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Case Report

Pathology Section

Mucinous Cystadenocarcinoma Coexisting with Invasive Ductal Carcinoma of the Breast: A Rare Case Report

SANDEEP MANI[1], SWETHA LAKSHMI NARLA[2]

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ABSTRACT

Mucinous Cystadenocarcinoma (MCA) of the breast is a rare variant of primary breast cancer with an unknown aetiology and pathogenesis. It resembles MCA of the ovary and pancreas and accounts for about one to four percent of primary breast cancers. Less than 25 cases of primary breast MCA have been reported in the literature. These tumours belong to the family of mucin-producing carcinomas of the breast, which includes mucinous carcinoma, signet ring cell carcinoma, columnar cell mucinous carcinoma, and MCA. MCA presents as a well-circumscribed, solid, and cystic mass. It contains large cystic spaces filled with mucin and is lined by atypical columnar cells with intracytoplasmic mucin. In addition to routine examination of Haematoxylin and Eosin (H&E)-stained slides, immunohistochemistry is necessary for the accurate diagnosis of primary breast MCA and to differentiate it from pure mucinous carcinoma. These tumours typically do not express hormonal receptors, making them triple-negative. The authors report a case of a 49-year-old woman who presented with a lump in her left breast. Ultrasonography (USG) suggested the possibility of carcinoma or atypical fibroadenoma. Fine Needle Aspiration Cytology (FNAC) indicated features suggestive of carcinoma. A trucut biopsy revealed infiltrating ductal carcinoma with mucinous features. Subsequently, a left-modified radical mastectomy was performed, and the patient was diagnosed with mixed-type carcinoma, comprising an 80-85% MCA component and a 15-20% invasive ductal carcinoma component.

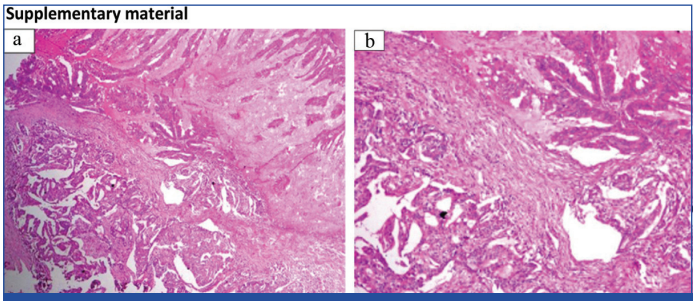
Keywords: Mixed carcinoma, Mucin-producing carcinomas, Postmenopausal

CASE REPORT

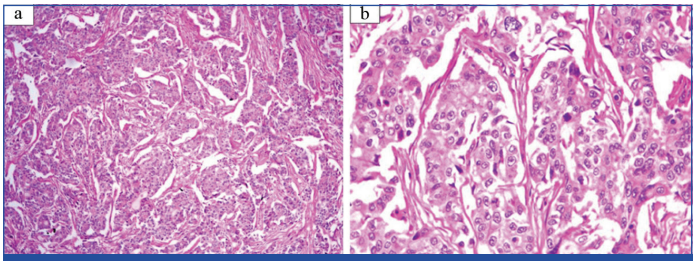
A 49-year-old woman noticed a lump in her left breast for around one to two months. She did not have any significant pain, discharge, trauma, past, or family history. On palpation, an ill-defined soft-to-firm mass measuring approximately 20×20 mm was noted in the upper outer quadrant of the left breast with an unremarkable nipple and areola. The examination of the right breast was unremarkable. No palpable axillary lymph nodes were seen. Ultrasonography of the left breast performed elsewhere showed a heterogenous hypoechoic mass with irregular margins measuring 24×18 mm, with evidence of calcification noted at the center of the mass. Due to its circumscription, the possibility of carcinoma versus atypical fibroadenoma was suggested and FNAC correlation was advised. FNAC of the left breast lump was performed elsewhere, stating that smears are cellular with cohesive groups and singly scattered atypical cells having hyperchromatic nuclei, an irregular nuclear membrane, nucleoli, and an increased nuclear-cytoplasmic ratio, which are reported as features suggestive of carcinoma. Positron Emission Tomography-Computed Tomography (PET-CT) was done, which showed a hypermetabolic malignant mass in the left breast abutting the chest wall. The right breast was normal. No significantly enlarged axillary nodes were seen, and there were no hypermetabolic areas suggesting nodal metastasis. Imaging features were suggestive of left breast malignancy with no regional or distant metastasis. As a part of the work-up, trucut biopsy of the left breast mass was done, which showed features of infiltrating ductal carcinoma with mucinous features, the Elston-Ellis modification of the Scarff-Bloom Richardson grading system (NMBRS) Grade 2. Immunohistochemistry was positive for Oestrogen Receptor (ER), negative for Progesterone Receptor (PR), and Human Epidermal Growth Factor Receptor 2 (HER2). After a thorough preoperative evaluation, the patient underwent a left modified radical mastectomy. Gross examination showed a well-circumscribed grayish-white, firm, lobulated lesion with cystic spaces filled with mucinous material measuring 3×2.7×2.2 cm. The rest of the breast tissue showed few fibrous areas, and the overlying skin, nipple, and areola were unremarkable. The lesion had a closest clearance of 0.8 centimetres from the deep resected margin. On dissection, 18 lymph nodes were identified in the axillary fat, ranging in size from 0.4 to 1.2 centimetres with greyish-tan cut surfaces.

