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Case Report

# Adenomyoepithelioma with carcinoma of the breast: A report of two cases and a review of the literature

Jing Xu[a,b,*], Xiaoyan Tang[a], Yuko Iida[c], Fumi Fuchinoue[a], Tomomi Kusumi[d], Norito Yagihashi[e], Kae Kawachi[f], Satoru Shimizu[g], Shinobu Masuda[a]

[a] Department of Pathology, Nihon University School of Medicine, Tokyo, Japan
[b] Department of Pathology, Qingdao Central Hospital, The Second Affiliated Hospital of Qingdao University Medical College, Qingdao, China
[c] Department of Respiratory Medicine, Nihon University School of Medicine, Tokyo, Japan
[d] Department of Pathology, Aomori City Hospital, Aomori, Japan
[e] Division of Pathology and Clinical Laboratory, Hirosaki National Hospital, Aomori, Japan
[f] Department of Pathology, Kanagawa Cancer Center, Yokohama, Kanagawa, Japan
[g] Department of Breast and Endocrine Surgery, Kanagawa Cancer Center, Yokohama, Kanagawa, Japan

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ABSTRACT

We herein described two cases of adenomyoepithelioma (AME) with carcinoma of the breast. Both of them were Japanese women, and they presented with a mass in their breast. Post-operative specimens revealed encapsulated and well-circumscribed tumors with local invasion, necrosis, cytological atypia, and a high mitotic rate. In immunohistochemistry, coincidentally with the loose adhesion pattern of myoepithelial cells in both cases, the intensities of E-cadherin and beta-catenin were much weaker in myoepithelial than luminal epithelial cells, with almost negative finding of beta-catenin in one case. We first found deletion of CDH1 and polysomy of CEP16 in myoepithelial cells by double color-fluorescence in situ hybridization. The two cases have been followed up for 5–8 years, and both remained free from local recurrence and distant metastases. We also presented an overview of 47 cases of AME with carcinoma in English-language literatures.



## 1. Introduction

In 1970, Hamperl [1] described adenomyoepithelioma (AME) of the breast for the first time, defined as a neoplasm composed of ductal or luminal and myoepithelial cells. Most of the AME described have been considered to be benign, but either or both cell types can progress to a malignant state and give rise to metastases in rare instances. The 4th ed. of WHO Classification of Tumors of the Breast [2] divided myoepithelial lesions into myoepithelial and epithelial–myoepithelial lesions. Malignant AME are primarily termed AME with carcinoma, including carcinoma derived from luminal epithelium (CLE), carcinoma derived from myoepithelium (CME), and epithelial–myoepithelial carcinoma (EMC). We herein report 2 cases of AME with carcinoma, review cases reported in the English-language literature, and reclassify all the cases according to the revised WHO Classification.

## 2. Materials and methods

### 2.1. Immunohistochemistry

Immunohistochemical analysis for cytokeratin (CK)-pan (clones AE1/AE3, Dako), CK7 (clones Ov-TL 12130, Dako), alpha-smooth muscle actin (SMA) (clones 1A4, Dako), CD10 (clones 56C6, Novocastra), P63 (clones 4A4, HISROFINE), E-cadherin (clones NCH-38, HISROFINE), beta-catenin (clones beta-catenin-1, Dako), estrogen receptor (ER) (clones 1D5, Dako), progesterone receptor (PR) (clones PgR636, Dako) and Her-2 (polyclonal, Dako) was performed on 5-μm-thick sections utilizing standard protocols on a Ventana Benchmark XT autostainer. The biphasic epithelial character of the tumor was confirmed by IHC.

### 2.2. Double color-fluorescence in situ hybridization (D-FISH)

Formalin-fixed and paraffin-embedded sections were used for D-FISH. Pretreatment and hybridization were performed along with the protocol provided by Empire Genomics (Buffalo, New York, USA). The E-cadherin probe (CDH1, 16q22.1, Empire genomics) on

* Corresponding author at: Department of Pathology, Nihon University School of Medicine, 30-1 Oyaguchi-Kamicho, Itabashi-Ku, Tokyo 173-8610, Japan.
*E-mail address:* katherine_xu@163.com (J. Xu).

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chromosome 16q22 was labeled in red and the centromere of the chromosome 16 probe (CEP16, D16Z3, Abbott Japan, Tokyo, Japan) was labeled in green. Twenty myoepithelial cells were counted. CDH1 deletion was defined as a state in which cells with less than one CDH1 signal accounted for more than 60% of the total. CEP16 polysomy was defined as a state in which cells with more than three CEP16 signals accounted for more than 30% of the total [3].

## 3. Results

### 3.1. Case 1

A 54-year-old Japanese woman consulted for a mass, which had gradually increased in size, in the inner region of her left breast. Mammography and ultrasonography led to a suspicious of malignancy. Fine-needle aspiration cytology (FNAC) also suggested malignancy. Lumpectomy was therefore performed, and the surgical margin was negative. She remained free from local recurrence and distant metastases for 5 years after the operation.

The lumpectomy specimen disclosed a well-defined, firm, and gray intracystic mass with a cross-sectional area of 23 mm × 16 mm (Fig. 1a). Microscopically, with foci of coagulative necrosis, the tumor was composed of luminal epithelial and myoepithelial cells with alveolar or papillary arrangements (Fig. 1b and c). The luminal epithelial cells were flattened or cuboidal and located toward the center of the glands. The myoepithelial cells were round or polygonal and showed predominantly clear cytoplasm (Fig. 1c). These biphasic epithelial cells showed an unbalanced proliferation of inner and outer cells following the loss of polarity and, in some areas, they were gathered into nests. Both the inner and outer cells had medium-sized atypical nuclei. Up to 15 mitoses/10 high-power fields (HPF) were counted (Fig. 1c). We may reclassify this case as epithelial–myoepithelial carcinoma (EMC).

