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# Combination of Adenomyoepithelioma and Adenoid Cystic Carcinoma of the Breast: A Case Report of an Uncommon Histopathological Entity

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Data Collection B  
Statistical Analysis C  
Data Interpretation D  
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**Patient:** Female, 48-year-old  
**Final Diagnosis:** Adenoid cystic carcinoma and adenomyoepithelioma of the breast  
**Symptoms:** Palpable breast mass  
**Medication:** —  
**Clinical Procedure:** —  
**Specialty:** Oncology

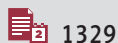
**Objective:** Rare coexistence of disease or pathology  
**Background:** Adenomyoepithelioma and adenoid cystic carcinoma are uncommon types of breast tumors. Adenoid cystic carcinoma accounts for 0.1% of breast neoplasms and typically presents as a tender breast tumor, mostly in the subareolar area. Adenoid cystic carcinoma usually appears in women in the fifth or sixth decade of life and predominantly presents as a mixed tumor, with cribriform, tubular, and solid growth characteristics. Adenomyoepithelioma of the breast shows epithelial and smooth muscle characteristics. Adenomyoepithelioma rarely goes through malignant transformation and is an uncommon type of benign breast tumor.

**Case Report:** Our study reviews the current published literature regarding the combination of these 2 rare neoplasms of the breast and shows a rare case of a 48-year-old woman with a combination of adenoid cystic carcinoma and adenomyoepithelioma.

**Conclusions:** The combination of adenoid cystic carcinoma and adenomyoepithelioma should be part of the differential diagnosis in breast cancer. More research is needed regarding the optimal therapy, which is currently surgical excision.

**Keywords:** Adenomyoepithelioma • Breast Neoplasms • Carcinoma, Adenoid Cystic • Mastectomy • Mastectomy, Segmental

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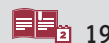
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## Background

There are only a few case reports in the literature regarding the combination of adenomyoepithelioma (AME) and adenoid cystic carcinoma (ACC) in breast cancer [1,2]. AME is a rare type of benign breast neoplasm, and if it goes through malignant transformation, it becomes challenging to make the correct diagnosis and differentiate among other benign diseases, such as sclerosing adenosis, tubular adenoma, and intraductal papilloma [3]. Malignant AME is characterized by the differentiation of epithelial and myoepithelial cells, in which 1 or both parts can show malignant attributes [4]. ACC rarely occurs in the breast. Additionally, ACC is formed by epithelial and myoepithelial cells that can present classic tubular, cribriform, or basaloid features. Fine needle aspiration cytology can provide the diagnosis for ACC of the breast, and treatment is mainly based on surgical excision; more research is needed regarding radiotherapy and chemotherapy for ACC [5].

