

Malignant Adenomyoepithelioma of Breast Cytologically Masquerading as Adenoid Cystic Carcinoma: Immunohistochemistry With Review of Literature



Medical Science

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ABSTRACT

Background: Adenomyoepithelioma (AME) breast is a rare epithelial – myoepithelial tumor. Rarely undergoes malignant change. We report a rare case of malignant adenomyoepithelioma (MAME) cytologically masquerading as adenoid cystic carcinoma (ACC) with literature review.

Case report: We here report a case of 50 year old woman with malignant adenomyoepithelioma, whose cytomorphological features were indicative of ACC. Histologically the tumor showed biphasic proliferation of epithelial and myoepithelial cells with focal areas of ACC like pattern. Malignancy was evidenced by infiltration into the surrounding tissue with focal area of necrosis. Immunohistochemistry (IHC) confirmed the diagnosis.

Conclusion: MAME is a rare neoplasm of breast shows spectrum of histological pattern due to which it causes diagnostic confusion. The cytological diagnosis of this neoplasm can be challenging. The cytopathologist should aware of the variable morphological pattern of MAME.

INTRODUCTION:

Adenomyoepithelioma (AME) is an uncommon epithelial myoepithelial neoplasm with different morphological features. In 1970, Hamperl described the first case of AME of breast (Qureshi, Kayani et al. 2009). WHO (2012) has categorized this tumor as benign and malignant (Petrozza, Pasciuti et al 2013). Malignant transformation of either one or both components has been documented in rare tumors, and distant metastases or even death can occur. Because of varied morphology cytologically misinterpreted as fibroadenoma, myoepithelioma, tubular adenoma or carcinoma (Iyengar, Ali et al 2006). Since its recognition few malignant cases have been documented. We here report a case of 50 year old woman with malignant adenomyoepithelioma (MAME), whose cytomorphological features were indicative of Adenoid cystic carcinoma. We have reviewed the available literature.

CLINICAL PRESENTATION AND RESULTS:

A 50 year old woman presented with a history of lump in the right breast one year duration, which was gradually increasing in size. On examination 4.5x3cms hard, partially mobile lump was found. Fine needle aspiration (FNA) cytology was performed. Cytological smears showed cellular loosely cohesive clusters of atypical cells with hyperchromatic nuclei, inconspicuous nucleoli and many hyaline globules were seen admixed with within cellular clusters (Figure 1). Based on these features possibility of ACC was suggested. Trucut biopsy was done based on cytological diagnosis. Trucut biopsy showed cribriform pattern with hyaline globules suggestive of ACC (Figure 2a). Modified radical mastectomy was performed based cytological and trucut biopsy diagnosis. Grossly the tumor was 4x3cm, grey white, lobulated mass with irregular margins involving upper and lower inner quadrant. Nipple and areola were grossly unremarkable. Six lymph nodes were isolated. Microscopically tumor exhibited lobular growth pattern composed of tubulo glandular arrangement lined by inner luminal epithelial cells outer myoepithelial cells with clear cell morphology (Figure 2b). These lobules were separated by pink hyaline material and some of the tubules also showed the same material (Figure 2c). Both epithelial and myoepithelial cells exhibited pleomorphism, atypia and mitoses. Area of necrosis and stromal invasion also noted (Figure 2d). Immunohistochemically the luminal epithelial cells were positive for cytokeratin (CK) (Figure 3a) and luminal membranous positivity for epithelial membrane antigen (EMA) (Figure 3b) and the clear cell myoepithelial cells were positive for S100, smooth

muscle actin (SMA) and p63 confirmed the biphasic component (Figure 3c, d, e). Six lymphnodes were isolated, none of which showed tumor deposit.

DISCUSSION:

AME was first described by Hamperl in 1970, a rare epithelial myoepithelial tumor of breast. Malignant transformation can arise from either of these components or both. It was further histologically classified by Tassoali in 1991 into three variants: spindle cell, tubular and lobulated (Qureshi, Kayani et al. 2009). 2012 WHO has classified AME into benign and malignant (Kalyani and Murthy 2014). Though the histogenesis of this tumor is still unclear, histological, immunohistochemical and ultrastructural features suggest that these tumors arise from the stem cells in the terminal duct lobular unit of breast with an intermediate epithelial/myoepithelial differentiation (Petrozza, Pasciuti et al 2013). Most cases are sporadic. No familial predisposition has been described till now. A review of literature revealed that point mutation of p53 gene has been described in myoepithelial components of these tumors but not in epithelial tumors (Han, Mori et al 2006). A case of MAME with coincident multiple gastrointestinal stromal tumor has been described in a neurofibromatosis type 1 patient (Hegy, Thway et al 2009).

The clinical presentation of MAME has been described in several articles. Literature review revealed that it has been reported in women aged between 26-76 years. Size of the tumor may vary from 1-15cm. tumors > 2cm can have cystic change, necrosis and calcification (Qureshi, Kayani et al. 2009, Kalyani and Murthy 2014). In our case patient was 50 years old. Grossly the tumor was 4.5 cm in size, grey white lobulated solitary mass involving upper and lower inner quadrant.

