Adenomyoepithelioma A Rare Breast Tumor: Case Studies With Review Of The Literature

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Citation

Abstract

Introduction
Adenomyoepithelioma is a rare, benign proliferative tumor that can involve the breast tissue. The diagnostic appearance of the lesion can give rise to a difficult differential diagnosis with breast carcinoma. There is the potential for malignant evolution of this lesion. It usually presents as a solitary, unilateral, painless mass at the periphery of the breast. Accurate diagnosis and differentiation from more aggressive tumors is important.

Materials and Methods
In two cases of breast lump, fine needle aspiration cytology (FNAC) was done and stained with H & E and Papanicolaou stains. The formalin-fixed tissue sections were stained with hematoxylin and eosin, and in one case immunohistochemistry was performed with smooth muscle actin (SMA).

Case 1: A 30-year-old female presented with a firm lump in the upper quadrant of the right breast along with axillary lymphadenopathy since 6 months. On ultrasound it was reported as duct ectasia. FNAC was suggestive of proliferative breast disease with atypia (possibility of duct cell carcinoma). Modified radical mastectomy was done and sent for histopathology. The histopathological diagnosis was adenomyoepithelioma – breast (right), tubular type.

Case 2: A 25-year-old female presented with a firm lump in the left breast, occupying all quadrants. On FNAC the aspirates were suggestive of fibroadenoma. Peroperatively it was found to be a cystic swelling occupying the whole breast. The mass was excised and sent for histopathology. The histopathological diagnosis was adenomyoepithelioma with apocrine metaplasia and cystic degeneration – breast (left), tubular type.

Results
Two cases of breast lump were managed surgically. Both the cases were females with the mean age being 27 years. Both cases were of adenomyoepithelioma (tubular type) with one case showing apocrine metaplasia and cystic change.

Conclusion
Prognosis of patients with benign adenomyoepithelioma of the breast is usually good, but it has a potential for local recurrence, especially in the tubular and lobulated variants. Total surgical excision with an adequate margin of uninvolved breast tissue is therefore recommended.

INTRODUCTION
Benign adenomyoepithelioma of the breast is a rare tumor characterized by biphasic proliferation of both an inner layer of epithelial cells and a prominent peripheral layer of myoepithelial cells. It was first described by Hamperl[1] in 1970; more than 60 cases have been reported since then. All cases except 2 occurred in females.[2,3] Benign adenomyoepitheliomas outnumber their malignant counterparts by far. Malignancy may arise either through malignant transformation of 1 of the 2 cellular components or through malignant transformation of both.[6] The difficult differential diagnosis, potential for recurrence and malignant evolution of this lesion merit a careful approach.

MATERIALS AND METHODS
In two cases of breast lump, FNAC was done and stained with H & E and Papanicolaou stains. The formalin-fixed tissue sections were stained with hematoxylin and eosin, and in one case immunohistochemistry was performed with smooth muscle actin (SMA).

Case 1: A 30-year-old female presented with a firm lump in the upper quadrant of the right breast along with axillary lymphadenopathy since 6 months. On ultrasound it was reported as duct ectasia. FNAC was suggestive of proliferative breast disease with atypia (possibility of duct cell carcinoma) (Figure 1, 2).
Figure 1
Figure 1: Cytological aspirate shows cell-rich smear with sheets of cohesive ductal epithelial cells revealing mild nuclear atypia and few individually dispersed bare nuclei and myoepithelial cells (10X).

Modified radical mastectomy was done and sent for histopathology. The specimen of breast along with axillary pad of fat measured 18 x 17 x 6 cm. There was a well circumscribed grey white solid mass measuring 3.5 x 3 x 3 cm. The mass was situated 0.2 cm beneath the nipple and 0.5 cm away from the lower resected margin. Nine lymph nodes were dissected from the axillary pad of fat. The lymph nodes measured 0.2-2 cm in diameter. Histopathological sections from the breast mass showed a well delineated tumor composed of predominantly round to irregular tubular structures lined by basal myoepithelial cells with focal cell proliferation having clear cytoplasm (Figure 3).

Figure 2
Figure 2: Cytological aspirate shows cell-rich smear with a large sheet of cohesive ductal epithelial cells revealing mild nuclear atypia and few individually dispersed bare nuclei and myoepithelial cells (40X).

Figure 3
Figure 3: Photomicrograph (4X) shows a well delineated tumor with lobules showing tubular pattern.

