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## **MUCINOUS CARCINOMA ABOUT 03 CASES**

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#### SUMMARY

Mucinous carcinoma represents 1 to 7% of breast cancers and may have clinical and mammographic characteristics of a benign lesion. Histologically, there are two types of colloid carcinoma: pure colloid carcinoma, in which there is no infiltrating ductal carcinoma component, and mixed colloid carcinoma, in which there are foci of infiltrating ductal carcinoma in addition to the colloid component. This distinction is crucial because of its prognostic value. Clinically, mucinous carcinoma, like most breast cancers, is revealed by a palpable breast nodule usually located in the superolateral quadrant. Node invasion is the main prognostic marker for colloid carcinoma of the breast. The diagnosis is made on the basis of mammography and breast ultrasound. The immunohistochemical study of hormone receptors often revealed a strong presence. Therapeutic management is based on surgery with or without chemotherapy and adjuvant hormonal therapy. In this work, we review the different epidemiological, diagnostic, anatomopathological, therapeutic and evolutionary particularities of mucinous breast carcinoma.

## INTRODUCTION

Mucinous carcinoma of the breast is a rare variety, representing 1 to 7% of breast cancers<sup>[1]</sup>, and has a more favorable prognosis than infiltrating ductal carcinoma.<sup>[2]</sup> It is important to distinguish between its two forms, pure and mixed, because the therapeutic attitude and prognosis depend on them. It is defined by the WHO as an infiltrating carcinoma characterized by the presence of a significant amount of extracellular mucus surrounding the tumor cells and sufficient to be visible macroscopically and recognizable histologically.<sup>[3]</sup> Pure CMs are characterized by a mucinous component greater than or equal to 90% of the tumor volume. Mixed CMs have both an infiltrative ductal component and a mucinous component: the mucinous component is greater than or equal to 50%.<sup>[4-5]</sup> The purpose of this work is to analyze the epidemiological, clinical, therapeutic and evolutionary characteristics of this type of cancer according to a retrospective study.

## **OBSERVATION**

We counted 3 cases of CM of the breast of which 2 mixed and 1 pure. This represents 0.7% of the breast cancers treated at the maternity hospital during the same period. The average age of our patients was 57 years, with extremes of 51 and 59 years. 2 patients were postmenopausal at the time of diagnosis, the 3rd patient was still in genital activity. The average time to consultation was 11.2 months (1-24 months). No familial

cancer was noted. One of the patients had a history of breast pathology, a bilateral cystic dystrophy.

On clinical examination, all 3 patients had a breast nodule, the tumor was well limited in 1 patient. It was unique in all 3 patients. Axillary adenopathies were palpated in 1 patient. Breast ultrasound and mammography, performed in all cases, showed a homogeneous image with clear polylobed or polycyclic contours in 1 case (Fig. 1).



**FIG 1.** 

In the remaining cases, it was a very hyperechoic heterogeneous image with irregular spiculated contours; microcalcifications were reported in only one case. The mean tumor size was 5 cm (3-7 cm). In only one patient, curage showed lymph node involvement. Treatment was started with surgery, which was radical according to Patey in all 3 cases. The anatomopathological study of the surgical specimen confirmed the diagnosis of colloid carcinoma. Macroscopically, the tumor was poorly limited in 2 cases, whitish, gelatinous and soft in all cases. The mean size of the tumor was 4.2 cm (1.8 to 7 cm). Histological examination showed a carcinomatous tumor proliferation consisting of trabeculae, masses and glands floating in mucus-filled cavities. Mitoses were rare. Foci of intracanal carcinoma were found in 2 cases. These tumors were grade I in only 1 of the cases and grade II in both cases. According to the PTNM classification, the tumors were classified as pT1NOMO, PT2NOMO, p T3N2aMO. Hormone receptors were expressed in all 3 cases, Her2 was expressed in 2 cases. All our patients underwent postoperative radiotherapy; this irradiation was delivered according to a conventional spread and fractionation, at a rate of 2 Gy per session, five sessions per week. All our patients received hormone therapy. With a mean follow-up of 30 months, complete remission was maintained in all 3 patients.

