Case Series

Adenomyoepithelioma of the Breast: A Case Series

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Abstract

Adenomyoepithelioma (AME) is a rare biphasic breast tumor composed of epithelial and myoepithelial components. The majority of them are benign, and some can undergo malignant transformation, posing significant diagnostic and therapeutic challenges. We report three cases in postmenopausal women (ages 63–72) who presented with palpable breast masses, all radiologically categorized as BI-RADS 4B and confirmed by histopathology to have a classic AME pattern. Case 1 demonstrated malignant transformation into triple-negative invasive breast carcinoma and was treated with wide excision and chemotherapy, while Cases 2 and 3 were benign AMEs exhibiting sebaceous differentiation and were managed with mastectomy and local excision, respectively; all patients remained disease-free at 1–3 years of follow-up. This series underscores that careful morphological assessment and immunohistochemical staining for myoepithelial markers are crucial to distinguish AME from differential diagnoses like fibroadenoma or papilloma. Although most classic AMEs follow a benign course and are cured by complete excision, malignant variants, characterized by infiltrative growth, high mitotic rate, and atypia, lack a consensus management strategy and are typically treated with excision with or without adjuvant therapy.

Keywords: adenomyoepithelioma; breast tumour; malignant transformation; myoepithelial cells

Introduction

Adenomyoepithelioma (AME) is a rare breast tumour initially described in 1970 [1]. A wide age range of presentations has been documented; however, its incidence increases with age [2]. The usual presentation is a palpable breast mass, although some cases are incidentally detected on screening [2]. As the name implies, it is of a biphasic nature and is composed of epithelial and myoepithelial cells [2]. WHO has divided them into benign and malignant categories [3]. Several morphological variants have been described, which include classic form, tubular, lobular, and spindled forms [3]. The typical features include a glandular proliferation which is lined by a dual epithelium with myoepithelial proliferation [3]. Prominent, plump myoepithelial cells which are increased in size and number are helpful features which aid in excluding other differentials such as intraductal papillomas, tubular adenomas, and other carcinomas [3, 4]. Immunohistochemical stains such as high molecular weight cytokeratins, p63, and h-calponin aid in identifying myoepithelial cells [3]. Malignant transformation is very rare, and less than 40 cases have been reported [2]. Epithelial, myoepithelial, or both components can undergo malignant transformation. The invasive component is usually negative for ER and Her2.

Majority of classic AME follow a benign clinical course [3]. However, rare distant metastasis has been reported even in the histologically benign ones [3]. The prognosis of malignant AME depends on the histological type of invasive carcinoma [3]. However, due to its rarity, the treatment following excision is still controversial [5].

In this case series, we describe one case of AME with malignant transformation and two cases of benign AME.

Case reports

This case series details three cases of AME that illustrate the spectrum of this rare breast tumor, from benign variants with unusual sebaceous differentiation to a case of malignant transformation into triple-negative carcinoma. A detailed description of each case is presented below, and a comparative overview of the features is presented in Table 1.

Case 1

A 69-year-old patient presented with a non-tender breast mass for 2 months duration. Mammogram and USS showed a well-circumscribed hyperdense mass (BI-RADS 4B). The core needle biopsy showed a lesion with a glandular proliferation, which was lined by a dual layer of epithelium and myoepithelium with the stroma containing numerous myoepithelial cells, which showed strong nuclear positivity with p63 (strong nuclear staining). ER showed a weak positivity, and Her2 was negative. Based on the morphological and immunohistochemical features, an AME was suspected. Then the patient underwent a wide local excision of the lesion. Macroscopically, a relatively well-circumscribed lesion with a maximum dimension of 26mm was noted. Microscopically, features suggestive of a classic AME composed of glandular spaces lined by a dual epithelium were seen, which was similar to the core biopsy findings (Figure 1A). The intervening stroma showed a proliferation of myoepithelial cells as demonstrated by P63 immunostain (Figure 1B). The periphery of the lesion showed malignant transformation into an invasive breast carcinoma, NST, composed of infiltrating acini, trabeculae, and solid nests of cells devoid of a myoepithelial layer in an inflamed desmoplastic stroma (Figure 1C and D). Necrotic areas were also seen. The invasive carcinoma belonged to Nottingham grade III. The invasive carcinoma was negative for ER, PR, and Her2. The sentinel lymph node biopsy of the patient was negative.

The patient was given adjuvant chemotherapy and is currently disease-free after one year of follow-up.