Histologically, the left breast tissue showed a malignant tumour with dual histomorphologic features [Table/Fig-1-3]. One component showed expanded ducts with papillary proliferations and hierarchical branching. These papillae were lined by columnar cells with stratification. Both intracellular and extracellular mucin were seen. The degree of cytological atypia was variable, with some showing

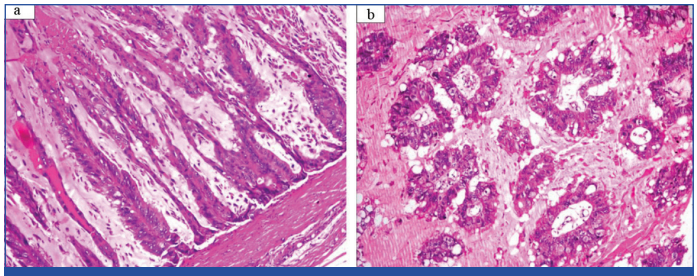
Supplementary material



[Table/Fig-1]: Malignant tumour with dual histomorphological features {a&b in 10x and 20x, respectively (H&E)}.



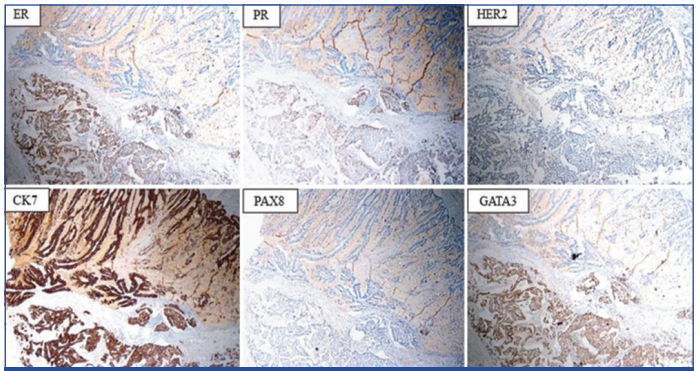
[Table/Fig-2]: Invasive ductal carcinoma components arranged as nests and islands {a&b in 10x and 20x, respectively (H&E)}.



[Table/Fig-3]: Mucinous component showing both intracellular and extracellular mucinous areas with papillary proliferations and hierarchial branching {a&b in 10x and 20x, respectively (H&E)}.

bland mucinous epithelium with basally placed nuclei and abundant intracytoplasmic mucin, while others displayed severe nuclear atypia with mucin depletion. This represents the MCA component. In addition, there were infiltrating areas seen as a second component, arranged as nests and islands separated by desmoplastic stroma with a moderate peritumoural lymphoid response. This represents the invasive ductal carcinoma component. Mitotic activity of 20-22 per 10 high-power fields was seen in both components, with rare atypical forms of mitoses noted in the invasive ductal carcinoma component. The adjacent breast tissue showed solid, cribriform, and papillary patterns of intermediate-grade Ductal Carcinoma In-situ (DCIS). There was no lymphovascular or perineural invasion, and no evidence of necrosis. All margins were free of tumours. Focal fibrosis was noted in the adjacent breast parenchyma. All 18 lymph nodes submitted showed reactive changes. A second opinion was obtained from a senior consultant, and the case was reported as a mixed-type carcinoma {MCA component (80-85%) and invasive ductal carcinoma component (15-20%)}.

The MCA components in Immunohistochemistry (IHC) showed positive immunoreactivity with cytokeratin seven (diffuse cytoplasmic) and androgen receptor (weak nuclear) and were negative for ER ("0" nuclear immunostain), PR ("0" nuclear immunostain), HER2 ("0" membraneimmunostain), GATA Binding Protein 3 (GATA-3) (nuclear), Paired-Box Gene 8 (PAX-8) (nuclear), Cytokeratin 5/6 (CK5/6) (cytoplasmic), CK20 (cytoplasmic), and Caudal-Type Homeobox 2 (CDX2) (nuclear) [Table/Fig-4]. Evaluation of ER and PR was done based on the Allred score, which combines the percentage of positive cells and the intensity of the reaction product. Immunostains in the invasive ductal carcinoma component showed positive staining for ER (70-75%, 2+ immunostain, 7/8 Allred score), PR (40-45%, 1+ immunostain, 5/8 Allred score), Cytokeratin 7 (diffuse), GATA-3, Androgen receptor (weak), and negative staining for CK20, HER2 ("0" immunostain), CDX2, PAX8, and CK5/6. Hence, it was confirmed as a mixed-type carcinoma. However, proliferation marker p53 and further genetic studies for chromosomal aberrations were not performed. The patient did not receive any adjuvant chemotherapy or radiotherapy following surgery.