As IHC confirmed, the inner epithelial components were strongly positive for CK-pan and CK7 (Fig. 1e), whereas the outer myoepithelial components were strongly positive for SMA, CD10 (Fig. 1f), and CK-pan, and weakly positive for P63. Concerning E-cadherin, the intensity was much weaker in myoepithelial than luminal epithelial components (Fig. 1g), but for beta-catenin, only a few luminal cells were dot-positive in the cytoplasm, and the myoepithelial cells were negative (Fig. 1h). Beta-catenin nuclear staining was not observed. ER, PR and Her-2 were negative.

In D-FISH findings, case 1 showed polysomy of CEP16 (Fig. 1d).

### 3.2. Case 2

A 48-year-old Japanese woman had noticed a mass in the upper outer region of her left breast. Mammography showed a well-defined tumor. Ultrasonography showed an intracystic tumor. The FNAC diagnosis was adenocarcinoma. Breast-conserving surgery accompanied by sentinel lymph node (SLN) biopsy was performed. No metastatic carcinoma was identified in the SLN. She remained free from local recurrence and distant metastases for 8 years after her operation.

The tumor was an encapsulated lesion measuring 20 mm × 18 mm × 17 mm and had clear excision margins (Fig. 2a). Microscopically, the tumor was mostly well circumscribed and surrounded by a pseudo-capsule of hyalinized connective tissue. The tumor consisted of biphasic epithelial cell proliferation with a cystic component, and tumor cells partially infiltrated the pseudocapsule (Fig. 2b). The inner epithelial cells with pale eosinophilic cytoplasm surrounded the lumina, and were arranged in a monolayer. Outer myoepithelial cells with clear cytoplasm and weakened cellular cohesion proliferated around the inner epithelial cells, which were polygonal to plasmacytoid in shape and had hyperchromatic nuclei, showing nuclear atypia (Fig. 2c). The average mitosis rate was up to 5 mitoses per 10 HPF. We may reclassify this case as carcinoma derived from myoepithelium (CME).

As IHC confirmed, the inner epithelial components were strongly positive for CK-pan and CK7 (Fig. 2e), whereas the outer myoepithelial components were strongly positive for SMA, CD10 (Fig. 2f), and CK-pan, and weakly positive for P63. The outer myoepithelial cells were also positive for CK7 (Fig. 2e). Concerning E-cadherin and beta-catenin, the intensity was much weaker in myoepithelial than luminal epithelial components (Fig. 2g and h), and beta-catenin nuclear staining was not observed. ER and PR were weakly positive, and Her-2 was negative.

In D-FISH findings, case 2 showed CDH1 deletion (Fig. 2d).

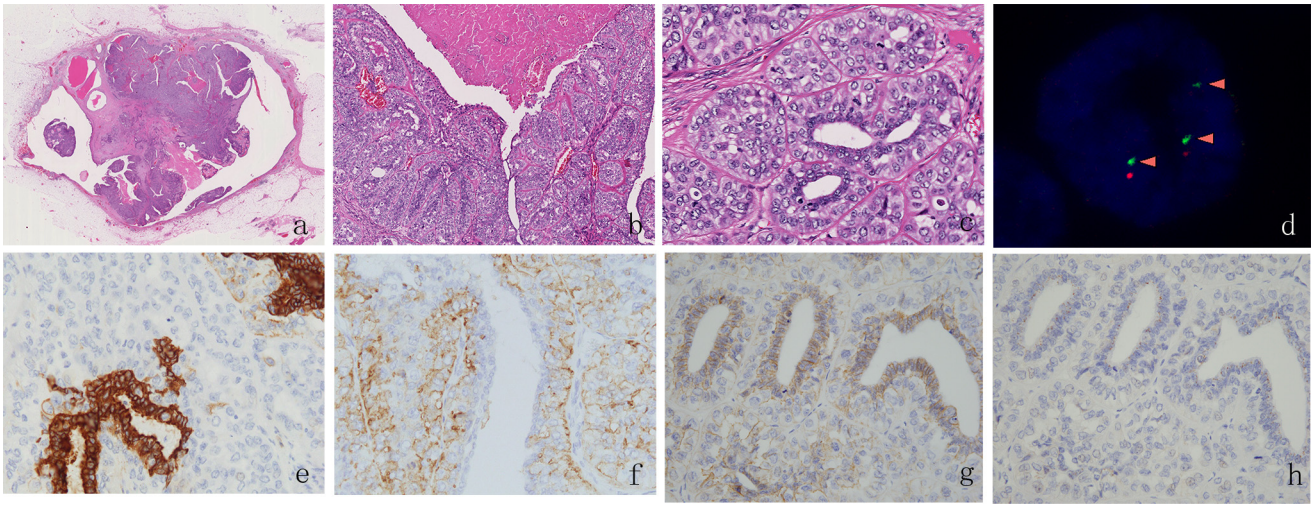


**Fig. 1.** Case 1, hematoxylin and eosin staining (HE) (a–c), D-FISH (d), IHC (e–h). (a) The tumor was a well-defined and intracystic mass, with papillary arrangements. (b) It showed biphasic differentiation with epithelial and myoepithelial cells, and coagulation necrosis was also noted. (c) These biphasic epithelial cells showed an unbalanced proliferation of inner and outer cells, and mitoses were conspicuous. (d) Myoepithelial cells showed polysomy of CEP16 (red arrowhead). (e) CK7 was positive in luminal cells. (f) CD10 was positive in myoepithelial components. (g) The E-cadherin intensity was much weaker in myoepithelial than luminal epithelial cells. (h) Beta-catenin was dot-positive in the cytoplasm of a few luminal cells, but myoepithelial cells were negative. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)