Case Report

A Case of Adenoid Cystic Carcinoma (ACC) of the Breast and Review of the Utility of Preoperative Imaging Diagnose

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A case of adenoid cystic carcinoma (ACC) of the breast in a 66-year-old woman is reported herein. ACC accounts for about 0.1% of all breast cancers. Our patient presented with a small, elastic and hard mass, measuring 2.0×2.0 cm, between both outer quadrants of the right breast. Although physical examination, ultrasonography and magnetic resonance (MR) mammography suggested a benign tumor, aspiration biopsy cytology (ABC) was performed twice, and the second ABC specimen was evaluated as suspicious for breast carcinoma. Breast conserving surgery with a level II lymph node dissection was subsequently performed. There was no lymph node metastases and estrogen receptor (ER) status was negative. Light microscopy revealed various growth patterns, with the cells showing biphasic cellularity. According to immunohistochemical analyses, CEA, actin and vimentin were positive, S-100 protein was negative, and the cytokeratin reaction was partially positive.

Therefore, ACC of the breast was diagnosed. Although ACC of the breast is a rare neoplasm, it should be considered in the differential diagnosis even if various diagnostic imaging studies suggest a benign tumor of the breast. Awareness of this tumor will help prevent misdiagnosis.

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Key words: Breast cancer, ACC (Adenoid cystic carcinoma), Preoperative imaging diagnose.

Adenoid cystic carcinoma (ACC) of the breast is a rare neoplasm accounting for about 0.1% of all breast cancers[1,2]. While common in salivary gland, this tumor also occurs at other sites such as in the nasopharynx, tracheal-bronchial tree, uterine cervix, Bartholin glands, skin, and other locations[3], and the prognosis for ACC of the breast is thought to be better than that of ACC at these other locations.

A case of ACC of the breast, detected on annual screening for breast cancer, and the preoperative imaging studies of the lesion are reported along with a discussion of other cases that have been reported in the literature.

Case Report

A 66 year-old Japanese woman presented in May of 1995 with a small mass in the right breast, on her yearly screening for breast cancer. When she visited our department in August of 1995, the mass was suspected to be fibroadenoma by palpation, mammography, and ultrasonography. Aspiration biopsy cytology (ABC) was then performed. Since the cytological findings were negative, the patient was scheduled for follow-up. A routine follow-up check did not show any changes in March 1996, 7 months after the initial vist. ABC was performed again and this time it was suspicious for breast carcinoma.

On physical examination, the tumor was found at the boundary between both outer quadrants of the right breast, and was mobile and elastic hard, measuring 2.0×2.0 cm with clear margins. There was neither abnormal nipple discharge nor skin redness. Axillary and subclavicular lymph nodes were not palpable. All conventional laboratory examinations, including various tumor markers (CEA and CA15-3), were normal. She had no

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Abbreviations:
ACC, Adenoid cystic carcinoma; ABC, Aspiration biopsy cytology; CEA, Carcioembrionic antigen, CA15-3, Carbohydrate antigen 15-3; MR, Magnetic resonance, Gd-DTPA, Gadolinium diethylenetriamine-pentaacetic acid; H-E, Hematoxylin-Eosin histopathological staining method; ER, Estrogen receptor, PgR, Progesterone receptor; EMA, Epithelial membrane antigen; EIA, Enzyme immunoassay

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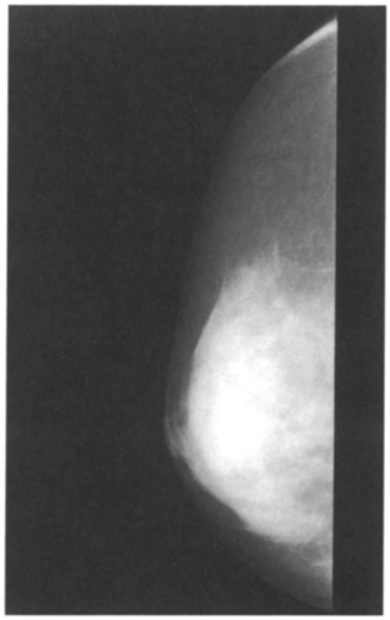

Fig 1. Mediolateral mammography showed neither tumor nor microcalcifications.

