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Original Article

Imaging Features of Benign and Malignant Adenomyoepithelioma of Breast – A Rare Entity

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Abstract

Purpose: The aim of the study was to retrospectively analyze the imaging features of AME of breast and possible imaging features that differentiate AME from other breast lesions and benign AME from the malignant AME.

Materials and Methods: The histologically proven cases of AME from 2004 to 2020 were identified from the pathology database. A total of 7 cases were identified. The clinical details were obtained from the hospital case records and the imaging database. The histopathology results were blinded and the USG and mammography of the patients were retrospectively reviewed. All the cases were analyzed individually by two radiologists and the breast imaging reporting and data system (BIRADS) category was assigned.

Results: A total of seven female patients were analyzed. The mean age was of 54 years (Range 32–76 years). The mammography was not available for all the patients. The USG findings such as size, shape, orientation, margin, echogenicity, posterior features, presence of calcifications, and vascularity as well as associated findings such as architectural distortion and skin thickening were evaluated. The lesions were classified according to American College of Radiology BIRADS. Radiological and histopathological correlation was done.

Conclusion: There is neither specific imaging feature to differentiate AME from other breast lesions nor in differentiating benign AME from malignant lesions. Imaging aids in the evaluation of occult axillary node involvement or to evaluate for distant metastasis. Despite being a rare entity it is essential to consider these lesions in the differential diagnosis of solid/solid cystic lesions due to the necessity of complete excision.

Key words: Adenomyoepithelioma, Biphasic tumor of breast, Recurrent breast lesion, Solid cystic breast tumor

INTRODUCTION

Adenomyoepithelioma (AME) of the breast is characterized by simultaneous proliferation of ductal epithelial and myoepithelial elements. Even though the majority of these lesions are benign they have the tendency to recur locally and may undergo malignant transformation. Despite being rare, it is essential to consider this entity in the differential diagnosis of solid or solid cystic lesions noted in mammogram or ultrasound (USG). However, a definite diagnosis is achieved with histopathologic correlation. In this retrospective study, we intend to study the various imaging features AME of the breast in mammogram and USG.

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MATERIALS AND METHODS

The histologically proven cases of AME from 2004 to 2020 were identified from the pathology database. A total of seven cases were identified. The clinical details were obtained from the hospital case records and the imaging database. The histopathology results were blinded and the USG and mammography of the patients were retrospectively reviewed from the imaging database. All the cases were analyzed individually by two breast

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radiologists and the breast imaging reporting and data system (BIRADS) category was assigned.

All seven patients had undergone preoperative imaging with sonomammography. Sonomammography was performed using a linear array high-frequency transducer (7–15 MHZ) in the Toshiba Aplio 500 machine. The mammogram was available for four patients. Conventional craniocaudal and mediolateral oblique views along with digital tomosynthesis were performed on the AMULET Innovality machine. One patient had undergone a contrast-enhanced computed tomography scan as metastatic work up for malignant AME. USG-guided core needle biopsy (CNB) was performed using 14G automated gun and the samples were immersed in formalin and sent for histopathological examination.

We retrospectively analyzed the USG findings for factors such as size, shape, orientation, margin, echogenicity, posterior features, presence of calcifications, and vascularity as well as associated findings such as architectural distortion and skin thickening (ST) on USG. The lesions were classified according to American College of Radiology BIRADS. Radiological and histopathological correlation was done.

RESULTS

A total of seven female patients were analyzed. The mean age was of 54 years (Range 32–76 years). The initial clinical presentation was a palpable non-tender mass in six patients. One patient was detected on routine screening breast imaging. Clinical examination was otherwise unremarkable, with no evidence of associated lymphadenopathy or nipple retraction in any cases. USG-guided CNB was done in all patients.

Details of the clinical and pathological features of seven adenomyoepithelial tumors seen at our institution are summarized in Table 1.