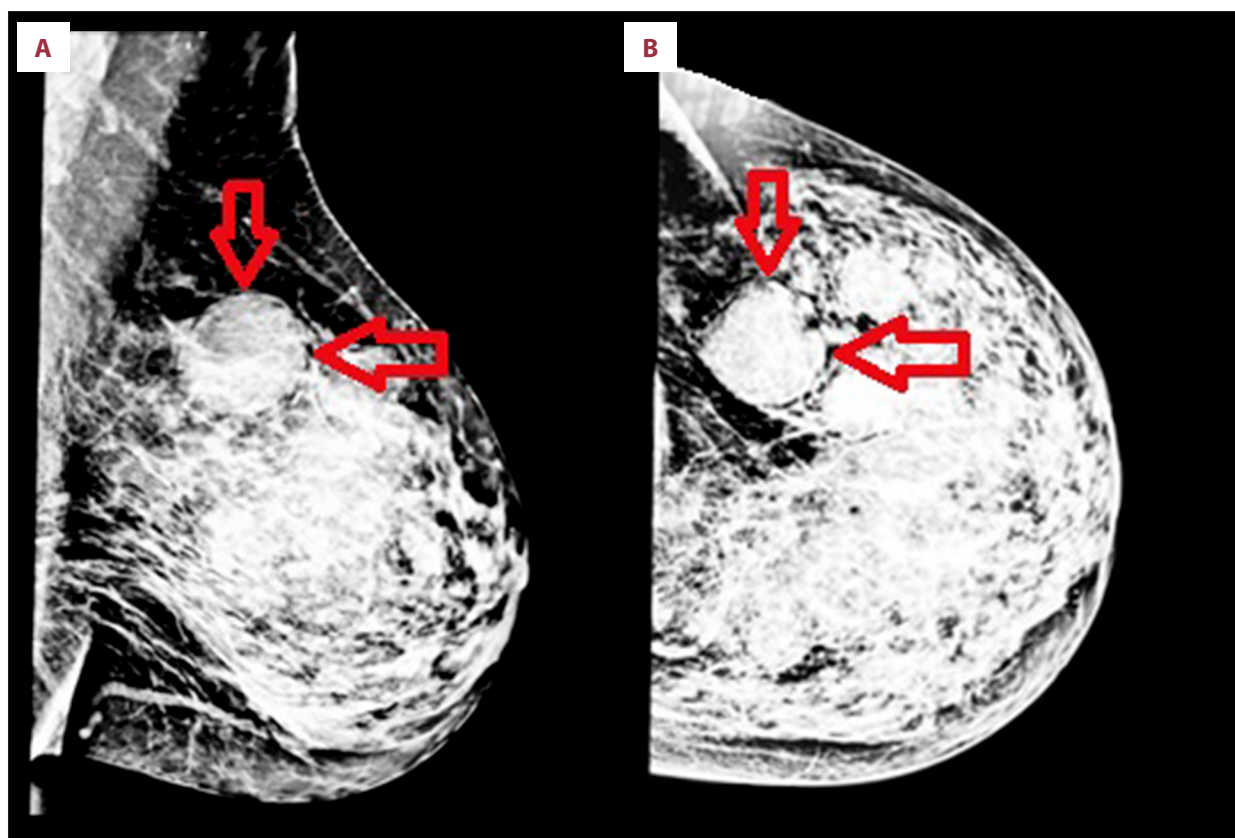
## Case Report

We describe a 48-year-old female patient in generally good health, who scored 0 on her Eastern Cooperative Oncology Group (ECOG)

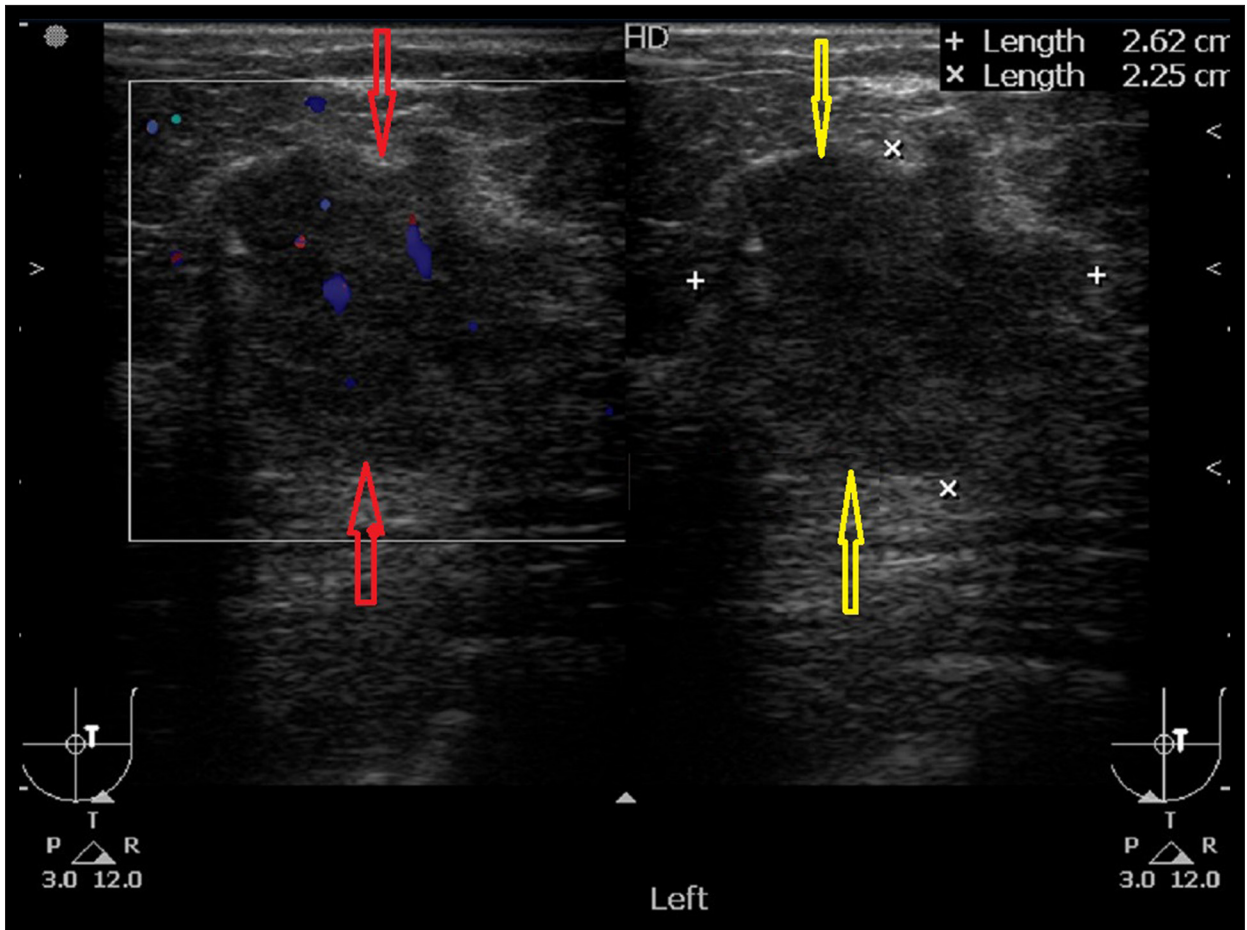
performance status. Her medical history was free of disease, except for a family history of paternal lung cancer. In July 2019, during self-examination, she discovered a palpable mass located in the upper outer quadrant of her left breast. The patient underwent several clinical examinations, including thorax and abdominal computed tomography (CT) scans, in addition to ultrasonography of both mammary glands. The mammographic findings were not conclusive (Figure 1). The ultrasonography showed a large hypoechoic, lobular mass of about 26×23×30 mm (Figure 2). The CT scan findings did not show any signs of metastases.