#### DISCUSSION

Mucinous carcinoma of the breast is a rare histological entity with particular anatomical, immunohistochemical and evolutionary features that preferentially affects women over 60 years of age. It represents 7% of all malignant breast tumors after the age of 75 and 1% before the age of 35.<sup>[4]</sup> This is consistent with the results in our series, with a median age of 57 years. Men can be affected, but very rarely.<sup>[5]</sup> There is no specific risk factor for colloid carcinoma. Colloid carcinomas often present as well-limited, mobile or even lobulated masses<sup>[6]</sup>, which can be mistaken for benign formations. A sensation of suffusion, crumpling or fluctuation is reported when colloid carcinomas of the breast are palpated.<sup>[7]</sup> A breast nodule is the most frequent revealing sign, found in more than 80% of cases.<sup>[6]</sup> It is most often an isolated nodule discovered by chance or a routine examination. Lee<sup>[8]</sup> during reported galactorrhagia as a revealing sign of colloidal carcinoma. Mastodynia and inflammatory signs have not been analyzed in the literature. Nipple changes have been noted in the literature, and nipple retraction or protrusion may be observed in cases of colloid carcinoma.<sup>[8]</sup> For the majority of authors, breast cancer, by its different histological types, is most often localized in the upper external quadrant. In our study, in accordance with the literature, the most frequent site was the upper-external quadrant in the right breast. The tumor size is generally small, Diab<sup>[10]</sup> specifies the tumor size in 1177 cases of colloid carcinoma: 54% of the patients presented with tumors of 2cm. According to CHTOUROU<sup>[11]</sup>, the average tumor diameter was 9.5 cm. The authors reported that CMMs are often larger in diameter than CMPs. To explain this phenomenon, they suggested that mucinous carcinomas are initially pure and during their growth a ductal cell clone appears which will proliferate and constitute the infiltrating ductal contingent. This would explain the larger diameter of MMCs.[12] It is accepted that colloid carcinomas are less prone to lymph node invasion than other histological types.<sup>[13]</sup> The frequency of lymph node metastasis increases with tumor size.<sup>[10]</sup> The frequency of lymph node metastases increases with the size of the tumor.<sup>[10]</sup> The frequency of pure mucinous carcinoma is between 2 and 14% and between 45 and 64% in mixed forms.<sup>[14]</sup> In our study, lymph node involvement was noted in one patient. Axillary lymph node involvement in CM patients, although rare, seems to worsen the prognosis of breast cancer with a higher risk of recurrence and distant metastasis.<sup>[1]</sup> The most suggestive mammographic appearance of pure colloid carcinoma is a dense, circumscribed and poly-lobed opacity with finely irregular or regular contours. The typical image suggested is the so-called <<cotton ball>> in relation to tumor reflow of surrounding tissue without true invasion, however, despite this reassuring imaging character, malignancy must always be ruled out in relation to the advanced age of the patients. The absence of a spiculation image on mammography is explained by the

absence of significant fibrosis and inflammation.<sup>[12]</sup> Mixed colloid carcinoma appears as a mass with irregular contours and ill-defined or even spiculated boundaries with the glandular tissue.<sup>[11]</sup> Chopra<sup>[15]</sup> reports that the spiculations are inversely proportional to the amount of mucus. Microcalcifications are not characteristic, but are found in 20% of cases.<sup>[15]</sup> Mammography may be normal in 5 to 17% of cases.<sup>[16]</sup> The ultrasound appearance differs according to the type of colloid carcinoma, the pure one presents as a welllimited heterogeneous isoechogenic mass with posterior enhancement, The latter is explained by the large amount of water in the tumor and the transmission of ultrasound through the mucus.<sup>[15]</sup> The mixed type presents as a heterogeneous hypoechoic mass with posterior acoustic attenuation, which reflects the infiltrative nature of the tumor.<sup>[11]</sup> Colloid carcinoma of the breast should also be considered on ultrasound in the presence of a complex image (liquid and solid) with posterior enhancement in an elderly woman.<sup>[6]</sup> Macroscopically, colloid carcinoma presents as a well-limited tumor mass that crackles on palpation.<sup>[17]</sup> The tumor surface is gelatinous, stringy on section, and the consistency is  $\text{soft}^{[3]}$  with a grayish or yellowish-gray color. Halsted<sup>[7]</sup> in 1915 gave one of the first morphological descriptions of colloid carcinoma of the breast, he reported that "the tactile impression is difficult to describe, being definable as a jelly under tension, it is a strange sensation of elasticity transmitted to the fingers". Colloid carcinoma of the breast is defined by the WHO as a carcinoma containing large amounts of extracellular epithelial mucus sufficient to be macroscopically visible to the naked eye, and microscopically recognizable around and within the tumor cells. Histologically, there are islands of regular epithelial cells with extensive lakes of extracellular mucus, separated by sparse fibrous septa. The tumor cells are small with a dark nucleus within which a small nucleolus is visible. The distinction between pure and mixed types is crucial because of its prognostic impact: Pure colloid carcinoma is characterized by the presence of tumor tissue completely surrounded by abundant extracellular mucus, with no infiltrating ductal component. This tissue does not exceed 10% of the overall tumor volume. The transition between the mucus and the surrounding connective tissue is abrupt; the abundant mucus acts as a mechanical barrier, which attenuates cell invasion and makes this type less aggressive than the mixed type. The transition between the extracellular mucus and the adjacent carcinomatous tissue is gradual, with local overlap between the two territories. Pure colloid carcinomas of the breast are in the majority of cases low-grade carcinomas (according to the SBR score); the association of pure colloid carcinoma with an intracanal carcinoma has been reported in 17% of cases.<sup>[11]</sup> The immunohistochemical study of hormone receptors for estrogen and progesterone has often revealed a strong presence, especially of estrogen.<sup>[11]</sup> Hormone receptors are strongly positive in our cases. The expression of Her2/neu and P53 is often absent, these antibodies are considered to be