The luminal epithelial lining was cuboidal to columnar with round to oval vesicular nuclei having eosinophilic cytoplasm and apocrine snouts. The intervening stroma was edematous (Figure 4, 5).

Figure 4
Figure 4: Photomicrograph (10X) shows tumor arranged in tubular architecture with biphasic proliferation of glandular epithelial cells and surrounding myoepithelial cells along with the intervening stroma.
Figure 5
Figure 5: Photomicrograph (40X) showing the proliferating basal myoepithelial cells with a clear cytoplasm, and the luminal epithelial cells.

No significant mitotic activity observed. There was no local invasion and the adjacent breast parenchyma revealed the normal breast lobules along with the intervening stroma. Reactive changes were observed in all 9 resected lymph nodes. The histopathological diagnosis was adenomyoepithelioma – breast (right), tubular type.

Case 2: A 25-year-old female presented with a firm lump in the left breast occupying all quadrants. On FNAC the aspirates were suggestive of fibroadenoma (Figure 6).

Figure 6
Figure 6: Cytological aspirate shows cellular smear of elongated, branching fragment of ductal epithelium and dispersed single bipolar nuclei in the background (40X).

Peroperatively it was found to be a cystic swelling occupying whole of the breast (Figure 7).

Figure 7
Figure 7: Showing a large cystic swelling occupying whole of the breast.

The mass was excised and sent for histopathology. The smooth, well encapsulated, grey white to yellow cystic mass measured 10 x 9 x 5 cm. Cystic cavity was filled with yellow pultaceous and calcified material (Figure 8, 9).

Figure 8
Figure 8: Smooth, well encapsulated, grey-white to yellow cystic external surface of the mass.
Histopathologically, sections from the cyst wall showed a compressed tumor tissue exhibiting proliferating glandular structures of varying size with intervening fibrocollagenous stroma. The glands with basal lamina were lined by basal cuboidal cells with clear cytoplasm and luminal columnar cells with apocrine metaplastic change. The cells revealed benign nuclear features (Figures 10-13).

Figure 9
Figure 9: Cut section of the cystic mass showing yellow pultaceous material.

Figure 10
Figure 10: Photomicrograph (4X) showing tumor arranged in lobules and having tubular structures of varying size with intervening fibrocollagenous stroma.

Figure 11
Figure 11: Photomicrograph (4X) showing tubular arrangement of the tumor with few cystically dilated glands.

Figure 12
Figure 12: Photomicrograph (40X) showing the proliferating myoepithelial cells with a clear cytoplasm, and the epithelial cells. Apocrine metaplasia seen in few glands.
Figure 13
Figure 13: Photomicrograph (40X) showing cystically dilated glands lined by clear myoepithelial cells and the luminal epithelial cells.

The inner fibrous wall of the cystic mass showed foamy degenerative cells and the cyst lumen was filled with acellular proteinaceous material (Figure 14).

Figure 14
Figure 14: Photomicrograph (40X) showing fibrous cystic wall with lining of foamy degenerative cells.

Upon immunostaining with smooth muscle actin (SMA), the myoepithelial cells showed strong positivity (Figure 15, 16).

Figure 15
Figure 15: Immunostain for SMA protein showing positivity in the proliferating myoepithelial cells, while the epithelial cells fail to react (10X).

Figure 16
Figure 16: Immunostain for SMA protein showing positivity in the proliferating myoepithelial cells, while the epithelial cells fail to react (40X).

It was diagnosed as adenomyoepithelioma with apocrine metaplasia and cystic degeneration – breast (left), tubular type.

RESULTS
Two cases of breast lump were managed surgically. Both the cases were females with the mean age being 27 years. Both cases were of adenomyoepithelioma (tubular type) with one case showing apocrine metaplasia and cystic change.

DISCUSSION
Myoepithelial cells are a normal component of the breast
metaplasia a central location in the acini. They may display apocrine
Epithelial cells by contrast have eosinophilic cytoplasm and
resembling the cells of leiomyomata, or be eosinophilic.
location in individual acini. They may also be spindled,
frequent, clear, abundant cytoplasm and their peripheral
myoepithelial cells in adenomyoepitheliomas include their
metaplasia may be encountered.
apocrine, squamous, mucinous, sebaceous or even chondroid
a tubular pattern to spindle cell or even clear cell. Focal
component, and the extent of fibrosis. Histology varies from
myoepithelial cells admixed with luminal elements: its
hallmark of benignity. Recently, however, breast neoplasms
have been described that are entirely or partially composed
of myoepithelial cells. Neoplasms of purely myoepithelial
origin have been called myoepitheliomas and may be benign
or malignant in approximately equal proportions. Tumors
derived from myoepithelial cells have been reported in skin,
salivary glands, breast and lungs; mammary tumors
containing myoepithelial elements are not frequent. Tumors
with bicellular proliferation of both epithelial and
myoepithelial cells are called adenomyoepitheliomas.

