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Adenoid Cystic Carcinoma of the Breast: Truly Uncommon or Easily Overlooked?

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Abstract. *Background: Adenoid cystic carcinoma of the breast is an uncommon histologic form of breast cancer, comprising in most series less than 1% of all mammary cancers. Due to the rarity, little information about its presentation on image studies has been noted in the literature. Here we report two additional cases with emphasis on the intriguing image presentations. Case one: A 67-year-old woman came to our clinic with the chief complaint of mastodynia. No obvious palpable mass of breast was found on physical examination. Mammography showed a small well-defined nodule in the medial part of the left breast without mammographic evidence of malignancy. Ultrasonography showed a 1.5 cm nodule with well-defined margin and heterogenous echogenicity in the medial part of the left breast. Unusually, a painful sensation was experienced on compression by the probe. The final pathological report was adenoid cystic carcinoma. Case two: A 48-year-old woman also came to our clinic with the chief complaint of mastodynia. No obvious palpable mass of breast was found on physical examination. Mammography showed dense mammary tissue with no mammographic evidence of malignancy. Ultrasonography showed two contiguous well-defined nodules with heterogenous echogenicity in the upper, middle part of the left breast. Unusually, a painful sensation was also noted on compression by the probe. Histopathological examination showed typical features of an adenoid cystic carcinoma. Conclusion: Adenoid cystic carcinoma of the breast fails to show the typical appearance of invasive ductal carcinoma on both mammogram and ultrasonography, probably due to its relatively well-defined nature with less surrounding architectural disruption and fibrosis. Hence a "negative" finding or a benign-looking breast lesion on mammography cannot completely exclude the existence of this disease. The presence of a painful breast lesion without obvious inflammatory evidence while compressed is a meaningful clue, which should lead to the suspicion of adenoid cystic carcinoma of the breast.*

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Adenoid cystic carcinoma of the breast is an uncommon histological form of breast cancer, in most series comprising less than 1% of all mammary cancers. The cell origin in the breast remains unclear. It is not known whether these tumors derive from ductal, myoepithelial or stem cells. Clinical experience has shown that this entity has a low propensity for metastasis and an excellent clinical prognosis (1,2). Due to the rarity, little information about its presentation on image studies has been noted in the literature. Here we report two additional cases with emphasis on the intriguing image presentations.

Case One

A 67- year-old woman came to our clinic with the chief complaint of mastodynia. No obvious palpable mass of the breast was found on physical examination. Mammography showed a small well-defined nodule (arrow) in the medial part of the left breast, without mammographic evidence of malignancy (Figure 1). Ultrasonography showed a 1.5 cm nodule with well-defined margin and heterogenous echogenicity (arrows, Figure 2) in the medial part of the left breast. Unusually, a painful sensation was experienced on compression by the probe. Further inspection and palpation revealed no obvious inflammatory changes. Excisional biopsy was arranged and frozen section examination showed carcinoma. The patient underwent left modified radical mastectomy later and the final pathological report was adenoid cystic carcinoma. All the 16 dissected lymph nodes were free of metastasis. The estrogen receptors were negative by immunperoxidase staining (3,4). Neither chemotherapy nor hormonal therapy was given. She is well with a follow-up period of 45 months.

Figure 1. *Mammography showed a small well-defined nodule (arrow) in the medial part of the left breast without mammographic evidence of malignancy.*

Figure 2. *Ultrasonography showed a 1.5 cm nodule with well-defined margin and heterogenous echogenicity (arrows) in the medial part of the left breast.*

Case Two

A 48- year-old woman also came to our clinic with the chief complaint of mastodynia. Past history revealed that a breast lump had been noted by a screening one year previously and regular follow-up had been suggested. No obvious palpable mass of the breast was found on physical examination. Mammography showed dense mammary tissue with no mammographic evidence of malignancy. Ultrasonography showed two contiguous well-defined nodules with heterogenous echogenicity (arrows, Figure 3) in the upper, middle part of the left breast. Additionally a painful sensation was experienced on compression by the probe. Further inspection and palpation revealed no obvious inflammatory changes. Operation was arranged and frozen section examination showed carcinoma. Modified radical mastectomy was performed. Histopathological examination showed typical features of an adenoid cystic carcinoma characterized by proliferation of cuboidal neoplastic epithelial cells forming tubular and cribriform glands with variable amounts of basophilic or hyalinized eosinophilic material. The neoplastic cells bore hyperchromatic and irregular-shaped nuclei, and pale eosinophilic to amphophilic cytoplasm. Stromal invasion of the neoplastic epithelial cords and ductules with perineural infiltration was noted (Figure 4). All the dissected lymph nodes were free of metastasis. Estrogen receptors were negative and HER-2 was 0 by immunoperoxidase staining.