In September 2019, a core biopsy was performed, and the pathology report suggested the presence of breast carcinoma of a nonspecific type. Further immunohistochemical study showed pieces of an uncommon breast neoplasm that combined characteristics of AME and ACC, which was negative to estrogen and progesterone receptors as well as to Her2-neu protein, but positive to keratins AE1/AE3 and antigen CD117 (characteristic of adenoid cystic carcinoma) as well as to protein p63, smooth muscle actin, and epithelial membrane antigen, which is typical for AME (Figures 3-5).

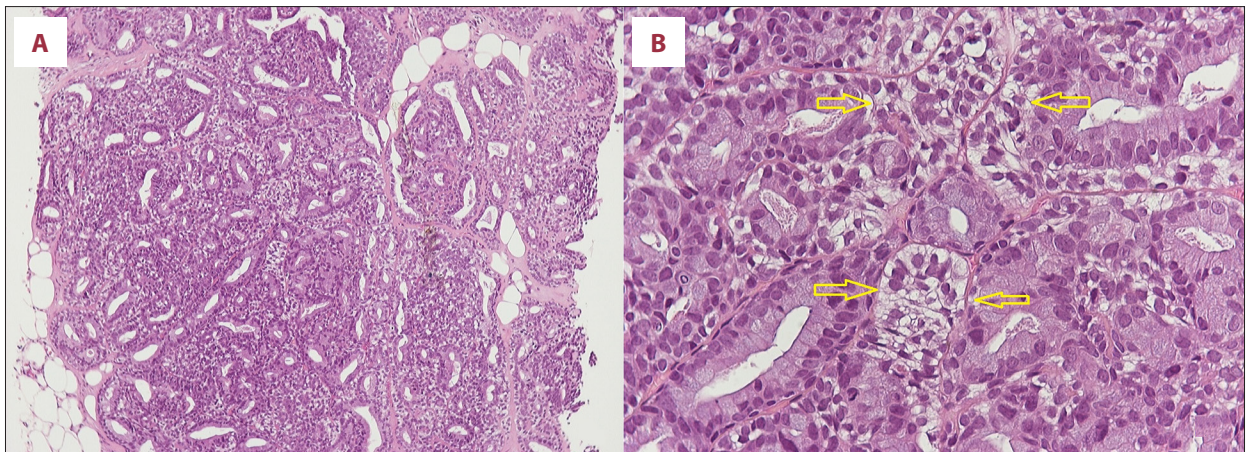
In October 2019, the patient was admitted to the Surgical Department of our hospital for a planned lumpectomy. Detailed