[Table/Fig-4]: Immunohistochemistry of ER, PR, HER2, CK7, PAX8, and GATA-3 in the MCA component (upper half of image) and IDC component (lower half of image) (10x, IHC).

DISCUSSION

Primary mucinous carcinoma (Mucinous cystadenocarcinoma) of the breast is an invasive breast carcinoma with an unknown aetiology and pathogenesis. It was first described by Koenig C and Tavassoli FA in 1998 [1]. Most of these tumours are reported in postmenopausal Asian women, with a median age of 61 years, a median tumour size of 3 cm, and distinctive clinical behaviour. They have a favourable prognosis, with a longer five-year disease-free survival rate of around 90%. Distant metastasis has not been documented. Making a definitive diagnosis of primary breast MCA based on cytology and core needle biopsy is challenging due to its overlap with pure mucinous carcinoma. Grossly, MCA of the breast shows well-circumscribed solid and cystic areas with mucin-filled spaces. Histologically, these tumours are characterised by cystic spaces with tall columnar cell linings exhibiting stratification, tufting, and papillary formations. These cells contain abundant intracytoplasmic mucin, and mucinis also seen within the cystic spaces. These cystic structures lack myoepithelial cells at the periphery [2,3]. These tumours are negative for ER, PR, and HER2. However, rare cases have been reported expressing ER [4], and rare cases also show positive HER2 expression, which can be confirmed by gene amplification. Some cases express CK5/6 [2]. The literature mentions that MCA can develop from a metaplastic process of DCIS [5]. In addition to the MCA component, the present case had a second component of invasive ductal carcinoma with adjacent areas of intermediate-grade DCIS. Thorough examination of the lesion is essential to exclude any associated invasive carcinoma. MCA shows positivity for MUC 5 (mucin) and negativity for MUC 6 and MUC 2 [6].

The differential diagnosis of mucin-producing breast tumours includes columnar cell mucinous carcinoma, signet ring cell carcinoma, mucinous carcinoma, and MCA. They can be differentiated based on histological differences and specific immunohistochemical characteristics. Mucinous carcinomas have clusters of epithelial tumour cells suspended in pools of extracellular mucin. Signet ring cell carcinomas have cells with intracellular mucin. Columnar cell mucinous carcinomas have elongated glands lined by columnar cells with clear cytoplasm and basally located nuclei. MCAs are characterised by cystic structures lined by tall columnar cells with abundant intracytoplasmic mucin [1]. Positivity for CK7 and negativity for CK20, PAX8, and CDX2 help to exclude metastatic MCA from distant organs such as the pancreas, ovary, and appendix [7]. Pure mucinous carcinomas are strongly and diffusely positive for ER and PR, which helps distinguish them from MCA. Despite being triple-negative and having a high proliferation index, MCA of the breast has a favourable biological behaviour and prognosis. Axillary lymph node involvement is uncommon, and distant metastases have not been documented in the literature. Therefore, it is important to accurately diagnose MCA of the breast for appropriate management. Most previously reported cases underwent mastectomy followed by adjuvant therapy, resulting in good prognosis and longer five-year disease-free survival rates [7-10]. However, in the present case, radical mastectomy was performed without adjuvant therapy, and the patient was lost to follow-up.

Although MCA of the breast shares similarities with its counterparts in the pancreas and ovary, they appear to have different embryological origins. While ovarian and pancreatic MCA cases exhibit somatic mutations in the KRAS gene, the genetic profile of breast MCA is not extensively studied due to its rarity [11]. No further genetic work-up was conducted in the present case.

CONCLUSION(S)

Mucinous carcinoma of the breast has a unique morphology that helps distinguish it from other mucin-producing breast tumours. These tumours differ from mucinous carcinoma of the ovary and pancreas in terms of immunophenotype and embryogenesis.

Furthermore, they exhibit a favourable prognosis and longer survival. Therefore, it is crucial to accurately identify this rare variant of breast tumour to develop appropriate treatment protocols.

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PARTICULARS OF CONTRIBUTORS:
1. DNB, Resident, Department of Histopathology, Apollo Cancer Centre, Tamil Nadu, Chennai, India.
2. Consultant, Department of Histopathology, Apollo Cancer Centre, Tamil Nadu, Chennai, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Sandeep Mani,
63/7, Sri Krishna Nagar, Samichettipalayam, Jothipuram Post,
Coimbatore-641047, Tamil Nadu, India.
E-mail: sandysandeep1607@gmail.com

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