Case Report

Breast adenomyoepithelioma with ductal carcinoma *in situ*: An unusual entity

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ABSTRACT

Adenomyoepithelioma is a rare biphasic tumor characterized by the proliferation of inner glandular epithelial cells and outer myoepithelial cells. These tumors have a low-grade potential for local recurrence and malignant transformation. Here, we present the case of a 51-year-old female who presented with a right breast lump for 1 month. Mammography was suggestive of BIRADS 4/5 for the right breast while BIRADS 1 for the left breast. FNAC was reported as benign breast disease, whereas, trucut biopsy of the same lesion was suggestive of invasive ductal carcinoma with ductal carcinoma *in situ* (DCIS). A final diagnosis of adenomyoepithelioma with DCIS component was confirmed on the right modified radical mastectomy. We, hereby, describe an extremely unusual case of biphasic breast adenomyoepithelioma that depicted benign features on FNAC and features of an invasive ductal carcinoma on trucut biopsy. Its distinct histomorphology with a characteristic epithelial-myoepithelial immunohistochemical profile on modified radical mastectomy specimen led to a definitive diagnosis of adenomyoepithelioma with DCIS.

Key words: Adenomyoepithelioma, Breast, Ductal carcinoma *in situ*, Immunohistochemistry

Breast adenomyoepithelioma (AME) is an unusual, biphasic neoplasm that occurs more commonly among middle-aged females. It was first reported by Hamperl in 1970 and described by Tavassoli in 1991 [1]. AME depicts well-circumscribed, encapsulated, and multinodular architecture with a spectrum of histomorphological patterns depending on the distribution of proliferating tall lining epithelial cells (arising from terminal duct lobular unit) and spindled/clear/polygonal myoepithelial basal cells. AME can also be found in the salivary gland, lung, and skin/adnexa. Among more than 150 cases reported, approximately 40 tumors exhibit malignant profiles as infiltrative borders, high mitosis, severe atypia, necrosis, and/or metastasis of either epithelial or myoepithelial cells with a tendency for local invasion and recurrence [2,3]. Only five cases of adenomyoepithelioma with ductal carcinoma *in situ* (DCIS) have been reported in the English literature to date as shown in Table 1 [4-6].

Here, we will highlight fine-needle aspiration cytology (FNAC) features with trucut breast biopsy findings and further confirmation of histomorphology of AME with DCIS on modified radical mastectomy (MRM) specimen.

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CASE REPORT

A 51-year-old premenopausal P2L2 woman is a known case of hypothyroidism for the past 10 years. She noticed a lump of 5 × 4 cm in the upper-outer quadrant of the right breast for 1 month. On examination, the vitals were stable. No nipple discharge/axillary lymphadenopathy was present.

Hematology parameters reveal hemoglobin of 12.5 gm/dl, total leukocytes count of 7500/mm^3, and platelets of 2.7 × 10^5/mm^3. Biochemical values comprise serum bilirubin of 0.9 gm/dl, serum urea of 18 mg/dl, serum creatinine of 0.8 mg/dl, serum cholesterol of 177 mg/dl, and blood sugar fasting of 89 gm/dl. X-ray chest PA view and echocardiography were within normal limits. Ultrasonography of the right breast showed multiple cystic-like lesions, the largest measuring 9.6 × 5.6 mm with a dilated ductal system (BIRADS III/IV).

Mammography of the right breast revealed an ill-defined, moderately increased density in the superolateral quadrant of the right breast (BIRADS 4/5) and mildly increased density in the left breast (BIRADS 1) (Fig. 1). FNAC of the lump was performed and showed a bimodal population of epithelial and myoepithelial cells arranged in cohesive patterns with bare nuclei in the background thus reported as benign breast disease (Figs. 2a-c). Trucut biopsy of the lesion was reported as infiltrating ductal carcinoma with DCIS (Figs. 2d-f).

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The patient underwent the right MRM with axillary lymph nodes dissection. Gross examination of the right MRM specimen measuring 17.4 × 16.8 × 4.9 cm showed multifocal circumscribed growths, largest in the outer upper quadrant measuring 2.1 × 1.2 × 0.9 cm. The growth is well away from all resected margins with an unremarkable nipple-areola.

