CASE REPORT

Malignant myoepithelioma of the breast: case report with review of literature

SUGUNA BV MD, GEETHAMANI V MD, NIVEDITHA SR MD, DNB and MONIKA Lamba Saini MD, DNB*

Department of Pathology, Kempegowda Institute of Medical Sciences, Bangalore and *Department of Pathology, Cliniques St Luc, Universite Catholique de Louvain, Brussels, Belgium

Abstract

Myoepithelial lesions of the breast are extremely rare and can present with a diverse morphology. We report a case of malignant myoepithelioma characterized by proliferation of atypical oval to polygonal cells expressing typical myoepithelial markers. A 45-year-old lady presented with a mass in the left breast. Fine needle aspiration yielded a cellular smear with large papillae-like clusters of monomorphous cells with naked nuclei in the background. A diagnosis of sub-areolar sclerosing duct hyperplasia was made on cytology and the patient underwent excision. The surgical specimen showed a grey-white 5x3 cm mass on cut surface. Histopathology revealed mitotically active (5-6 per 10hpf) oval to polygonal cells tumor cells with clear to eosinophilic cytoplasm arranged in the form of nodules separated by dense sclerotic stroma mimicking clear cell or adenoid-cystic carcinoma. A diagnosis of malignant myoepithelioma was made as the cells were CK14 and SMA positive, and negative for ER and PR on immunohistochemistry. We discuss the unusual morphological features of malignant myoepithelioma, cytological findings and the important differential diagnoses of malignant myoepithelial lesions. A high degree of suspicion with a keen eye for morphological details coupled with relevant immunohistochemistry will aid in arriving at the diagnosis.

Keywords: myoepithelioma, immunohistochemistry, breast, CK14, SMA

INTRODUCTION

Myoepithelial carcinomas of the breast show neoplastic cells with myoepithelial phenotype. Myoepithelial cells are present between ductal epithelial cells and normal basement membrane and have structural characteristics of both smooth muscle and epithelial cells.1 WHO defines malignant myoepithelioma as an infiltrating tumor composed purely of myoepithelial cells (predominantly spindle) with identifiable mitotic activity.2 Pure myoepithelial carcinomas are characterized by an infiltrating proliferation of plump, atypical spindle cells, with identifiable mitotic figures.

Myoepithelial neoplasms composed of polygonal cells with clear cytoplasm are relatively uncommon and have received less attention than spindle cell myoepithelial lesions. The histogenesis of these tumours is not recognized and they are probably misclassified as clear cell, apocrine, secretory or adenoid-cystic carcinoma.3 Also, the trapping of ductular structures in a fibrotic core mimics the appearance of infiltrating carcinoma.4 We present a case which illustrates these diagnostic challenges.

CASE REPORT

A 45-year-old female presented with a firm to hard lump measuring 6 cm in diameter in the sub-areolar region of the left breast. General physical and systemic examination was unremarkable. Routine laboratory parameters were with normal limits. A fine needle aspiration was done which yielded a cellular smear with large papillae-like clusters of monomorphous cells with naked nuclei in the background (Fig 1). A diagnosis of sub-areolar sclerosing duct hyperplasia was made and excision was advised.

Pathology

The excised specimen measured 10x7x3 cms. Cut surface revealed a well-defined, firm to hard grey white 5x3x2 cm mass. Histopathology revealed...
tumour cells arranged in the form of nodules separated by dense sclerotic stroma (Fig 2). Cells were oval to polygonal with eosinophilic to clear cytoplasm (Fig 3). Moderate nuclear pleomorphism with prominent nucleoli was seen. Focal comedo-necrosis and myxoid change were noted. Five to six mitotic figures per 10 hpf were present. Immunohistochemistry (IHC) showed a diffuse cytoplasmic positivity for CK14 and SMA (Fig 4). The cells were negative for ER, PR, synaptophysin and chromogranin. A diagnosis of myoepithelial carcinoma was made.

The patient received adjuvant radiotherapy and is presently doing well.

**DISCUSSION**

Malignant myoepitheliomas of the breast are a rare entity. Myoepithelial carcinomas are also termed basal-like as the myoepithelial cells are present between ductal epithelial cells and normal basement membrane and are located in the basal area of the lobules. The mean age of presentation is usually in the fifth decade. They present as painless nodules in elderly patients. Prasad et al reported a series of myoepithelial carcinomas in patients in the 31-70 year age group with a mean size of 3.5 cms.