Breast adenomyoepithelioma arises from a mixture of
epithelial and myoepithelial cells and is a rare, myoepithelial
cell-rich neoplasm. It is closely related to
adenomyoepithelial (apocrine) adenosis and sometimes also
considered an uncommon variant of intraductal
papilloma.

The exact etiology of breast adenomyoepithelioma is still
obscure. All cases have been sporadic and no familial
aggregation has been observed. Kiaer et al. reported a case
of sequential changes from adenomyoepithelial adenosis into
adenomyoepithelioma which eventually became low grade
malignant adenomyoepithelioma during the course of 18
years. From this observation, Choi et al. proposed that
adenomyoepithelioma was derived from a myoepithelial,
long-standing, underlying breast disease such as adenosis
and fibroadenoma. The association of adenomyoepithelioma
with adenosis has been documented.

The lesion is usually well circumscribed and consists of
myoepithelial cells admixed with luminal elements: its
histology depends on the relative proportion of luminal and
myoepithelial cells, the existence of any papillary
component, and the extent of fibrosis. Histology varies from
a tubular pattern to spindle cell or even clear cell. Focal
apocrine, squamous, mucinous, sebaceous or even chondroid
metaplasia may be encountered. Distinctive features of
myoepithelial cells in adenomyoepitheliomas include their
frequent, clear, abundant cytoplasm and their peripheral
location in individual acini. They may also be spindled,
resembling the cells of leiomyomatia, or be eosinophilic.
Epithelial cells by contrast have eosinophilic cytoplasm and
a central location in the acini. They may display apocrine
metaplasia as was seen in our case 2. Epithelial lumina
may be reduced to slit-like spaces by the expansion of
myoepithelial cells.

Tavassoli proposed a classification system of
myoepithelial lesions of the breast. These lesions were
divided into: myoepitheliosis, adenomyoepithelioma and
malignant myoepithelioma. Tavassoli classified
adenomyoepitheliomas as spindle cell, lobulated, and tubular
(or adenosis) types with carcinoma arising in
adenomyoepithelioma. The most common pattern is the
tubular type with features characterized by proliferation of
glandular cells and surrounding myoepithelial cells of
abundant clear cytoplasm, as was seen in both our cases.

Differential diagnosis of adenomyoepithelioma includes
sclerosing adenosis, fibroadenoma, tubular adenoma, and
pleomorphic adenoma. Tubular adenoma, sclerosing
adenosis, and fibroadenoma have less prominent
proliferative features compared with adenomyoepithelioma.
Pleomorphic adenoma usually has prominent areas of
chondroid and osseous differentiation. Proliferative
myoepithelial cells with clear cytoplasm may mimic
malignancy in an intraoperative frozen section; therefore, it
is difficult to make an accurate diagnosis. Accurate
diagnosis can be difficult based solely on radiological
observation; therefore, histological examination results are
required to make the precise diagnosis.

Benign adenomyoepitheliomas have mammographic
findings, which are often suggestive of a benign lesion. The
sonographic appearance may vary from a cystic to a solid
mass. In our case 1, ultrasound findings were suggestive of
duct ectasia.

Fine needle aspiration cytology (FNAC) is usually a good
choice for diagnosis of breast lumps: a diagnostic accuracy
of 96.9% and positive predictive value of 98.4% have been
reported. Cytologically, adenomyoepithelioma usually
shows moderate to high cellularity. In our case 1, FNAC
report was proliferative breast disease with atypia suggestive
of duct cell carcinoma, and in case 2, FNAC was suggestive
of fibroadenoma.