Hematoxylin and eosin-stained sections from growth showed a biphasic tumor comprised circumscribed, multinodular patterns with a compact proliferation of epithelial and myoepithelial cells. Small round or oval glandular lumen lined by cuboidal epithelial cells surrounded by polygonal-/spindle-shaped myoepithelial cells seen. Predominant areas of pure spindled myoepithelial cell proliferation with focal palisaded arrangements were seen in the background. Foci of solid, cribriform intraductal papillary ductal carcinoma *in situ* (intermediate nuclear Grade 2), apocrine changes, adenosis, hyalinization, and sclerosis were seen (Figs. 3a-d). No cellular pleomorphism/mitosis/necrosis or invasion of the surrounding tissue was present. Nineteen axillary lymph nodes were dissected, all were free from tumor. Due to the prominence of spindle cell components, differential diagnosis of myoepithelioma, leiomyoma, schwannoma, neurofibroma, and fibroadenoma with sclerosing adenosis were considered.

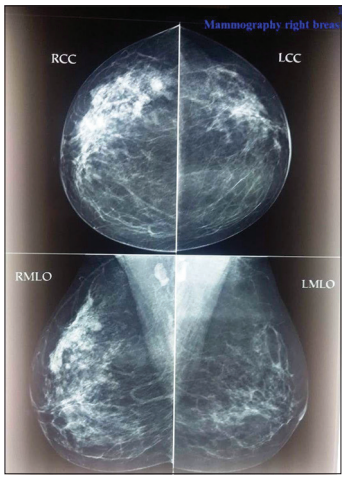

Figure 1: Mammography of the right breast shows an ill-defined lesion with moderately increased density in superolateral quadrant

The immunohistochemical profile showed CK7, estrogen receptor (ER; Allred score 4/8), and progesterone receptor (PR; Allred score 4/8) positive in epithelial/DCIS component, whereas, vimentin, S100, calponin, and p63 positivity indicate myoepithelial nature of spindle cells (Figs. 3e-l). Therefore, based on characteristic histomorphological features and immunohistochemical profile, a definitive diagnosis of the lobulated variant of adenomyoepithelioma with DCIS was offered. The previous trucut biopsy slides were reviewed and observed that AME can be misdiagnosed as invasive ductal carcinoma due to pathogenic heterogeneity and the multinodular nature of the tumor. The patient did not receive any adjuvant chemo/radiotherapy and is presently doing well with 6 monthly follow-up.

DISCUSSION

The World Health Organization (WHO) defines adenomyoepithelioma as benign tumors composed of a biphasic proliferation of phenotypically variable myoepithelial cells around small epithelial-lined spaces. Tavassoli described these tumors to have (a) spindle growth pattern (predominance of spindled myoepithelial cells with sparse/compressed epithelial-lined spaces resembling leiomyoma), (b) tubular growth pattern (small, round tubules lined by luminal epithelial cells and more prominent/hyperplastic myoepithelial cells resembling tubular adenoma), and (c) most common lobular growth pattern (solid nests of eosinophilic/clear/plasmacytoid myoepithelial cells proliferating around epithelial-lined spaces) [1]. Its lobulated AME or adenomyoepithelial adenosis shows thick fibrocollagenous septa with multinodular architecture and forms microscopic satellite nodules at the periphery of the tumor. The glandular structures are composed of an inner layer of epithelial ductal cells having eosinophilic cytoplasm, sharp margin, round nucleus, inconspicuous nucleoli surrounded by nests or nodules of the proliferating outer layer of myoepithelial cells. The histomorphological similarity of lobulated AME with myoepithelial/stromal cell-rich structures makes pre-operative