USG features of benign and malignant are summarized in Table 2. The size of the lesions ranged from 1 to 4.2 cm. All the benign AMEs (n = 4) showed circumscribed margin, parallel orientation, posterior enhancement, and were categorized under BIRADS 4A [Figures 1 and 2]. Among the benign AMEs (n = 4), two lesions (n = 2) were oval, complex cystic-solid with mild vascularity in solid components, and two others (n = 2) were irregular, hypoechoic with minimal internal vascularity.

The malignant lesions revealed irregular shape, spiculated margin, non-parallel orientation, a combined pattern of posterior features, and vascularity and were categorized under BIRADS 4C [Figures 3 and 4]. The internal echogenicity of two lesions was complex cystic and solid, one lesion was solid hypoechoic. Surrounding architectural distortion and ST were seen in one of the malignant lesions. None of the lesions had associated suspicious axillary lymphadenopathy. One malignant lesion (invasive carcinoma of no special type arising in a background of AME) had metastasis to the lung and liver.

All four patients with benign AME underwent an excision biopsy. Two malignant patients had undergone modified radical mastectomy. One patient with malignancy had an image-guided Tru-Cut biopsy and lost to follow-up. None of the patients received chemotherapy or radiotherapy. Follow-up of the four (two benign and two malignant lesions) out of seven patients are uneventful. The remaining two benign and one malignant patient were lost to follow-up.

DISCUSSION

Hamperl was the first person to describe AME in 1970.[1] The normal acini and ductal network are lined by an inner epithelial layer and an outer layer of myoepithelial cells, and a basement membrane separating the myoepithelial cells from the stroma.[2,3] Adenomyoepithelial tumors are characterized histologically by the simultaneous proliferation of ductal epithelial and myoepithelial cells.

Most commonly these lesions are seen in women.[4] It is seen in women of all ages, ranging from 20 to 90 years with a mean age of 60 years.[5,6] Rare cases have been described

Table 1: Summary of clinical and histopathological features

Pt	Age	Symptom	Side	Multiplicity	Procedure	Histopathology
1	56	Palpable mass	Right	Single	CNB, EX	AME
2	32	Asymptomatic (screening USG)	Left	Single	CNB	AME
3	49	Palpable mass	Left	Single	CNB, Ex	Sclerosing adenosis with AME
4	33	Palpable mass	Left	Single	CNB	AME
5	69	Palpable mass	Right	Single	CNB, MRM	Invasive carcinoma of no special type arising in a background of AME
6	76	Palpable mass	Right	Single	CNB, Ex	Adenomyoepithelial carcinoma
7	67	Palpable mass	Left	Single	CNB, MRM	Carcinosarcoma in a background of AME

CNB = Ultrasonography-guided core needle biopsy, Ex: Excision; Pt: Patient; MRM: Modified radical mastectomy; USG: Ultrasound; AME: Adenomyoepithelioma

Table 2: Summary of USG features of benign and malignant AME

Patient	Shape	Size (cm)	Orientation	Margin	Echogenicity	Posterior features	Calcification	Associated Features (SAD, ST)	Vascularity	BIRADS
1	Oval	1.5 × 0.7	Parallel	Circumscribed	Complex cystic and solid	E	No	No	No	4A
2	Irregular	1.4 × 1.0	Parallel	Circumscribed	Hypoechoic	E	No	No	Yes	4A
3	Oval	1.1 × 0.8	Parallel	Circumscribed	Complex cystic and solid	E	No	No	No	4A
4	Irregular	4.2 × 2.5	Parallel	Circumscribed	Hypoechoic	E	No	No	Yes	4A
5	Irregular	1.0 × 0.9	Non parallel	Spiculated	Hypoechoic	Combined pattern	No	No	Yes	4
6	Irregular	3.5 × 3.0	Non parallel	Spiculated	Complex cystic and solid	Combined pattern	No	SAD, ST	Yes	4C
7	Irregular	2.8 × 2.2	Non parallel	Spiculated	Complex cystic and solid	Combined pattern	No	ST	Yes	4C