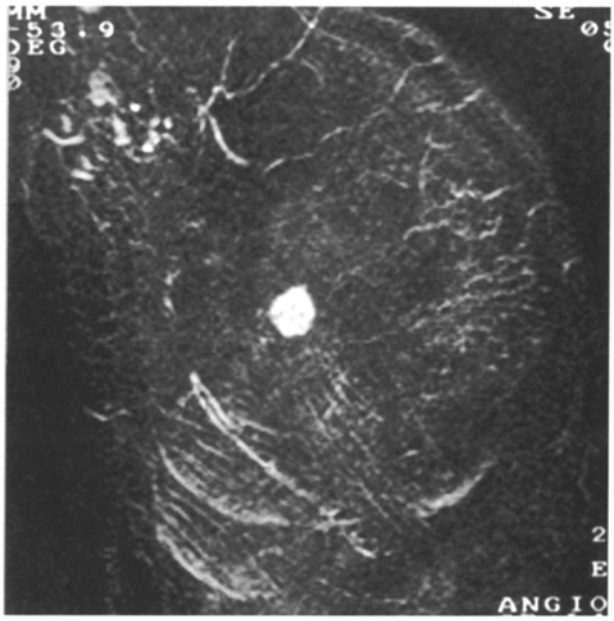

Fig 3. MR mammography showed a breast mass about 1.2 cm in size. Delayed enhancement was demonstrated after injection of Gd-DTPA, suggesting a benign neoplasm.

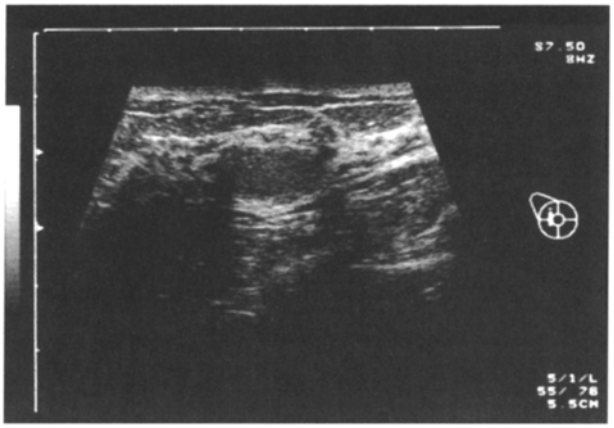

Fig 2. Ultrasonography shows a round, homogeneous, and hypoechoic mass with partially poorly-defined borders. Tumor measuring 1.7×1.4×0.8 cm in diameter is imaged in the right breast. Images were obtained using SSA-250A with a 7.5 MHz annular array prove (Toshiba, Medical Systems, Tokyo, Japan)

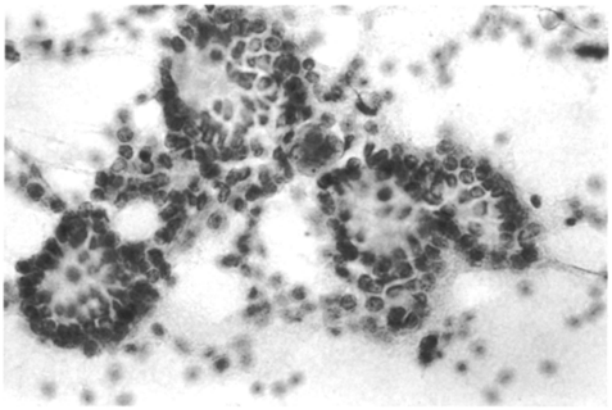

Fig 4. ABC material of ACC showing sheets of malignant cells, homogeneous central spaces surrounded by basaloid cells, with some showing a cribriform-like arrangement. (Papanicolau-staining, original magnification ×200)

noteworthy past medical or family history.

Although mammography showed neither tumor nor microcalcifications (Fig 1), ultrasonography revealed a $1.7 \times 1.4 \times 0.8$ cm, round and hypoechoic mass in the right breast (Fig 2). The internal echo of the mass was homogeneous, with enhancement of the posterior echo, suggesting fibroadenoma, but its margins were partially ill-defined. A diagnosis of breast carcinoma could not be completely excluded. Therefore, Magnetic Resonance (MR) mammography was performed using a 1.5-T magnet (Gyro scan R-4.5, Phillips, Best, The Netherlands). MR mammography showed a breast mass of about 1.2 cm in size. Delayed enhancement was demonstrated after injection of gadolinium diethylenetriamine-pentaacetic acid (Gd-DTPA), suggesting a benign neoplasm (Fig 3).

This tumor had been aspirated using ultrasonographic guidance and 21-gauge (0.8mm) needles. ABC findings showed highly cellular smears as well as rare mitotic figures including small,

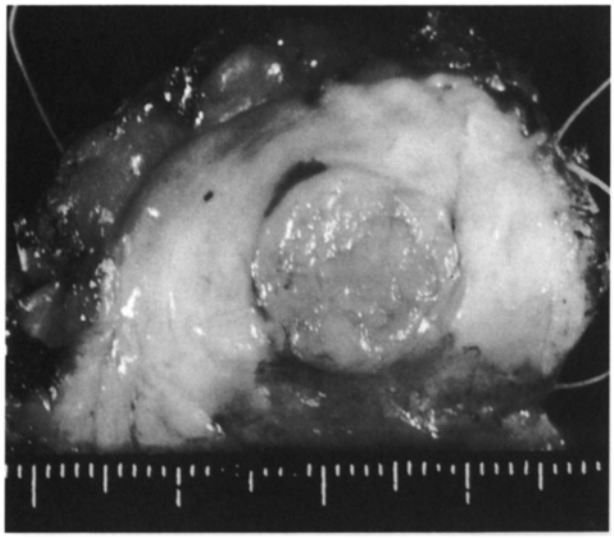

Fig 5. The cut surface of the tumor shows a nodular, gray-white lesion, measuring 1.5×1.5 cm.