Discussion

The microscopic pattern of adenoid cystic carcinoma of the breast is identical to that of the tumor seen in other sites. The most striking histological feature of this entity is the presence of cribriform nests of cells. These nests typically are composed of two morphological cell types: cuboidal epithelial cells and myoepithelial cells. The proportion of each component may vary among different tumors (1). Adenoid cystic carcinoma of the breast may be confused with cribriform ductal carcinoma *in situ* and invasive cribriform carcinoma, although cribriform carcinoma is usually well-differentiated. Their neoplastic cells typically have bigger, more vesicular nuclei and more voluminous cytoplasm than adenoid cystic carcinoma. Besides, invasive cribriform carcinoma does not have the cylindromatous pattern and mucin production that characterizes adenoid cystic

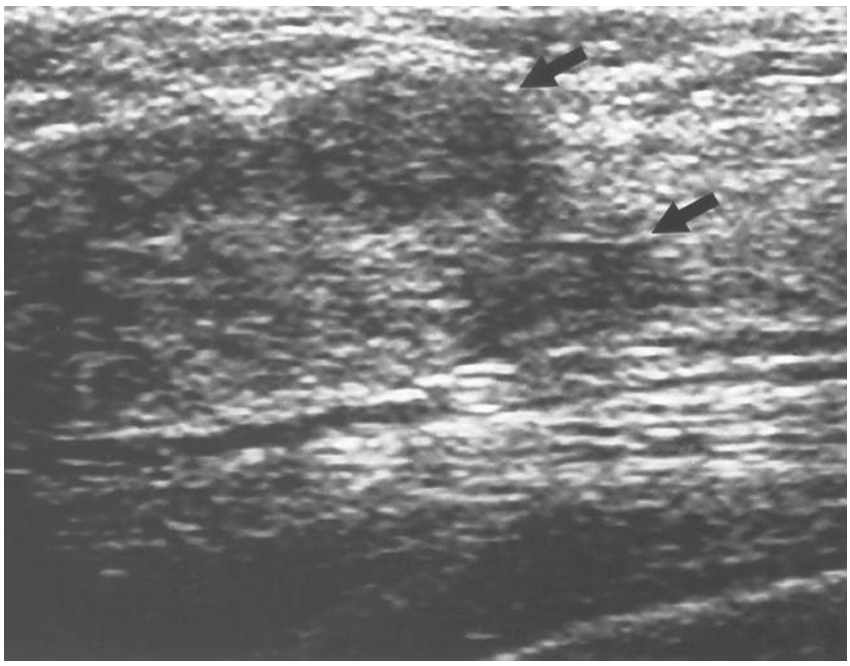

Figure 3. *Ultrasonography showed two contiguous well-defined nodules with heterogenous echogenicity (arrows) in the upper, middle part of the left breast.*

