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Adenomyoepithelioma of the breast misdiagnosed as invasive ductal carcinoma

İnvaziv duktal karsinom olarak hatalı tanı alan memenin adenomiyoepiteliyoması

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ABSTRACT

The consultation material of total mastectomy and axillary lymph node dissection specimens taken from a 34-year-old female with a previous diagnosis of invasive ductal carcinoma was evaluated. Microscopic examination of the 6,5 cm well-circumscribed tumor revealed rounded tubules lined by both epithelial and myoepithelial cells in a myxomatous stroma. Obvious smooth muscle differentiation and area of fibroadenoma were also noted. Immunohistochemically, myoepithelial cells and cells with smooth muscle differentiation exhibited vimentin and smooth muscle actin. Myoepithelial cells were also reactive for S100 protein and epithelial membrane antigen. Luminal epithelial cells revealed positive reaction for epithelial membrane antigen and pan-cytokeratin (AE1/AE3), but displayed only focal staining with carcinoembryonic antigen. Based on these findings a final diagnosis of adenomyoepithelioma was made. Differential diagnosis of adenomyoepithelioma from its malignant counterpart and invasive ductal carcinoma may occasionally be challenging. Moreover, although considered an indolent neoplasm but with a potential risk for recurrence and sometimes metastasis, adenomyoepithelioma of the breast requires long-term follow-up.

Key words: Adenomyoepithelioma, breast, benign, malign

ÖZET

Bir başka merkezde invaziv duktal karsinom tanısı alan 34 yaşındaki kadın hastanın total mastektomi ve aksiller lenf nodu diseksiyonunu içeren konsültasyon materyali değerlendirilmiştir. Mastektomi materyalinde saptanan 6,5 cm boyutundaki düzgün sınırlı kitlenin mikroskobik incelemesinde, mikzoid stromada epiteliyal ve myoepiteliyal hücreler ile döşeli tübül yapıları izlenmiş, belirgin düz kas diferansiyasyonu ve bir alanda fibroadenom odağı dikkati çekmiştir. İmmünhistokimyasal olarak, myoepiteliyal ve düz kas diferansiyasyonu izlenen hücrelerde vimentin ve düz kas aktini ile, miyoepiteliyal hücrelerde ise S100 proteini ve epitelyal membrane antijeni ile reaksiyon belirlenmiştir. Lüminal epitelyal hücrelerde epitelyal membran antijeni, pan-sitokeratin (AE1/AE3) ve fokal olarak karsinoembriyonik antijen ile reaksiyon gözlenmiştir. Olguya adenomiyoepiteliyoma tanısı verilmiştir. Adenomiyoepiteliyomayı, malign eşdeğeri ve invaziv duktal karsinomdan ayırt etmek zor olabilir. Ayrıca, benign bir tümör olduğu düşünülse de, rekürrens ve nadiren metastaz yapabilme kapasitesinden dolayı, olgular uzun süre takip edilmelidir.

Anahtar sözcükler: Adenomiyoepiteliyoma, meme, benign, malign

INTRODUCTION

Myoepithelial cells are normally present in the breast localized between epithelial cells and the basal lamina of secretory elements of the mammary duct system (1,2). Tumors derived from these cells have been described in skin, salivary glands, breast and lungs (1,2). Adenomyoepithelioma (AME) of the breast is a rare lesion, and usually affects adult female patients (1,2). Rare cases have been described in males (3,4). It usually presents as a palpable nodule, ranging from 0.5 cm to 7 cm at its greatest diameter (1,2). AME has a bicellular pattern consisting of epithelial and myoepithelial cells,

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which are regularly distributed in the tubular structures, based on peculiar histological and ultrastructural features of the lesion. AME is considered to be a benign or a low grade malignant lesion, and carcinoma arising in an AME of the breast is a rare entity (1,2,5). The morphologic appearance of this tumor varies, leading to erroneous diagnoses of other types of benign or even malignant lesions. The tumor has a potential for local recurrence, therefore, wide excision is recommended for proper diagnosis and treatment (1,2,6). We report a case of adenomyoepithelioma in the breast formerly diagnosed as an invasive ductal carcinoma.