E: Enhancement; SAD: Surrounding architectural distortion; ST: Skin thickening; Pt: Patient; BIRADS: Breast imaging reporting and data system AME: Adenomyoepithelioma

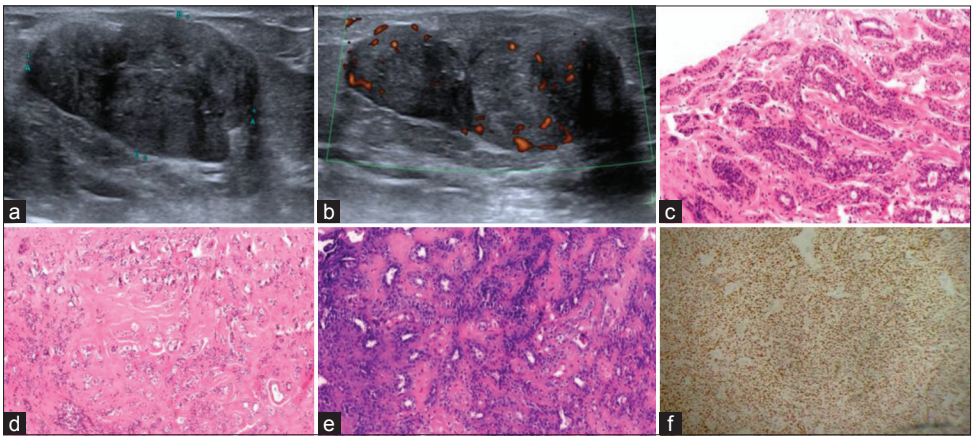

Figure 1: (a) and (b) Grey scale ultrasound reveals an irregular (>3 lobulations) solid hypoechoic lesion with increase internal vascularity. Breast imaging reporting and data system-4A; (c) HPE-Microscopy showing the proliferating ductal component (H and E × 400); (d) histopathology showing the proliferating myoepithelial cells with a clear morphology (H and E × 200); (e) histopathology showing the ducts surrounded by proliferating myoepithelial cells (H and E × 400); (f) nuclear positivity for P 63 highlighting myoepithelial cells (IHC × 200)

