Introduction

Pure mucinous carcinoma (PMC) of the breast is a group of invasive breast carcinomas with a good-prognosis compared to other breast malignant neoplasia such as ductal or lobular variants. It characterized by clusters of epithelial tumor cells suspended in pools of extracellular mucin.1 Mucinous carcinoma (MC) represents about 4% of all invasive breast cancers and PMC accounts for approximately 2% of all malignant breast tumors.2 It often occurs in perimenopausal and post-menopausal women, with a median patient age of 71 years.2 Other terms that are used to identify this tumor include gelatinous carcinoma, colloid carcinoma, mucous carcinoma, and mucoid carcinoma.3 The 10-year survival rate is about 90.4%. From a histological point of view, it is important to differentiate PMC from mixed types of ductal carcinoma with mucinous component (mixed mucinous breast cancer—MMC). Interestingly, the latter have an identical prognosis compared to non-mucinous tumors. Axillary lymph nodes are rarely involved; nevertheless, a nodal metastatic disease can worsen the survival rates and it is considered as one of the most important prognostic factors.4

Herein, we report a case of an 80-years-old woman with pure mucinous carcinoma of the left breast.

Case Report

Case

We present a case of an 80-year-old woman, who had a gradually enlarging lump in her left breast 6 months ago. She had no personal or family history of breast or ovarian cancer. Except this mass, she was in good health.

Methods

Our patient underwent a complete clinical examination with an ultrasound and a mammography leading to the realization of a breast biopsy. For which a careful microscopic examination with molecular profile research has been established.

Observations

The physical exam showed a mass at the upper outer quadrant of the left breast. The mass was soft and well circumscribed. It measured of about 16 × 10 cm without axillary lymphadenopathy. Mammography showed a well circumscribed, lobulated mass mimicking a benign process. Sonographically, the tumor was hypoechogenic with posterior acoustic enhancement in the...
upper outer quadrant of the left breast. The radiologist’s conclusion was a suspicious finding (ACR 4A) (Figure 1).

The core needle biopsy was performed with ultrasound guidance. Pathological examination showed a microlobulated proliferation including a well differentiated carcinoma classified in Type 1 of Scarff Blood Richardson (SBR 1). At low magnification, there were nests of tumor cells floating in large lakes of extracellular mucin divided by delicate fibrous septa containing capillary blood vessels. The tumor contained more than 90% of mucin. At 20× magnification, malignant cells showed mild to moderate nuclear atypia. Mitotic figures were rare, with 4 mitotic figures per 10 high power fields (40×) (Figure 2). No lymphovascular emboli or perineural spread were seen. Tumor infiltrating lymphocytes (Tils) were absent.

The neoplastic cells were strongly positive for ER, PR, without superexpression of HER-2/neu, and a weak proliferation.
index evaluated by Ki-67 (Figure 3). The tumor was classified as luminal A molecular subtype.

We proposed a breast conserving surgery for our patient and she got hormone treatment with a good clinical course.

Discussion

The definition of pure mucinous carcinoma consists of nests of tumor cells floating in lakes of mucin, whereas the mixed form also contains common infiltrating ductal carcinoma not specific type (NST). The percentage of the mucinous component is used to distinguish between pure and mixed mucinous carcinoma. However, pure mucinous carcinomas are generally defined as containing more than 90% mucin, and mixed mucinous carcinomas are those containing 50% to 90% of mucin. The presence of less than 50% mucin is considered as ductal carcinoma with a mucinous component.

Clinically, these mucin-containing cancers often present as soft masses due to their semisolid mucin constituents. Most mucinous carcinomas are readily detected on mammography. They appear as low-density, well-defined or microlobulated oval masses and generally belong to the category of "well-circumscribed" breast carcinomas. Microlobulated margins have been associated with greater degrees of fibrosis associated with the non-mucinous components. Albeit rare, calcifications seen in conjunction with mucinous tumors frequently correspond to the invasive ductal component of the cancer in a mixed mucinous tumor. Sonographically, mucinous carcinomas typically present as complex masses of mixed echogenicity with solid and cystic-appearing components. However, up to 20% of these lesions may present as homogenous masses on ultrasound. They are isoechoic or hypoechoic to subcutaneous fat, with posterior acoustic enhancement. A microlobulated contour is often more readily demonstrated on sonography than mammography.

Gross examination of these tumors shows a glistening and gelatinous nodule with pushing margins and a soft, viscous consistency. The tumor size ranges from <1 to >20 cm. The histopathological appearances of PMC consist of clusters or sheets of neoplastic cells suspended in abundant extracellular mucin, partitioned by delicate fibrous septa containing capillary blood vessels. The tumor clusters vary in size and shape. Nuclear grade is low or intermediate. Tumors with high nuclear grade have been described, but they are best classified as invasive breast carcinoma-NST with mucin production. Furthermore, pure MC may be classified as hypocellular (PMC-A) and hypercellular (PMC-B). The difference between these 2 subtypes lays in their growth pattern. The hypocellular variant may have different growth patterns (tubular, cribriform, cord-like, papillary, or micropapillary), and the hypercellular type shows only a single pattern, spreading outward in solid nests that often show neuroendocrine differentiation. The mean metastatic rate is 15% and the prognosis is better compared to no special type breast cancer. Other mucin-producing carcinomas of the breast include a variety of carcinomas that are characterized by the

Figure 3. Immunohistochemistry 10× magnification: the neoplastic cells were strongly positive for ER (a), PR (b), without superexpression of HER2/neu (c), and a week proliferation index evaluated by Ki-67 (d).
production of abundant extracellular and/or intracellular mucin. Among these are mucinous cystadenocarcinoma, columnar cell mucinous carcinoma, and signet ring cell carcinoma. All of these tumors must be excluded to retain MCs. Carcinomas with signet-ring cells without extracellular mucin are not classified as MCs. Primary carcinomas of the breast with signet-ring cell differentiation must be distinguished from metastases to the breast from signet-ring cell carcinomas from other organs, in particular from the gastrointestinal tract.