CASE REPORT

The consultation material containing total mastectomy and axillary lymph node dissection specimens from a 34-year-old female which had been previously diagnosed as invasive ductal carcinoma was reevaluated. Gross examination revealed a well-circumscribed, mobile and yellowish, solid nodule, measuring 6.5x6x4 cm in size (Figure 1). Histopathologically, the tumor was well demarcated from the surrounding breast tissue through a thin fibrous capsule. The tumor was composed of rounded tubules lined by both epithelial and myoepithelial cells within a myxomatous stroma (Figure 2). Obvious smooth muscle differentiation and area of fibroadenomatous lesions were also noted (Figure 3 and 4). Prominent myoepithelial hyperplasia resulting in obliteration of some of the tubular lumens was present in areas with rounded tubules.

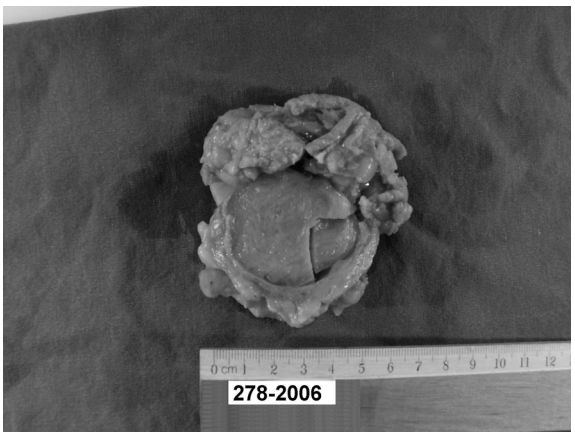

Figure 1. Gross appearance of the tumor; well-circumscribed tumor surrounded by a thin capsule.

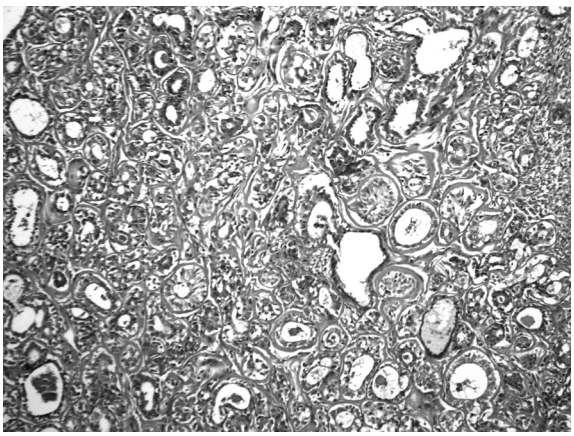

Figure 2. Irregular small glandular structures (HE x200).

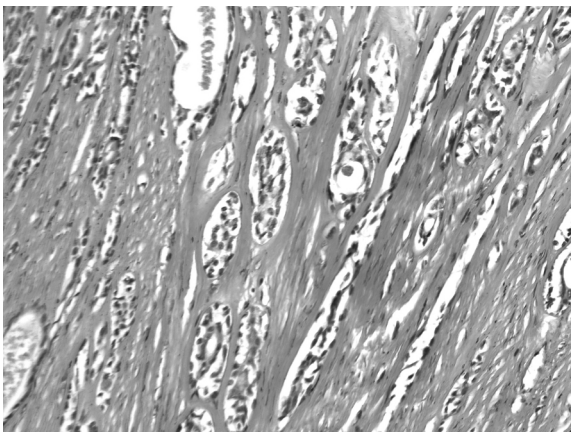

Figure 3. Prominent smooth muscle differentiation (HE x200).

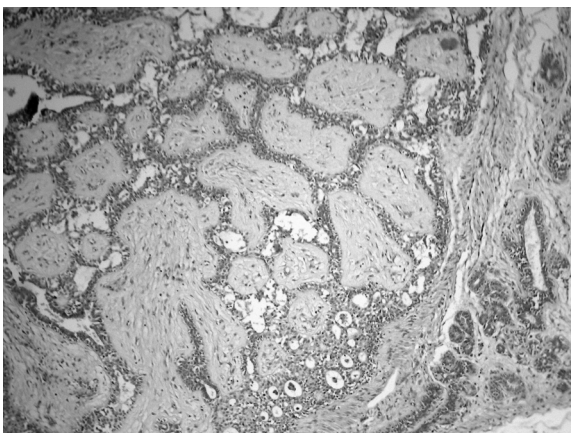

Figure 4. Fibroadenomatous area within the adenomyoepithelioma (HE x100).