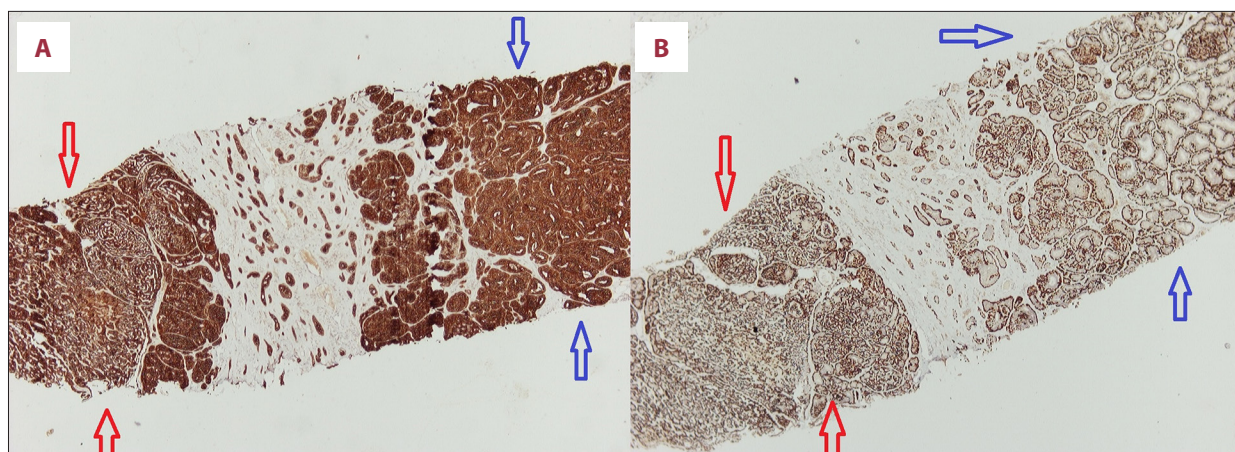
**Figure 1.** Mammographic depiction of left breast: (A) mediolateral view; (B) craniocaudal view. The arrows point toward the large mass in the upper left quadrant of the breast.



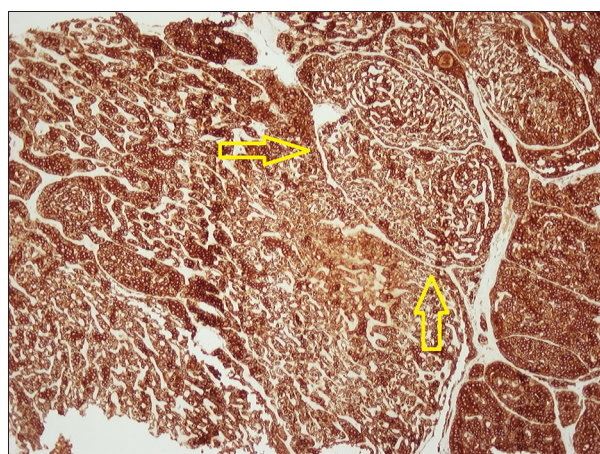
**Figure 2.** Ultrasonography depicting a large hypoechoic lobular mass with indistinct margins and posterior acoustic shadowing located in the upper outer quadrant of the left breast. The red and yellow arrows point toward its upper and lower limits.



**Figure 3.** Hematoxylin and eosin staining (A) ×100 and (B) ×400, showing characteristics of adenomyoepithelioma from core biopsy. The yellow arrows point toward the lighter-colored myoepithelial cells.



**Figure 4.** (A) Immunohistochemical staining for keratins AE1/AE3  $\times 40$  from core biopsy. Depicted are broad lesions characteristic of adenomyoepithelioma (AME) (blue arrows) and adenoid cystic carcinoma (ACC) (red arrows). (B) Immunohistochemical staining for protein p63  $\times 40$  from core biopsy. The blue arrows show the AME area, the red arrows show the ACC.



**Figure 5.** Immunohistochemical staining for keratins AE1/AE3  $\times 100$  from core biopsy. The yellow arrows point toward the characteristic cribriform structure of adenoid cystic carcinoma.

medical history of the patient, complete blood scan, and thorax X-ray were performed. All were within normal parameters. The level of cancer antigen 125 was 12 U/mL, and that of cancer antigen 15.3 was 18 U/mL; both were within the normal range, according to our laboratory.

A lumpectomy was performed, and macroscopically clean margins were achieved. The patient was discharged in good overall health on the first day after surgery. The histopathological report showed breast tissue with signs of chronic inflammatory response and foci of whitish ACC along with components similar to those of AME. Immunohistochemical analysis confirmed the results of the core biopsy, which were negative for estrogen and progesterone receptors, Her-2 neu protein, chromogranin, and synaptophysin.