Case 2

A 72-year-old patient presented with a left breast lump for 4 years and skin ulceration over the lump and nipple discharge for 3 weeks. On imaging, a complex cyst (BI-RADS 4B) was noted. The tru-cut biopsy showed tubular structures lined by a dual layer of cells with proliferation of myoepithelial-like cells. Then the patient underwent a mastectomy. Macroscopically, a cystic lesion with a solid polypoidal area was noted, measuring 50mm in maximum dimension. Morphologically, a biphasic neoplasm composed of glandular structures lined by epithelial and prominent myoepithelial cells was noted (Figure 2A). The stroma also contains sheets and single scattered myoepithelial cells which are positive with CK5/6 (strong cytoplasmic/membranous staining) and p63 immunostains (strong nuclear staining) (Figure 2C). Focal areas with sebaceous differentiation were also seen (Figure 2B). A few satellite nodules were also seen in the adjacent tissue. No invasive carcinoma component was seen. No papillary structures were seen, and a solid intraductal papilloma was considered as a differential diagnosis. However, it was excluded due to the presence of prominent myoepithelial cells and proliferation of myoepithelial cells in the stroma.

The patient did not have further treatment and is currently disease-free after 3 years of follow-up.

Case 3

A 63-year-old female patient presented with a left breast lump for 1 month. On imaging, a complex cyst was noted in the subareolar region. Then the patient underwent a wire-localized excision of the lesion, and macroscopically, a cystic area with a white nodule (12mm) was noted. Microscopically, a cystic and solid lesion with solid areas containing glandular proliferation was noted (Figure 3A). They are lined by epithelial cells and plump/prominent myoepithelial cells. Similar to the previous cases, a stromal myoepithelial cell proliferation was seen. The myoepithelial nature was confirmed by CK5/6 (strong cytoplasmic/membrane staining) immunostain (Figure 3C). Focal sebaceous differentiation was also noted (Figure 3B).

Discussion

AME, first described by Hamperl in 1970, is a rare breast tumour with biphasic morphology comprising epithelial and myoepithelial elements [1]. The three cases presented herein illustrate the clinical and pathological spectrum of AME, ranging from benign forms to those with malignant transformation, as summarized in Table 1. All patients were postmenopausal women, which aligns with the typical age of presentation [2]. They presented with a palpable mass, consistently categorized

Table 1: Comparative summary of clinical, radiological, and pathological features in three cases of AME.

Feature	Case 1 (Malignant AME)	Case 2 (Benign AME)	Case 3 (Benign AME)
Age	69	72	63
Presentation	Palpable mass (2 months)	Palpable mass (4 years) + ulceration/discharge	Palpable mass (1 month)
Radiology (BI-RADS)	4B (well-circumscribed mass)	4B (complex cyst)	4B (complex cyst)
Macroscopic Size	26 mm	50 mm	12 mm
Key Histology	Classic AME pattern	Classic AME pattern	Classic AME pattern
Special Features	–	Sebaceous differentiation, satellite nodules	Sebaceous differentiation
Malignant Transformation	Yes (IBC, NST, Grade 3: Triple-negative)	No	No
IHC (Carcinoma)	ER-, PR-, HER2-	N/A	N/A
Management	Wide Local Excision + Adjuvant Chemotherapy	Mastectomy	Wide Local Excision
Follow-up	Disease-free after 1 year	Disease-free after 3 years	Disease-free after 2 years

Abbreviation: IBC, NST: Invasive Breast Carcinoma, No Special Type

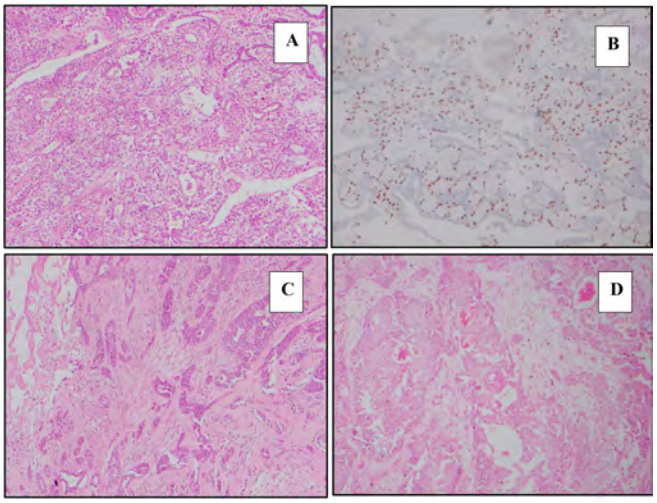

Figure 1: Case 1: (A) Adenomyoepithelioma component (H&E 100X). (B) P63 immunostain highlighting myoepithelial cells (100X). (C) Malignant transformation (H&E 40X). (D) Malignant transformation (H&E 100X).