Cytological features of benign myoepithelioma include a dual cell population of epithelial and spindle cells, and naked bipolar cells with a background of fibrillar myxoid material. The present case showed monomorphic oval cells in papillae like clusters prompting a diagnosis of sclerosing duct hyperplasia. However, the authors feel that presence of monomorphic cells with naked nuclei in a background of fibrillary myxoid material should raise the suspicion of myoepithelial lesions. The diagnostic criteria for malignant myoepithelioma on cytology are still ambiguous but the WHO definition and few previous cytological and histological descriptions of malignant myoepitheliomas in the literature describe a spindle cell population with unequivocal nuclear atypia, metachromatic background substance and mitoses.

Myoepithelial cells can show divergent

FIG. 1: Papillae-like clusters of monomorphic cells with naked nuclei in the background (FNAC, MGG, x40)

FIG. 2: Tumour cells arranged in nodules separated by dense sclerotic stroma (H&E, x10)
MALIGNANT MYOEPITHELIOMA OF BREAST

Malignant myoepithelioma of breast is a rare tumor, often leading to diagnostic challenges due to its diversity in morphology, therefore complicating the diagnostic process for myoepithelial carcinoma. Myoepithelial neoplasms composed of polygonal cells are relatively uncommon and usually mistaken as examples of clear cell or adenoid-cystic carcinoma. These lesions show an alveolar or nodular pattern of growth and resemble clear cell myoepithelial tumours arising in the salivary glands. The present case also showed oval cells with clear/eosinophilic cytoplasm arranged in a nodular pattern, thus posing a diagnostic challenge.

An appropriate panel of IHC markers is essential for diagnosis of myoepithelial carcinomas due to variability on light microscopy. As none of these markers are specific for myoepithelial differentiation, a combination of positive results, keen eye for morphologic details and excluding close differential diagnoses is essential for arriving at a correct diagnosis. These carcinomas do not show positivity for ER/ER-related genes or HER-2 neu as documented by array data and IHC. In fact, all ER negative breast cancers should be assessed for myoepithelial markers as Kesse-Adu et al have suggested that myoepithelial markers are expressed in 29% of ER negative breast cancers. The expression of cytoplasmic keratin is typical of myoepithelial cells or potential breast progenitor cells. Myoepithelial carcinomas exhibit immunopositivity for LMW keratin using antibodies Cam 5.2, CK 14 and 17. They are negative for CK 18, 19, and desmin.

Myoepithelial cells show positivity for SMA, S-100, and CD10. However, SMA positivity is also seen in myofibroblasts in myoepithelial lesions. Therefore, it is recommended to use a combination of SMA and CD10 to ascertain the nature of myoepithelial cells. The present case also showed polygonal cells arranged in the form of nodules separated by dense sclerotic stroma. Such lesions may sometimes raise the suspicion of infiltrating duct carcinoma due to entrapment of ductular structures in a dense fibrotic stroma. This dilemma can be resolved by using a combination of p63 and SMA as p63 is a sensitive and specific myoepithelial cell marker. Due to financial constraints of the

FIG. 3: Oval to elongated cells with prominent nucleoli and eosinophilic to clear cytoplasm (H&E, x40)

FIG 4: Cells showing SMA positivity (DAB, x10).
laboratory. p63 could not be ascertained in the present case. The differential diagnoses of myoepithelial carcinomas with predominantly spindle cells are leiomyosarcoma, metaplastic spindle cell carcinoma, pure spindle cell sarcoma, and fibronodular carcinoma.1, 11 Leiomyosarcomas typically show blunt-ended nuclei with abundant cytoplasm and positivity for desmin. Metaplastic carcinomas show areas of metaplastic differentiation. Pure spindle cell sarcoma lacks the epithelial component. Fibronodular carcinoma show proliferating spindle cells with a distinctive growth pattern.1 Another important differential diagnoses to be considered is breast fibromatosis which is an infiltrative fibroblastic and myofibroblastic proliferation.13 Since myoepithelial cells present with a varied morphology as seen in this case, it is necessary to broaden the possibilities of differential diagnoses beyond spindle cells to include metaplastic cells, clear cells, apocrine cells or secretory carcinoma.12 A suitable panel of markers including antibodies against epithelial and myoepithelial differentiation, mesenchymal, smooth muscle, neural differentiation would help in clinching the diagnosis of myoepithelial carcinoma.

Breast conservation surgery is appropriate treatment in selected patients but is associated with risk of local recurrence without adjuvant radiotherapy. The role of chemotherapy and choice of agent is not well defined. The role of hormonal therapy is also unknown.

REFERENCES