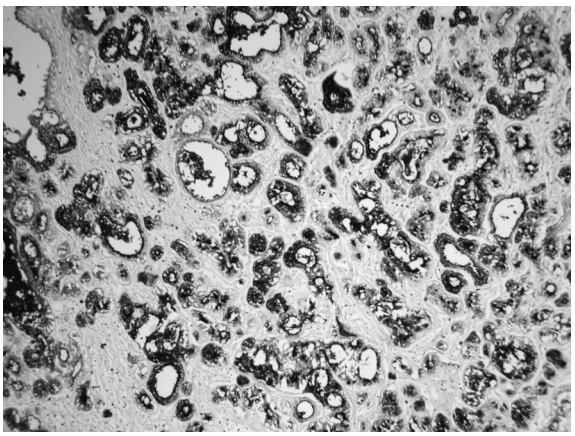

Figure 5. Strong staining for EMA in the epithelial and myoepithelial cells (B-SA, DAB x200).

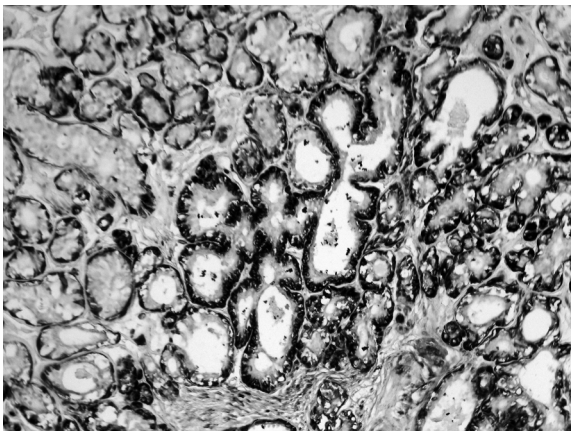

Figure 6. SMA decorated the outer myoepithelial layer (B-SA, DAB x200).

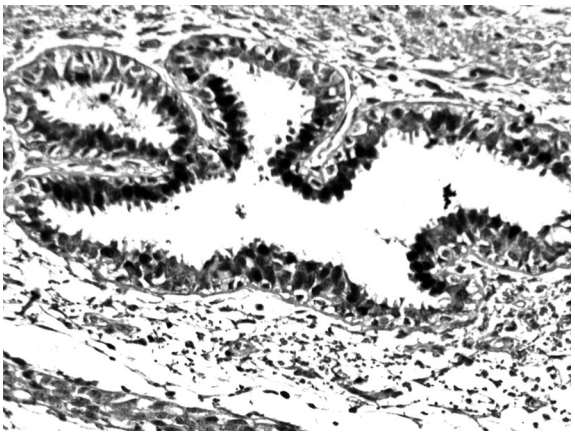

Figure 7. Estrogen receptor expression in the inner epithelial layer (B-SA, DAB x400).

The epithelial cells had flattened or cuboidal configuration with pink cytoplasm. They were located toward the center of the glands, some of which displayed apocrine metaplasia. The myoepithelial cells were round or polygonal with clear or eosinophilic cytoplasm. Occasional solid areas exclusively composed of myoepithelial cells were also found. Epithelial cells had minimal cytologic atypia, but the myoepithelial cells had neither cytologic atypia nor pleomorphism. The mitotic index was less than three in 10 high power fields (HPFs) for both elements. Apocrine metaplasia and myoepithelial cell proliferation involving the ducts were seen within the surrounding breast tissue. Immunostaining was performed using antibodies against epithelial and myoepithelial markers, including pan-cytokeratin (AE1/AE3), epithelial membrane antigen (EMA) (Figure 5), carcinoembryonic antigen (CEA), vimentin, smooth muscle actin (SMA) (Figure 6), S100 protein, estrogen receptor (ER) (Figure 7), progesterone receptor (PR) and Ki-67. Table 1 summarizes the immunohistochemical findings. The Ki-67 labeling index for epithelial and myoepithelial cells were 0.007 and 0.012. The axillary lymph nodes were free of tumor. A final diagnosis of adenomyoepithelioma was made. The patient has been well without any recurrences or metastases in 22 months of follow-up.