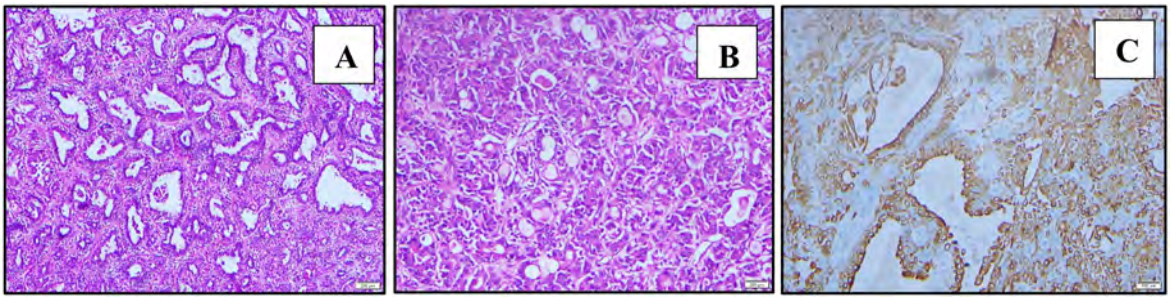

Figure 2: Case 2: (A) Adenomyoepithelioma with numerous stromal myoepithelial cells (H&E 100X). (B) Sebaceous differentiation (H&E 400X). (C) CK5/6 immunostain demonstrating myoepithelial cells (100X).

as BI-RADS 4B on imaging, underscoring the non-specific radiological features that make preoperative diagnosis challenging [2].

These tumours are predominantly benign, and of approximately 150 reported cases, around 40 have been malignant [2]. Macroscopically, the usual presentation is a circumscribed lesion with pushing margins. However, cystic and papillary areas have been described rarely [3], as in Case 2 and 3 where imaging and macroscopic findings showed cystic lesions. Several morphological variants have been described such as classic (glands surrounded by a myoepithelial proliferation), tubular, spindled, and lobular. Sebaceous and squamous differentiation had been described rarely [3]. All three of our cases had the

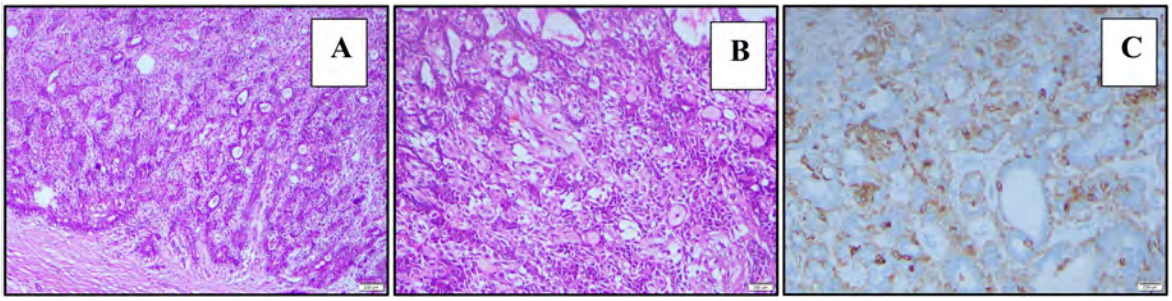

Figure 3: Case 3: (A) Adenomyoepithelioma with numerous myoepithelial cells and a circumscribed margin (H&E 40X). (B) Sebaceous differentiation (H&E 400X). (C) CK 5/6 immunostain demonstrating myoepithelial cells (100X).

classic pattern, and sebaceous differentiation is noted in Case 2 and 3.

Histological characteristics associated with malignancy include nuclear pleomorphism, high mitotic rate including abnormal mitoses, hyperplasia of glandular epithelial or myoepithelial cells, tissue invasion, and necrosis [6].

Malignant transformation can occur in either the epithelial or myoepithelial component, and in some cases, both compartments can show malignant transformation [3]. The malignant transformation of the epithelial component can range from invasive breast carcinoma, NST, to metaplastic carcinoma [3]. In Case 1, malignant transformation of the epithelial component into an invasive breast carcinoma, NST, is noted, with a triple-negative profile, which aligns with the immunohistochemical profiles described in the literature [3].

On molecular genetics, PIK3CA hotspot mutations occur in both ER positive and negative ones. AKT1 hotspot mutation is usually seen in ER positive cases [3]. HRAS p.GLn61 mutations are seen with ER negative cases with atypical histological features, and homozygous CDKN2A deletions are associated with malignant transformation of ER negative AME. TP53 mutations are generally not found [3].

The differential diagnosis includes fibroadenomas, fibrocystic changes, and papillomas. However, in those cases, a prominent myoepithelial layer or proliferation of myoepithelial cells in the stroma is not seen, which are typical morphological features of AME [3], which is present in our cases. Tubular carcinoma, adenoid cystic carcinoma, low-grade adenosquamous carcinoma, and metaplastic carcinoma are also possible differentials [3, 4]. Therefore, careful morphological assessment and myoepithelial markers are warranted [3, 4].

Despite its rarity, the majority of classic AME follow a benign clinical course, and complete surgical excision is curative [3], as seen in Case 2 and 3. However, a few cases with apparent benign histology have metastasized or recurred [3]. Due to the rarity of malignant AME, there is a lack of consensus on the management. The current recommendation is complete surgical excision with clear negative margins [7]. Metastasis can occur several years after excision, and lymph node metastases are rare [3]. The prognosis depends on the histological subtype of the invasive carcinoma [3].

Conclusion

This case series highlights the morphological spectrum of AME, including the diagnostic and therapeutic challenges. Our cases reaffirm that while the majority of AMEs follow a benign clinical course and are cured by complete surgical excision, there is potential for malignant transformation.

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