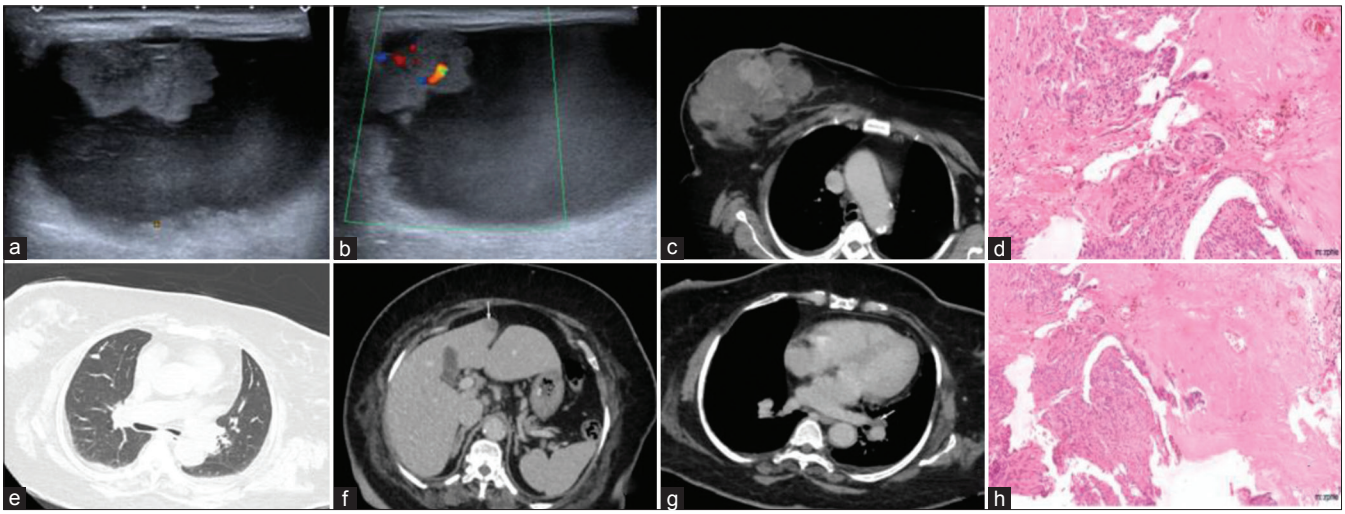

Figure 2: (a,b) Grey scale ultrasound reveals an irregular poorly circumscribed solid cystic lesion in right breast. Breast imaging reporting and data system category- 4C; (c) CT-scan reveals irregular solid cystic lesion with overlying skin thickening in the right breast. Solid component shows intense enhancement. Contrast-enhanced computed tomography scan reveals (e) suspicious right lung nodule; (f) hypodense lesion in liver; and (g) left hilar lymph node-suspicious for metastasis; and (d,h) HPE malignant adenomyoepithelioma

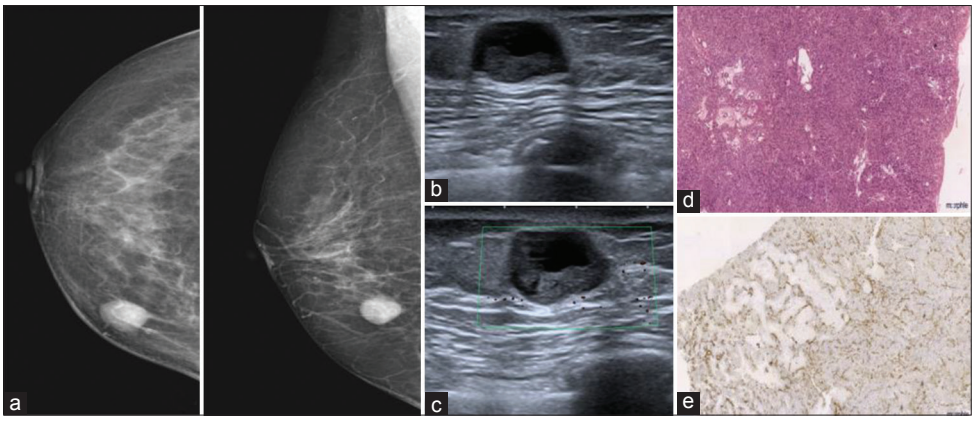

Figure 3: (a) Digital X-ray mammogram: Craniocaudal and mediolateral oblique view reveals an oval well circumscribed equal density lesion in the lower inner quadrant of right breast; (b) and (c) ultrasound shows a well-defined solid cystic lesion in the right breast with minimal internal vascularity in the solid component–breast imaging reporting and data system 4A; (d) histopathology of excision biopsy shows a diffuse sheets of tumor cells arranged in a syncytial pattern (H and E × 100); (e) IHC of the sample shows myoepithelial cells showing P63 nuclear positivity (IHC × 100)