In the cytological differential diagnosis,
adenomyoepithelioma may mimic other
myoepithelial/stromal cell-rich lesions: the classical example
is phyllodes tumor. In malignant phyllodes tumors, there is
an increase in cellular pleomorphism and mitotic activity of
the spindle cells. The rare, adenoid cystic carcinoma of the
breast represents another biphasic tumor. FNAC of adenoid
Adenomyoepithelioma is currently considered an indolent breast neoplasm but with a potential for local recurrence and distant metastasis, this is especially true if malignant transformation occurs within the original mass. Malignant neoplasms arising in adenomyoepitheliomas have been described in many patterns and have been subclassified as undifferentiated, myoepithelial, or epithelial. Malignant adenomyoepithelioma in which both cellular components underwent malignant transformation is exceptionally rare, and only 12 cases have been reported.

Malignant adenomyoepithelioma of the breast is a rare lesion characterized by malignant proliferation of epithelial and myoepithelial cells that show characteristic histologic and immunohistochemical features. Most of the cases demonstrate malignant transformation of only one cellular component, either epithelial or myoepithelial, though more often epithelial.

A focal infiltrative growth pattern increases with successive local recurrences. Complete surgical excision with adequate margins is required, especially in view of tendency for local recurrence and malignant transformation. The malignant type of adenomyoepithelioma can show nodal and distant metastases. Loose et al. have proposed three malignancy predictors, including high mitotic rate, cytologic atypia, and infiltrative peripheral border for benign adenomyoepitheliomas.

In the therapeutic approach to this disease, all findings and results should be assessed together to decide ultimate surgical planning so as to avoid unnecessary wide surgical resections and complications, but also to ensure a radical therapy for the patient. In our case 1, clinical examination and the FNAC, were strongly suggestive for breast malignancy so modified radical mastectomy was done. The potential for the adenomyoepithelioma to recur locally and, sometimes, to give distant metastasis could justify resorting to breast surgery.

The association of benign adenomyoepithelioma with a malignant lesion has been reported. The malignant lesions reported to arise from a benign adenomyoepithelioma, however, were all carcinomas. The evolution of malignant adenomyoepithelioma seems to begin with adenosis, with or without myoepithelial hyperplasia, proceed to benign adenomyoepithelioma, and end in a malignant tumor that still may contain residues of its precursor lesion.

Biphasic malignant adenomyoepithelioma is a rare breast neoplasm that may result in local recurrence or even distant metastasis: radical surgery is important to ensure good local control of disease. A correct preoperative diagnosis is also important for surgical planning. To date, only 13 cases of adenomyoepithelioma with detailed fine needle aspiration biopsy findings have been described in the literature.
neoplasm, so far only reported in women who range in age from 26 to 76 years. Tumor sizes range from 1 to 15 cm. Metastasis may occur, hematogenous rather than lymphatic, and so far has been seen in tumors 2 cm in diameter or larger.\[4\]

Not much is known about the natural history of biphasic malignant adenomyoepitheliomas. Of the 11 published cases, follow-up was reported in 4 cases and ranged from 12 to 64 months. Metastasis was described in 4 cases. Troiani et al. reported a case of malignant adenomyoepithelioma with lung metastasis. One of the 2 cases reported by Loose et al.[15] also showed lung and brain metastases. The primary tumors were 2 and 3.5 cm, respectively. Metastatic tumors were composed of both epithelial and myoepithelial cells. Simpson et al. described a unique case of malignant adenomyoepithelioma in which a carcinoma developed from the epithelial component and the tumor contained a metaplastic carcinoma with osteogenic and undifferentiated areas. In this case, the tumor recurred twice, metastasized, and caused death after 39 months. In these cases, the presence of distant metastasis was a clear sign of malignancy. Rasbridge and Millis reported 7 cases of adenomyoepithelioma, 5 of which were classified as malignant based on cytologic and architectural criteria. In one case, the patient died as a result of clinically suspected cerebral metastasis.\[4\]

However, as Loose et al.[15] suggested, the term malignant adenomyoepithelioma can also be applied to tumors that have not yet metastasized but are locally invasive and show high mitotic activity and marked cytologic atypia. In our cases, there was absence of local invasion, high mitotic activity, and cytologic atypia indicating the benign nature of the lesions. Although case 1 presented with axillary lymphadenopathy, on histopathology only reactive changes were observed.

CONCLUSION

Prognosis of patients with benign adenomyoepitheliomas of the breast is usually good, but it has the potential for local recurrence, especially in the tubular and lobulated variants. Total surgical excision with an adequate margin of uninvolved breast tissue is therefore recommended. Failure to achieve a free resection margin may result in local recurrence or rarely, malignant transformation.

References

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