The differential diagnosis of MC includes non-neoplastic mucocele–like lesions (MLLs) with stromal mucin and it may be challenging to distinguish MCs from MLLs, especially in core biopsy material. The absence of cytological atypia in the epithelium lining the mucin-filled ducts and the presence of myoepithelial cells adherent to the detached epithelial strips present in the mucin pools favor a non-atypical MLL over MC. MC is usually positive for ER and PR, and it is positive for AR in 80% of cases. ERBB2 (HEB2) overexpression and/or amplification is rare in MC but is found in >10% of MCs with a micropapillary pattern. Pure and mixed MCs express WT1 and GATA3.

The rarity of these entities has impaired the possibility of an extensive clinical evaluation. Most of the information on outcome and treatment comes from small series and case reports. Therefore, clear recommendations concerning clinical management are still lacking. The 2014 NCCN Guidelines include specific treatment recommendations for favorable mucinous histotypes. In a hormone receptor-positive tumor with absence of nodal involvement, adjuvant endocrine therapy can be avoided if tumor size is less than 1 cm. If T is between 1 and 3 cm, endocrine therapy should be considered, and it is recommended for T greater than 3 cm. However, with nodal involvement endocrine therapy is indicated with or without chemotherapy.

Pure MC is associated with low rates of local and distant recurrence and has an excellent 5-year disease–free survival. Late distant metastases may develop. There is no prognostic difference between type A and type B MCs. In one retrospective series, MCs with a >50% micropapillary component had a significantly worse prognosis. Data obtained from our case are similar to other clinical studies interested to clinical, pathological outcomes, biological profiles, and therapeutic methods of this rare tumor.

Our aim is mainly to add a new case in the series of this rare entity in breast cancer, hence to remind its diagnostic difficulties contrasting with the simplicity of effective management.

Conclusion
Mucinous carcinoma should be in the differential diagnosis when imaging microlobulated masses of the breast. Even though mucinous carcinoma is an invasive breast cancer, it tends to be a less aggressive type that responds well to treatment. A simple and rapid core needle biopsy gives important information about this tumor and optimize its treatment.

Author Contributions
Fayrouz Rabbi and Fatima Zohra Soussi collected the clinical findings. Ouafae Karmouni collected radiological images. Karima Idrissi Serhrouchni, Jinane Kharmoum and Mariame Chraibi analysed and interpreted the specimen. Karima Idrissi serhrouchni wrote the manuscript. All authors critically revised the manuscript.

Declaration of Patient Consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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REFERENCES
1. Rosai J. Rosai and Ackerman’s Surgical Pathology. Chapter 36. 10th ed. Elsevier; 2011:1383.
2. Di Saverio S, Gutierrez J, Arivor E. A retrospective review with long-term follow up of 11,400 cases of pure mucinous breast carcinoma. Breast Cancer Res. 2008;11:541-547.
3. Makki J. Diversity of breast carcinoma: histological subtypes and clinical relevance. Clin Med Insights Pathol. 2015;8:23-31.
4. Marrazzou E, Frusone F, Milana F, et al. Mucinous breast cancer: a narrative review of the literature and a retrospective tertiary single-centre analysis. Breast. 2020;49:87-92.
5. DiCierto MV, Orvieto E, Dominici M, Conte P, Guarrneri V. Rare breast cancer subtypes: histological, molecular, and clinical peculiarities. Oncologist. 2014;19:805-813.
6. Tan PH, Tse GM, Bay BH. Mucinous breast lesions: diagnostic challenges. J Clin Pathol. 2008;61:11-19.
7. Harvey JA. Unusual breast cancers: useful clues to expanding the differential diagnosis. Radiology. 2007;242:683-694.
8. Wilson TE, Helvie MA, Oberman HA, Joynt LK. Pure and mixed mucinous carcinoma of the breast: pathologic basis for differences in mammographic appearance. AJR Am J Roentgenol. 1995;165:285-289.
9. Conant EF, Dillon RL, Palazzo J, Ehrlich SM, Feig SA. Imaging findings in mucin-containing carcinomas of the breast: correlation with pathologic features. AJR Am J Roentgenol. 1994;163:821-824.
10. Lam WW, Chu WC, Tse GM, Ma TK. Sonographic appearance of mucinous carcinoma of the breast. AJR Am J Roentgenol. 2004;182:1069-1074.
11. Dilani L, Valeria AW, Reiko W, Ian AC. WHO Classification Pathology and Genetics of Tumours of the Breast. 5th ed. Chapter 2 IARC Press; 2019:123.
12. Ranade A, Batra R, Sandhu G, Chitale RA, Balderacchi J. Clinicopathological evaluation of 100 cases of mucinous carcinoma of breast with emphasis on axillary staging and special reference to a micropapillary pattern. J Clin Pathol. 2010;63:1043-1047.