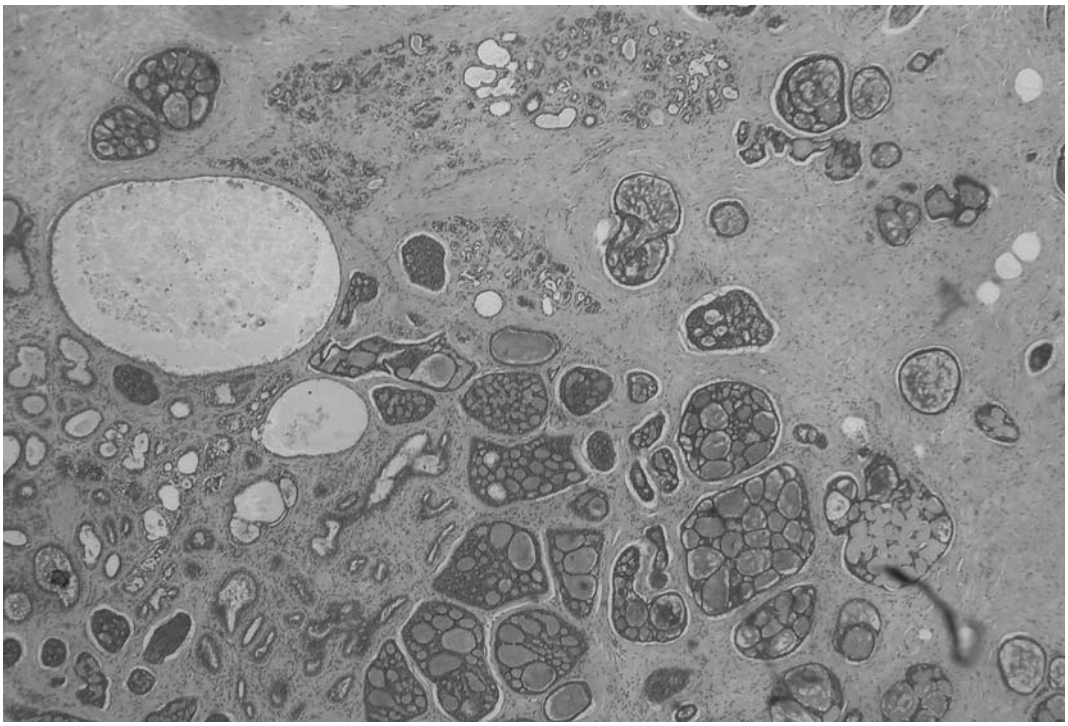

Figure 4. *Interconnecting cords and nests of tumor cells surround multiple, variably sized cyst-like spaces containing basophilic and hyalinized eosinophilic materials forming the characteristic cribriform pattern. Residual breast tissue is visible in the right lower region. (H&E 60X)*

carcinoma, and myoepithelial cells are not present (1,2). Collagenous spherulosis is an unusual benign ductal proliferation that should not be confused with adenoid cystic carcinoma. The epithelial proliferation in collagenous spherulosis is similar to that of intraductal hyperplasia. Besides the eosinphilc collagen spherules, collagenous spherulosis also

shows ovoid or slit-like spaces that render the typical appearance of benign intraductal hyperplasia (5,6).

Sumpio *et al.* (7) reported s series of 14 cases with adenoid cystic carcinoma of the breast, the main presenting symptom being a mass in the breast. In contrast, our two cases presented with non-palpable mass which could be attributed to their smaller size (<2 cm) and deeper locations. This highlights the importance of image study in detecting an early or more deeply-located breast lesion. Adenoid cystic carcinoma of the breast is a tumor with a prediction for perineural infiltration (8). This might explain the painful sensation on compression by the probe in our cases. The contractility of the myoepithelial component may be another explanation for this painful sensation (9). Hence, a painful breast lesion without obvious inflammatory evidence could rationally raise the suspicion of adenoid cystic carcinoma of the breast.

Mammography is usually regarded as the best image study for the screening of a breast malignancy. Review of the literature reveals little information about the presentation of adenoid cystic carcinoma on mammograms of the breast. In our first case, the mammography showed a small well-defined nodule (Figure 1,arrow) in the medial part of the left breast without mammographic evidence of malignancy. This probably could be attributed to the relatively well-defined nature with less surronding architectural disruption and fibrosis of adenoid cystic carcinoma of the breast. In case two, the mammography showed dense mammary tissue with no mammographic evidence of malignancy. Based on our experience, this mammography failed to show the characteristic changes of infiltrating ductal carcinoma, meaning that a "negative" finding or a benign-looking breast lesion on mammography can not completely exclude the existence of this disease. Similarly, there is again little information in the literature about the presentation of adenoid cystic carcinoma on ultrsonography. In our two cases, ultrasonography showed nodules with well-defined margin and heterogenous echogenicity (Figures 2 and 3), easily distinguishable from benign anechoic breast cyst. The best sonographic criteria for breast carcinoma are wide, jagged borders, architectural disruption, lack of compression and vertical orientation (10). Surprisingly, our cases lacked these characteristic changes usually shown in infiltrating ductal carcinoma. As stated before, this probably could be attributed to the relatively better defined nature with less surrounding architectural disruption and fibrosis of adenoid cystic carcinoma of the breast. The painful sensation on probe compression noted in our two cases was probably due to its perineural infiltration (8) or contractility of the myoepithelial component (9) and we stress that the presence of this unusual sign should rationally lead to a suspicion of adenoid cystic carcinoma of the breast.

Axillary lymph node metastases rarely develop. Distant metastases have been reported in the absence of axillary lymph node involvement and occur almost exclusively in the lung (11). This suggests that distant metastases probably predominantly develop by a hematogenous dissemination, and axillary lymph node dissection may not be necessary (11). Good local control can be achieved by lumpectomy with radiation or by simple mastectomy (2). With the favorable prognosis of this entity, adjuvant systemic therapy probably does not provide a clinically significant benefit (2). Annual chest X-ray follow-up and a thorough physical examination are still necessary despite the excellent prognosis of this disease.

In conclusion, adenoid cystic carcinoma of the breast fails to show the typical appearance of invasive ductal carcinoma on both mammogram and ultrasonography, probably due to its relatively well-defined nature with less surrounding architectural disruption and fibrosis. Hence a "negative" finding or a benign-looking breast lesion on mammography cannot completely exclude the existence of this disease. The presence of a painful breast lesion without obvious inflammatory evidence while compressed is a meaningful clue, which should lead to the suspicion of adenoid cystic carcinoma of the breast.

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