unfavorable histopronostic factors. However, Bcl2 expression is correlated with a more favorable prognosis. The treatment of choice for CM is surgery combined with adjuvant therapy: radiotherapy, chemotherapy and/or hormone therapy.<sup>[18]</sup> Conservative treatment in the pure type should be satisfactory both carcinologically and aesthetically given the favorable prognosis of this type; particular interest has been attributed to lymph node involvement in colloid carcinoma; it is known that colloid carcinomas of the breast are less prone to lymph node involvement than the other histological types.<sup>[19]</sup> The incidence of axillary metastases in pure MCC varies from 0 to 14% depending on the series.<sup>[4]</sup> This incidence</sup> seems to be correlated with the young age of the patient. aneuploidy, high nuclear grade and negativity of the osteogenic receptors. It has been shown that the presence of lymph node metastases is the only negative factor in pure MCC. The authors recommend that axillary curage should not be performed in pure MCC. Therefore, the sentinel node technique would be useful to detect patients with lymph node metastases and to better adapt the adjuvant treatment.<sup>[20]</sup> Radiation therapy is an integral part of treatment, as colloid carcinomas of the breast are radiosensitive. Partial and accelerated irradiation of the breast is currently the most recommended after conservative surgery.<sup>[3]</sup> Exclusive radiotherapy may be attempted in inoperable forms for local or general reasons.<sup>[16]</sup> Chemotherapy with doxorubicin combined with paclitaxel seems to have a good response in locally advanced forms of colloid carcinoma of the breast.<sup>[1-7]</sup> Hormone therapy is indicated whenever hormone receptors are positive.<sup>[11]</sup> Noell GH et al<sup>[21]</sup> in their study based on therapeutic trials compared patients who had postoperative irradiation, systemic treatment and the combination of both treatments. The rate of locoregional relapse was statistically lower with irradiation or the combination of systemic treatment and radiotherapy than with systemic treatment alone. In these numerous trials, an improvement in recurrence-free survival and even overall survival was noted in the groups of patients receiving radiotherapy. Thus, radiotherapy is an essential treatment in the management of CM. The attitude in our institute is similar to that adopted internationally with comparable results. Proudhom<sup>[22]</sup> in his meta-analysis demonstrated a decrease in the risk of local recurrence where adjuvant hormonal therapy was administered, this decrease was 37%. Ten-year survival decreased from 91% in the pure form to 46% in the mixed form.<sup>[23]</sup> Node invasion is the main prognostic marker for colloidal breast carcinoma;<sup>[23]</sup> the relative risk of relapse and death in node invasion is 2.69. The high number of invaded nodes and capsular rupture are negative prognostic factors. The amount of mucus, cellularity, tumor size and intracanal component are uncertain prognostic factors.<sup>[4]</sup> It is certain that the prognosis of colloid carcinomas of the breast is favorable, especially in its pure form, however, late relapses both locally and remotely may occur, hence the interest of long-term surveillance.

#### CONCLUSION

Mucinous carcinoma of the breast is a rare variety, occurring mainly after the menopause. The distinction between the variant, pure mixed which is important because the therapeutic attitude and the prognostic incidence depend on it. The therapeutic management is multidisciplinary combining chemotherapy, radiotherapy and surgery.

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