AME can have spectrum of histological patterns which include tubular, lobulated and spindled type. Myoepithelial cells can be plasmacytoid, clear cell variant or spindle cell type. Moreover myoepithelial cells are known to produce basement membrane like material which can be appreciated as hyaline globules and often confused as collagenous spherulosis. Presence of these hyaline globules can be mistaken for ACC as happened in our case. Because of varied morphology and hyaline globules cytologically misinterpreted as fibroadenoma, myoepithelioma, collagenous spherulosis, tubular adenoma or rarely ACC (Iyengar, Ali et al 2006, Kurashina, 2002). The histological criteria for MAME in-

clude infiltrative growth pattern, necrosis, nuclear pleomorphism, >3mitoses per 10 HPF, overgrowth of myoepithelial component (Kalyani and Murthy 2014). All these above mentioned features were noted in our case. Glandular elements can show apocrine/ sebaceous/ squamous or mucoepidermoid differentiation (Kalyani and Murthy 2014). Myoepithelial elements can show chondroid and osseous differentiation (Simpson, Cope et al 1998). Coexistence of fibroadenoma, adenosis and phyllodes tumor has been described in AME. Literature review revealed rare association of MAME with invasive lobular carcinoma and ACC (Honda and Iyama 2009, Yang, Wang et al. 2014). Though our case had cytological resemblance with ACC on FNA and core needle biopsy, histological examination of excised specimen revealed MAME with focal adenoid cystic like areas. IHC confirmed the diagnosis.

A variety of IHC stains are used to characterize the tumor immunologically. The myoepithelial markers are p63, SMA, calponin, S100, high molecular weight CK 5/6. The epithelial cell markers are EMA, CK and CEA. Our case myoepithelial cells were positive for SMA, S100 and p63. Epithelial component showed positivity for CK and membranous positivity for EMA.

Biological behavior of these tumors are not well established. Metastases appears to be hematogenous rather than lymphatic. Metastasis to lung, brain, liver, bone and thyroid has been described in literature (Kalyani and Murthy 2014, Jones, Tooze et al. 2003, Bult, Verwiel et al. 2000). Though lymphnode metastases is rare it has been described in two cases (Awamleh, Gudi et al. 2012). Our case did not show any metastasis. In our case malignant change was seen in both the components with infiltrative margins, necrosis. Both the components were confirmed immunohistochemically.

CONCLUSION:

MAME is a rare neoplasm of breast shows spectrum of histological pattern due to which it causes diagnostic confusion. The cytological diagnosis of this neoplasm can be challenging. Cytopathologist should be aware of the variable morphological pattern of AME. Also in the presence of hyaline globules, the differential diagnosis of AME should be considered along with collagenous spherulosis and ACC. IHC confirmation is needed in difficult cases.

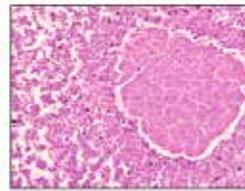


Figure 2d: Necrosis

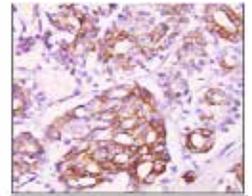


Figure 3a: IHC - CK positivity in epithelial component

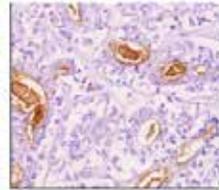


Figure3b: EMA, membranous positivity

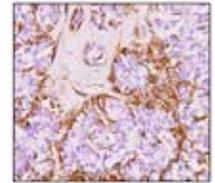


Figure3c: S100 positivity in myoepithelial component

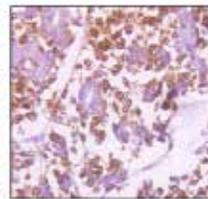


Figure3d: SMA positivity in myoepithelial component

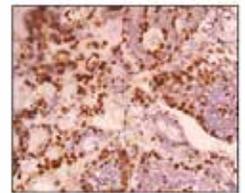


Figure3e: p63, nuclear positivity in myoepithelial component

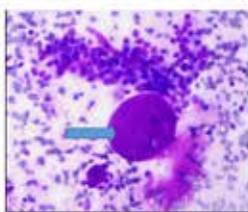


Figure 1: FNAC smear showing loosely cohesive clusters of atypical cells admixed with hyaline globules (arrow).

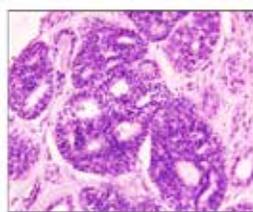


Figure 2a: Trucut biopsy showing ACC like pattern

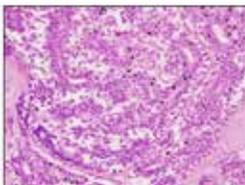


Figure 2b: Mastectomy sections showing tubulo glandular inner epithelial cells surrounded by clear cell myoepithelial cells

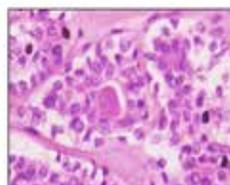


Figure 2c: hyaline globules

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