaplastic carcinoma, the tumor should not be related to the skin, nor be secondary to distant squamous cell carcinoma. Some authors [10,11,9] evoke the possibility of the birth of the tumor from a

mammary dermoid cyst, a chronic breast abscess, a complete epidermoid metaplasia of the mammary glandular tissue or from a phyllode cystosarcoma.

Primary metaplastic breast carcinoma is the prerogative of women [12]. The average age of onset is 54 years [13]. The clinical signs are similar to those of the other breast carcinomas [14,12]. Whightson et al. reported 2 cases of primary metaplastic breast carcinoma revealed by breast abscess [15]. Gaural et al. reported a case revealed by isolated axillary lymphadenopathy without clinical or radiological individualisable lesions [16].

Metaplastic carcinoma has no particular mammographic presentation; however, mammary ultrasound highlights the importance of the necrosis as well as the cystic appearance of lesions [17,18,19]. It is a cancer that affects both the right and left breast. It is rarely bilateral. The size of the tumor is variable depending on the stage of evolution. It is on average 5 cm with extremes ranging from 2 to 16 cm [18]. Large tumors tend to suffer from a central cystic degeneration, invading and ulcerating skin [11,19].

For some authors [9/15] the existence of a cystic mass or abscess in an elderly woman must be reminiscent of a metaplastic carcinoma. The preoperative diagnosis can be made by simple cytological aspiration [20,24].

However, histopathological examination is essential for the search of the main histopronostic criteria which shows that metaplastic carcinomas are most of the time high-grade and aggressive tumors, with a high frequency of vascular emboli and lymph node metastases [20, 21,22].

Like basal-type cancers, metaplastic carcinomas are in the vast majority of cases "triple-negative" (absence of hormone receptors or HER2 overexpression) [23,24].

Sheen et al reported a case of metaplastic carcinoma in which hormone receptor testing was positive [25]. The results of our series underline the literature data, the estrogen receptors are negative in 13 cases, the progesterone receptors are positive in 3 cases

Metaplastic carcinomas express one or more myoepithelial or basal type markers such as p63, 34\_E12, CK5 / 6, CK14, S100 protein, actin and EGFR [2, 3, 25, 26].

In the majority of metaplastic breast carcinomas, there is an overexpression of the HER1 / EGFR receptor. In a study of 20 cases of metaplastic breast carcinoma, they found that 14 patients were positive for the expression of EGFR [23]; this research should be included in the initial evaluation of breast carcinomas. New therapeutic possibilities have been suggested by the treatment with EGFR targeting agents such as gefitinib and cetuximab in an adjuvant strategy. It has been suggested that the expression of EGFR in the absence of hormone receptors or other receptors of the EGFR family could make metaplastic breast carcinoma even more sensitive to EGFR tyrosine kinase inhibitors [27].

The treatment usually involves a mastectomy with axillary lymph node dissection followed by chemotherapy and radiotherapy. Treatment is similar to invasive ductal breast carcinomas of the same stage of evolution [28,29,10,30]. Its prognosis would be more pejorative than other carcinomas.

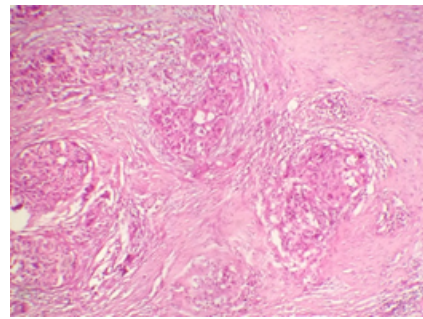
Dejager et al [31] used neoadjuvant treatment with 5-fluorouracil and cisplatin with a good response. A patient in our series has benefited from neo-adjuvant chemotherapy with anthracycline and docetaxel with disappearance of inflammatory signs, decreased tumor size, the patient was operated with negative surgical margins and negative lymph node dissection.

The prognosis of metaplastic carcinoma stays a controversial subject in the literature but is globally similar to that of the ductal carcinomas infiltrating the breast at the same stage of evolution [10, 17, 32, 33, 34]

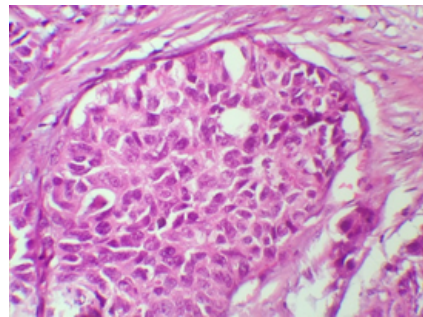
#### Conclusion:

It is important to identify metaplastic carcinoma among the other types of breast cancer, as their treatment is different and heavier. The treatment of choice stays surgery but a new molecular approach could

modify the low contribution of the conventional systemic treatments.



**Figure1: Breast parenchyma infiltrated by carcinomatous tumor proliferation, made of hoses of variable size (HE, x200)**



**Figure2: Tumor cells appear cohesive and have abundant cytoplasm and highly nucleated anisokaryotic nuclei (HE, x400)**

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