Table 1. Adenomyoepithelioma of the breast; immunohistochemical findings.

Antibody	Glandular Areas		Cells with Smooth Muscle Differentiation
	Inner Cells	Outer Cells	
Pan-cytokeratin (AE1/AE3)	Positive	Negative	Negative
EMA	Positive	Positive	Negative
CEA	Positive	Negative	Negative
Vimentin	Negative	Positive	Positive
SMA	Negative	Positive	Positive
S100 protein	Negative	Positive	Negative
ER	Positive	Negative	Negative
PR	Positive	Negative	Negative

EMA: Epithelial membrane antigen, CEA: Carcinoembryonic antigen, SMA: Smooth muscle actin, ER: Estrogen receptor, PR: Progesterone receptor.

DISCUSSION

Adenomyoepithelioma (AME) of the breast is an uncommon disorder characterized by the simultaneous proliferation of ductal epithelium and myoepithelial cells (1,2,6). The occurrence of AME in the breast was first described and illustrated by Hamperl in 1970 (7). Bult et al. (8) has reported 125 adenomyoepitheliomas up to year 2001 in the literature including benign and malign cases in their review article. Afterwards 78 additional adenomyoepithelioma cases were reported in the literature. Histogenesis of this tumor has been remained unclear, but it has been suggested that AME derives from myoepithelial overgrowth from long-standing adenosis, fibroadenoma, or other benign breast lesions (6). Tavassoli (2) proposed a classification system of myoepithelial lesions of the breast, dividing them into three types as myoepitheliosis, adenomyoepithelioma and malignant myoepithelioma. AME is subdivided into four subtypes as spindle cell, tubular, lobulated and carcinoma arising in adenomyoepithelioma. Combinations of growth patterns sometimes exist (1,2,9). Presented case has been classified as a tubular subtype. These different histological types behave differently both in clinical presentation and follow-up (1,2,9). Tubular variants and some lobuler tumors with high mitotic activity are particularly prone to local recurrence (2).

The majority of AMEs is grossly well circumscribed and they can even be encapsulated. However, AMEs may have lobulated, somewhat irregular appearance which may grossly mimic malignancy (10). The typical histologic appearance of an AME consists of acinar structures composed of an inner layer of epithelial cells with eosinophilic cytoplasm and a prominent peripheral layer of myoepithelial cells with clear cytoplasm (1,2). Minimal pleomorphism and low mitotic rate (usually less than 3 mitotic figures per 10 HPFs), as noted in this case, may be seen in both elements (11). Moreover, focal apocrine, squamous, mucinous, sebaceous or even chondroid and oseeous metaplasia may be encountered (1,2,9,12). Coexistent areas of fibroadenoma in this case support the hypothesis that myoepithelial overgrowth from benign breast lesions give rise to AME, and as might be expected smooth muscle differentiation may be encountered. Immunohistochemically, consistent with the current case, myoepithelial cells exhibit positive reactions for SMA, smooth muscle myosin, vimentin, EMA, cytokeratin 14, S100 protein, calponin and p63, while the luminal epithelial cells are strongly positive for cytokeratin, EMA and CEA. Contrary to normal myoepithelial cells, luminal cells possess receptors for ovarian steroid hormones and actively cycle in response to hormonal levels, however their growth regulation is largely unknown (1,2,11-14). On the other hand, AME's resemblance to usual ductal carcinoma -not uncommonly and as noted in the current case- and differentiation from its malignant counterparts are the most challenging issues complicating the diagnosis. In these circumstances, careful examination for myoepithelial differentiation verified by immunohistochemistry may be helpful.

AME is regarded as either a benign or a low-grade malignant lesion. The biologic behavior of AME still remains uncertain. In fact the presence of two-cell lineages alone is of no help in differentiating benign from malignant AME. Although high mitotic activity, cellular pleomorphism, high cellularity, necrosis, reactive stromal response (desmoplasia) and infiltrating (rather than pushing) borders (if present), are suggestive of a malignant behaviour, quite often some malignant AMEs have only one of the above characteristic features (1,2,6,12,15,16). Malignant change may involve only one cellular element, more often epithelial component rather than the myoepithelial component (1,2). Several cases with local recurrences and distant metastases to lung, liver, brain, bone, thyroid, chest wall and lymph nodes have been reported (6,8,13,17-19).