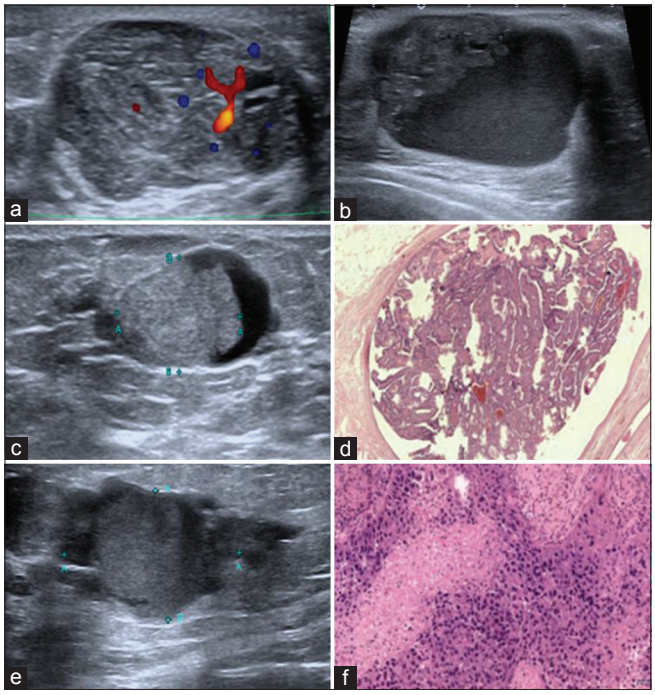

Figure 4: (a) Ultrasound reveals an oval, well circumscribed solid hypoechoic lesion with internal vascularity. HPE – Benign phyllodes tumor; (b) ultrasound shows a large cystic lesion with an eccentric irregular hypoechoic solid component. HPE – Invasive ductal carcinoma; (c) ultrasound reveals an oval well circumscribed solid lesion with eccentric cystic component; (d) HPE – benign intraductal papilloma; (e) Ultrasound reveals an irregular non-circumscribed hypoechoic mass with peripheral cystic changes; (f) HPE – invasive papillary carcinoma

in males.[5,6] Most of the adenomyoepithelial tumors are benign but malignant changes in the myoepithelial or, more commonly, epithelial component results in myoepithelial or epithelial carcinoma have been reported.[2,4,5,7,8] The occurrence of sarcoma and carcinosarcoma from AME has been described.[6]

The usual clinical presentation is a palpable, nontender, and centrally located mass, although a more peripheral distribution and a painful lesion may occur.[5] Rapid enlargement in a pre-existing lump may indicate malignant transformation[9] In our study, seven out of the six symptomatic patients presented with a non-tender palpable mass.

The most common mammographic abnormality is an irregular non-calcified mass with microlobulated margins.[2,7,8] Architectural distortion is usually associated with malignancy.[8] In our study, we had mammography of two patients with benign AME [Figure 3] which revealed a well-circumscribed oval equal density lesion with no associated architectural distortion or microcalcifications, and mammography of two malignant AME patients which revealed an irregular spiculated high-density mass with no associated microcalcifications.

On ultrasonography, benign lesions are commonly seen as circumscribed hypoechoic masses and may have posterior enhancement, while malignant tumors may show poorly defined margins and posterior shadowing.[8] In a study by Lee *et al.*, it is concluded benign AME appears as solid or complex echoic masses with suspicious malignant ultrasonographic features, which may be associated with adjacent duct ectasia.[10] In our study, USG evaluation, among the benign lesions, we found 2 lesions were oval-shaped but were complex solid cystic (50%) [Figure 3] and two irregular lesions were completely hypoechoic (>3 lobulations) [Figure 1] making it difficult to differentiate from a malignant entity based on shape and echo pattern. All the benign lesions were well-circumscribed, and parallelly oriented and had posterior acoustic enhancement. The three malignant lesions were irregular or solid cystic [Figure 2],

poorly circumscribed, non-parallel orientation with combined posterior features and mild internal vascularity. None of the lesions had adjacent ductal dilatation.

Metastases from malignant AME appear to be hematogenous rather than lymphatic. There is potential for local invasion and recurrence after excision of both benign and malignant lesions.[3] In the original Tavassoli study, the median recurrence time was 6.1 years and there were three recurrences in 27 cases.[7] Association of AME with concurrent ipsilateral breast cancer was reported in other studies.[7] Synchronous ductal carcinoma *in situ* or invasive ductal carcinoma have also been cited in several case reports.[11] In our study, one patient had metastasis to the lung and liver [Figure 2]. None of the patients had multicentric or contralateral breast involvement.