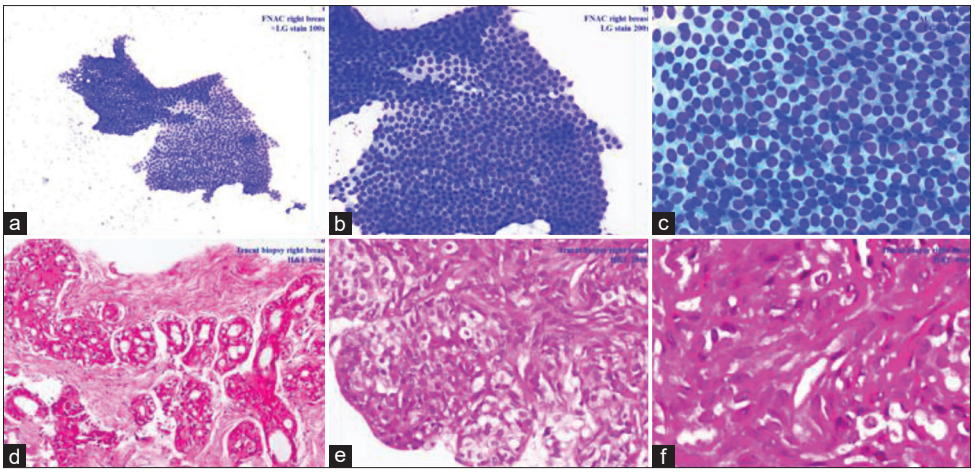

Figure 2: FNAC smears (a-c) show bimodal population of epithelial and myoepithelial cells arranged in cohesive patterns with bare nuclei in the background. H&E section of trucut biopsy (d-f) shows features of benign epithelial myoepithelial proliferation with foci of DCIS

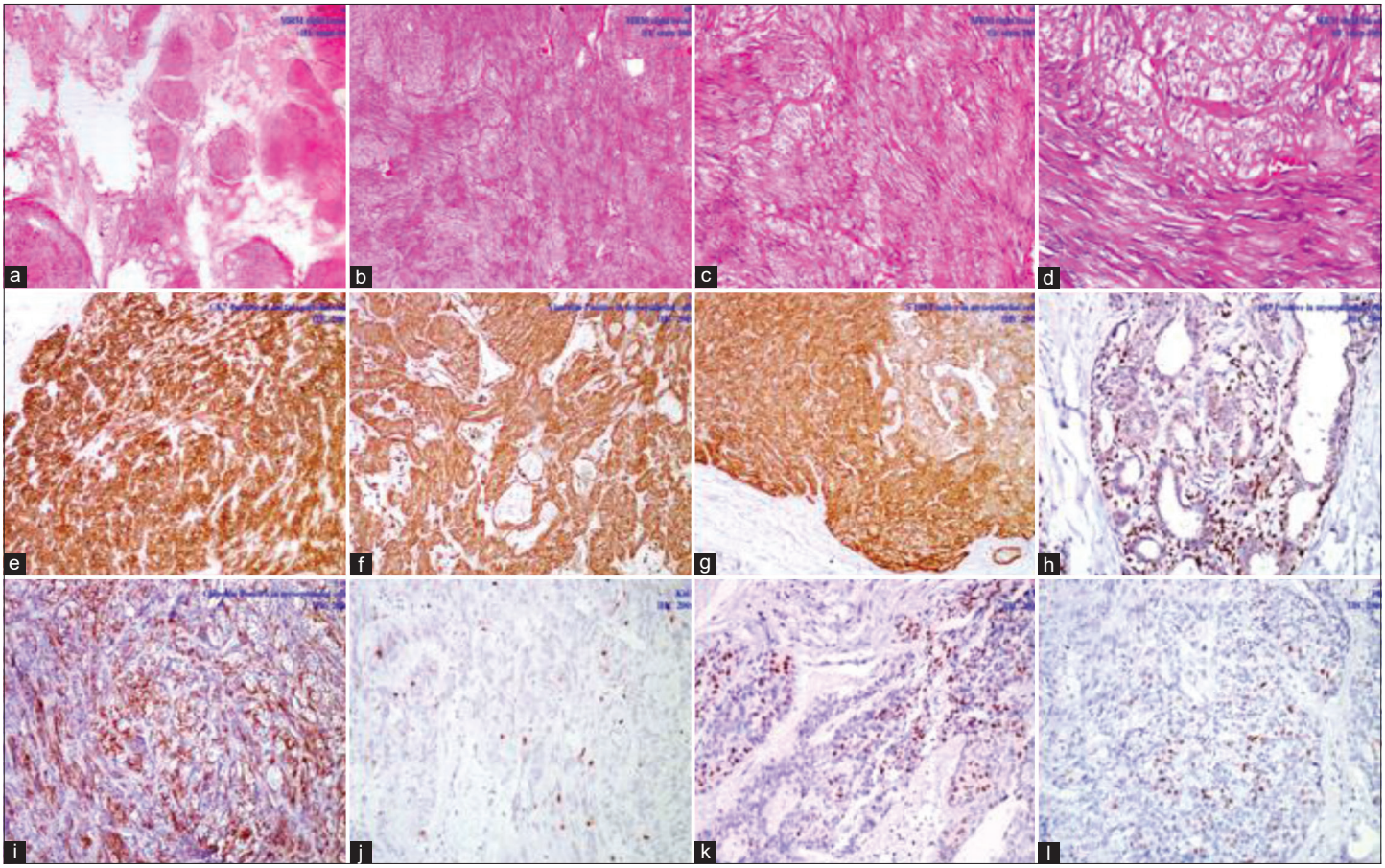

Figure 3: H&E sections of the right MRM show a biphasic tumor comprised circumscribed, multinodular pattern (a-d). Immunohistochemical profile of CK7 positivity in ductal epithelial cells (e; ×200), whereas, myoepithelial cells vimentin (f) S-100 (g), p63 (3h), calponin (i), and low ki67 (j) noted. Epithelial cells show nuclear positivity for ER (k) and PR (l)