In December 2019, the patient was admitted to our hospital for a planned total mastectomy. On the day of the surgery, 5 mL of methylene blue was injected at 5 points near the palpable mass, 1 mL per point of injection. Two sentinel lymph nodes were stained with methylene blue. They were sent for frozen sections, which were negative for local metastases. A simple mastectomy was performed. Gross examination of the tumor revealed the following: macroscopically, the total excised material was sized 25 $\times$ 14 $\times$ 4 cm, covered by an area of skin sized 14.5 $\times$ 5.5 cm that was also bearing the nipple. Sections revealed an area of white fibroelastic tissue sized 7.5 $\times$ 3.5 $\times$ 2.5 cm. Microscopically, components of ACC were concentrated in an area sized 1.5 $\times$ 0.5 cm. There were also foci with characteristics of both ACC and AME. The patient was discharged on the second day after surgery in good overall health. She did not undergo chemotherapy or radiotherapy. Follow-up and imaging surveillance have shown no breast cancer recurrence until now.

## Discussion

ACC is considered a low-grade lesion that usually originates in glandular tissues and in the salivary glands [2]. It rarely occurs in the breast, constituting about 0.1% of all breast tumors [1,5]. Mammary ACC has an excellent prognosis [2,5,6]. It predominantly affects women in the sixth decade of life [5]. The incidence of axillary lymph node metastases by ACC is relatively low [5]. Rare cases of distant metastases occur usually without prior lymph node involvement [5]. ACC is formed by basaloid (myoepithelial) and ductal (epithelial) cells with a typical tubular or cribriform architecture [1,2], with true glandular spaces, pseudolumens, and invagination of the stroma, which is histologically characteristic of ACC and absent in AME [1]. CD117 is an immunohistological marker that is positive in ACC

epithelial cells but is not present in AME [1]. It is possible for ACC and malignant AME to develop from the same pluripotent progenitor cells [1,2]. However, their different histological structures, distinct immunohistological profiles, and the organized papillary architecture of AME in contrast to ACC separate these 2 morphologically similar but distinct lesions [1,2,5].

AME is a relatively rare tumor that shows both epithelial and myoepithelial characteristics with bicellular proliferation. AMEs often affect the mammary glands [7,8]. This tumor usually presents in post-menopausal women over the age of 60 [8]. The first reported case of AME of the breast was published by Hamperl [9] in 1970, and this type of tumor was further classified by Tavassoli [6] in 1991. Tavassoli's classification separates AMEs into 3 distinct categories: tubular, lobulated, and spindle cell [6,10,11]. The myoepithelial cells can present spindle-shaped or round nuclei along with dispersed naked oval nuclei or clear cytoplasm [11]. The epithelial component of the AME can form into any of the following: solid, tubular, cystic, papillary, or trabecular structures or as apocrine metaplasia [11]. It often presents as a solitary palpable nodule ranging in size from 1 cm to 7 cm, often circumscribed but sometimes with lobulated, pushing borders [12]. AMEs are usually considered benign tumors; however, there is a possibility of malignancy. Cytologic criteria for the differentiation of malignant from benign cases of AME have not yet been established [11].

AMEs are inclined to local recurrence, even several years after the initial procedure. Distant metastases are a rare phenomenon and usually pertain to hematogenous rather than lymphatic spread [7,13]. The prognosis of patients with distant metastases is extremely poor [13-15]. The differential diagnosis of AME of the breast can include ACC, fibromatosis, myoepithelial hyperplasia, papilloma, spindle cell carcinoma, ductal adenoma or carcinoma in situ, undifferentiated carcinoma, phyllodes tumor and tubular adenoma with AME-like

areas. Few case reports have been published with a combined occurrence of AME and ACC, making this tumor an extremely rare entity [1,2].

In our case, diagnosis was obtained with excisional biopsy before the mastectomy, through pathology consultation and immunohistochemical study.

No specific guidelines have been established for the treatment of AME and ACC, except for complete surgical resection with healthy surgical borders to avoid local recurrence. The literature seems to suggest simple mastectomy combined with sentinel lymph node biopsy as the proper treatment for AME and ACC; however, as of this writing, a consensus has not yet been reached [13]. In cases of AME and ACC, close follow-up after complete surgical resection of the lesion is advised. While the application of adjuvant chemotherapy and radiotherapy has been mentioned, their effectiveness, especially in metastasized tumors, seems limited. Further research is necessary to establish guidelines for the treatment of this rare disease.

## Conclusions

The present report is of a combination of ACC and AME in a female patient with breast cancer. The combination of these 2 neoplasms is very rare. A consensus about the treatment of such a rare disease has not yet been reached. Further research is required to establish guidelines for the management of patients with this particular type of breast cancer.

## Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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