In conclusion, AME is an unusual breast neoplasm mostly with a benign course, but has a potential for local recurrence, and may simulate malignant lesions. Furthermore, malignant change of one or both cellular components may also occur. Therefore, it should be considered in the differential diagnosis of solid lesions of the breast and complete excision is necessary for accurate diagnosis and treatment of this unusual breast lesion with long term follow-up.

REFERENCES

1. Rosen PP. Myoepithelial neoplasms. In Rosen PP (ed). Rosen's Breast Pathology. 2nd ed. Philadelphia, Lippincott Williams&Wilkins, 2001. p.121-134.
2. Tavassoli FA. Miscellaneous Lesions. In Tavassoli FA (ed). Pathology of the Breast. 2nd ed. Norwalk, Appleton&Lange, 1992. p.595-609.
3. Tamura G, Monma N, Suzuki Y, Satodate R, Abe H. Adenomyoepithelioma (myoepithelioma) of the breast in a male. Hum Pathol 1993;24:678-681.
4. Berna JD, Arcas I, Balleter A, Bas A. Adenomyoepithelioma of the breast in a male. Am J Roentgenol 1997;169:917-918.
5. Loose JH, Patchefsky AS, Hollander IJ, Lavin LS, Cooper HS, Katz SM. Adenomyoepithelioma of the breast. A spectrum of biologic behavior. Am J Surg Pathol 1992;16:868-879.
6. Choi JS, Bae JY, Jung WH. Adenomyoepithelioma of the breast. Yonsei Med J 1996;37:284-289.
7. Hamperl H. The myothelia (myoepithelial cells). Normal state; regressive changes; hyperplasia; tumors. Curr Top Pathol 1970;53:161-220.
8. Bult P, Verwiel JMM, Wobbes T, Kooy-Smits MM, Biert J, Holland R. Malignant adenomyoepithelioma of the breast with metastasis in the thyroid gland 12 years after excision of the primary tumor. Case report and review of the literature. Virchows Arch 2000;436:158-166.
9. Gill TS, Clarke D, Douglas-Jones AG, Sweetland HM, Mansel RE. Adenomyoepithelioma of the breast: a diagnostic dilemma. Eur J Surg Oncol 2000;26:316-318.
10. Felipo F, Del Agua C, Eguizabal C, Vaquero M. Benign adenomyoepithelioma of the breast: a case with gross mimicking of malignancy. Breast J 2002;8:383-384.
11. McLaren BK, Smith J, Schuyler PA, Dupont WD, Page DL. Adenomyoepithelioma: Clinical, histologic, and immunohistologic evaluation of a series of related lesions. Am J Surg Pathol 2005;29:1294-1299.
12. Gatti G, Viale G, Simsek S, Zurrida S, Intra M, Caldarella P, et al. Adenomyoepithelioma of the breast, presenting as a cancer. Tumori 2004;90:337-339.
13. Kihara M, Yokomise H, Irie A, Kobayashi S, Kushida Y, Yamauchi A. Malignant adenomyoepithelioma of the breast with lung metastases: report of a case. Surg Today 2001;31:899-903.
14. Rosen PP. Adenomyoepithelioma of the breast. Hum Pathol 1987;18:1232-1237.
15. Harigopal M, Park K, Chen X, Rosen PP. Pathologic quiz case:a rapidly increasing breast mass in a postmenopausal woman. Malignant adenomyoepithelioma. Arch Pathol Lab Med 2004;128:235-236.
16. Dorpe JV, De Pauw A, Moerman P. Adenoid cystic carcinoma arising in an adenomyoepithelioma of the breast. Virchows Arch 1998;432:119-122.
17. Chen PC, Chen CK, Nicastri AD, Wait RB. Myoepithelial carcinoma of the breast with distant metastasis and accompanied by adenomyoepitheliomas. Histopathol 1994;24:543-548.
18. Takahashi II, Tashiro H, Wakasugi K, Onohara T, Nishizaki T, Ishikawa T, et al. Malignant adenomyoepithelioma of the breast: a case with distant metastases. Breast Cancer 1999;6:73-77.
19. Jones C, Tooze R, Lakhani SR. Malignant adenomyoepithelioma of the breast metastasizing to the liver. Virchows Arch 2003;442:504-506.