Table 1: Cases of adenomyoepithelioma with DCI

Author	Year	Age	CC	MMG findings	USG findings	MRI findings	Cytology	Operation	DCIS within or out of AME	Biopsy
Awamleh *et al*. [2]	2012	41	-	-	-	-	Benign	WLE	Within	AME+DCIS
Lee *et al*. [3]	2015	55	Mass	Well circumscribed	Solid cystic mass	Abnormal enhancement	-	BP-BT	Within	AME+DCIS
Warrier *et al*. [4]	2013	55	Mass	Within normal limits	Solid mass with dilated duct	No record	Benign with atypia	BP+SLNB+BT	Out	AME+DCIS
Zhu *et al*. [5]	2015	51	Mass	-	Heterogeneous, ovoid, irregular	-	-	BP	Out	AME+DCIS
Kemei *et al*. [6]	2015	71	Bloody discharge	Well circumscribed	-	Early peak washout	-	BT+SLNB	Out	AME+DCIS
Present case	-	51	Mass	Ill defined	Multiple cyst-like lesions	Not done	Benign	BT+SLNB	Out	AME+DCIS

CC: Chief complaint, MMG: Mammography, USG: Ultrasonography, MRI: Magnetic resonance imaging, WLE: Wide local excision, BP: Partial mastectomy, BT: Radical mastectomy, SLNB: Sentinel lymph node biopsy, AME: Adenomyoepithelioma, DCIS: Ductal carcinoma *in situ*

diagnosis difficult due to non-specific radiological findings on ultrasound and mammography including the index case [7].

The differential diagnosis include microglandular adenosis (highly infiltrative borders, non-lobular architecture with uniform round glands, and an absence of myoepithelial cells), tubular carcinoma (larger, irregular glands with angular pattern in desmoplastic stroma) fibroadenoma with sclerosing adenosis, pseudoangiomatous stromal hyperplasia (anastomosing vascular spaces and stromal myofibroblastic cells present), desmoid-type fibromatosis (infiltrative spindle cells arranged as fascicules in collagenous stroma), benign phyllodes (Bcl2 positive), pleomorphic adenoma (chondromyxoid stroma

with chondroid/osseous metaplasia), myofibroblastoma (bulging, curved clefts with whorled pattern), inflammatory myofibroblastic tumor, schwannoma, neurofibromas, nipple adenoma (florid ductal hyperplasia, pseudoinfiltrative pattern of stromal sclerosis entrapping glandular epithelium), and myxoid hamartoma or leiomyoma (exclusive spindle cell component, immunohistochemically positive for CD34 and negative for pan-cytokeratin, and actin) [8,9].

The diagnosis of AME on trucut core biopsy may be challenging/mistaken for invasive carcinoma due to morphologic heterogeneity, especially in tumors with compact glandular structures and clear cell epithelioid myoepithelial proliferation, as happened in the index case. However, careful observation of regularly spaced, unidirectional streaming of the rounded/ovoid glands, and prominent spindle or clear cell myoepithelium favor AME over invasive ductal carcinoma.

As AME has a propensity for hematogenous spread, therefore axillary dissection is considered overtreatment. Optimal treatment of adenomyoepithelioma is complete excision with appropriate margins or breast conservation surgery with long follow-up is recommended to prevent local recurrence. Local recurrences are managed by reexcision or radiotherapy. The response to imatinib therapy needs to be evaluated on a larger scale with further research.

CONCLUSION

We have described an extremely rare case of biphasic tumor of the breast with the presence of ductal epithelial cells and myoepithelial cells indicating benign features on FNAC. However, it was reported as invasive ductal carcinoma on trucut core biopsy due to its morphologic heterogeneity and multinodularity of disease. Due to this reason, the exact diagnosis is of paramount importance for accessing clinical behavior and optimal treatment of the disease.

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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