The differential diagnosis of the well-defined solid lesion on mammography and USG is fibroadenoma, phyllodes [Figure 4a], triple-negative breast tumors, medullary, and mucinous tumors. The differential diagnoses for a solid cystic lesion on USG are benign papillomas [Figure 4c and d], malignant papillary lesions [Figure 4e and f], and invasive ductal carcinoma [Figure 4b]. It is not always possible to differentiate these entities and histopathology correlation is essential.

Pathologically, hyperplasia of the breast can be in the epithelial and myoepithelial component and this can be seen in various benign and malignant conditions, ranging from adenomyoepithelial adenosis, pleomorphic adenoma, AME with carcinoma, and adenoid cystic carcinoma. The proliferation may form irregular multiple lobules, where the myoepithelial cells are seen surrounding the ductal epithelial cells. Fibrous and adipose tissue can be seen separating the lobules. The myoepithelial cells may show a range of morphologies from spindle cell to epithelioid or glycogen-rich clear cell type. The ducts may be forming tubules or may be compressed by the proliferating myoepithelial cells. Apocrine or squamous metaplasia may be noted in the ductal epithelial cells. The nuclei are generally of moderate size and round to oval. Usually, the mitosis will be low (<2 mitoses per ten high power fields). Chondromyxoid changes may be seen in the surrounding stroma.[12]

Fattanch further subdivided AME into spindle cell, tubular, and lobulated variants.[7] The spindle cell type shows a predominant spindle cell pattern, whereas, in the tubular cell variant, the ductal component is seen as forming tubules. The lobulated variant shows proliferating myoepithelial cells with compressed ductal elements.

Immunohistochemical staining confirms the nature of the cells, where the myoepithelial cells show cytoplasmic positivity for smooth muscle actin and calponin and nuclear positivity for P63. Immunohistochemistry of the luminal epithelial cell component is positive for low molecular weight cytokeratins (AE1/AE3 and CK 7, CK 8/18, CEA, EMA, and a variable ER expression).

The management of benign adenomyoepithelioma is complete excision as there is a potential risk of malignant transformation or recurrence. Regular follow-up of the ipsilateral as well as the contralateral breast is essential.

The treatment of malignant AME is not established except for complete excision at an early stage. Kihara *et al.* concluded that complete local excision is the only way to reduce the chance of local recurrence and distant metastases.[13] The role of axillary lymph node sampling/ effective adjuvant chemotherapy or post-operative radiotherapy is unclear. In a study by Bult *et al.* and Takahasi *et al.*, it is stated that chemotherapy was found ineffective in malignant cases.[14,15] Lee *et al.* reported that eribulin had a beneficial effect on malignant AME of the breast with multiple hepatic, pleural, and abdominal wall metastases.[16] Logie *et al.* suggest in the setting of AME with axillary metastasis, adjuvant radiotherapy may provide additional local control.[17]

The demerits of our study are it is a retrospective study; hence, clinical information is limited. The study sample is less, being the rare incidence of the disease. Mammography correlation could not be done for all the patients as few had done initial evaluation outside our institute for which images were not available.

To conclude, there is neither specific imaging feature to differentiate AME from other breast lesions nor in differentiating benign AME from malignant lesions. Imaging aids in the evaluation of occult axillary node involvement or to evaluate for distant metastasis. Despite being a rare entity it is essential to consider these lesions in the differential diagnosis of solid/solid cystic lesions due to the necessity of complete excision.

CONCLUSION

AME is an unusual breast neoplasm and should be considered in the differential diagnosis for a focal solid or solid cystic lesion in the breast. No specific features exist to identify this entity on imaging alone; hence, core biopsy is mandatory to establish the diagnosis. It is essential to do complete excision even in pathologically proven benign adenomyoepithelioma due to the risk of recurrence and malignant transformation. The post-surgical management of the malignant lesions remains controversial.

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