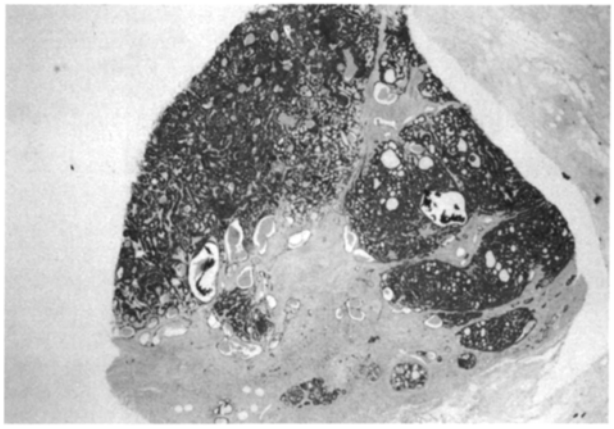

Fig 6. Low magnification view of an entire tumor showing central nodule that appeared grossly circumscribed. There are slightly invasive elements extending into the surrounding breast. ×12.5.

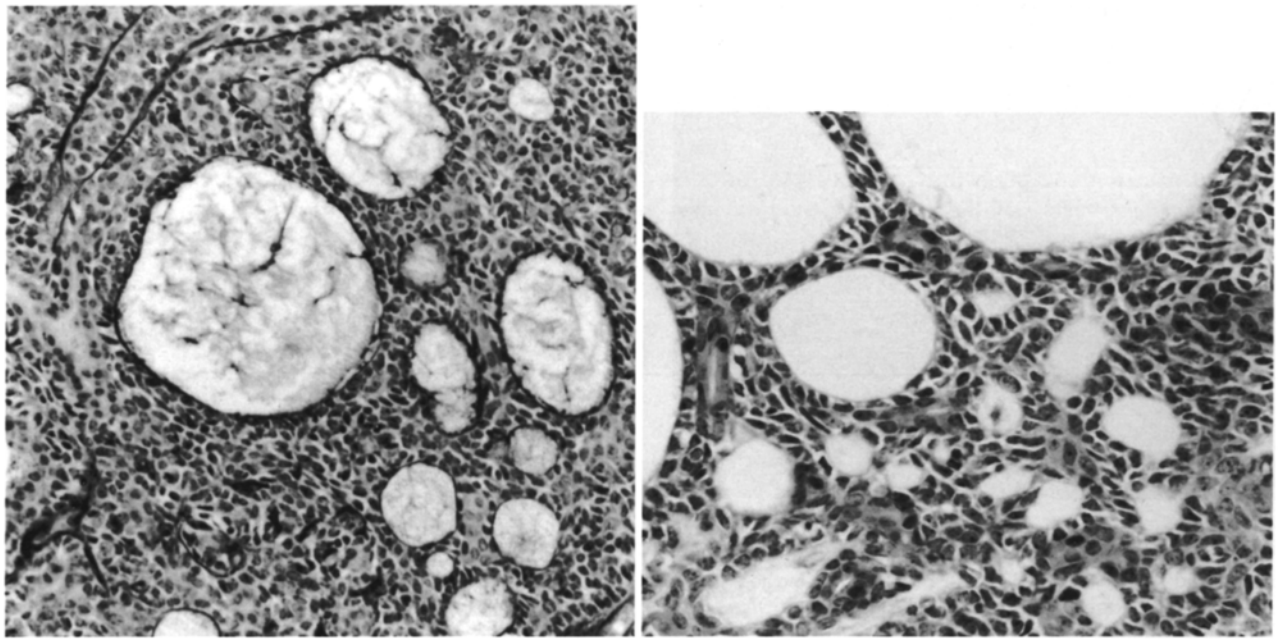

Fig 7. Histological examination revealed: Left, glandular subtype. The glandular type consists of epithelial cell nests permeated by numerous cylindric spaces, some of which are occupied by a hyaline stroma. PAS, original magnification, ×120. Right, histologic grade II, nuclear grade 1. Histologic grade II adenoid cystic carcinoma, grade II tumor contained solid areas that constituted less than 30% of the tumor volume. Nuclear grade 1 comprised mild cytologic atypia, with nuclei having slight variation in size and shape and rare mitotic figures (0-1 mitoses/10 high-power fields). H-E, original magnification, ×200.

uniform cells with centrally-located hyaline globules (Fig 4). The cytological findings were suggestive of a malignant tumor, especially ACC, but benign proliferative lesions could not be ruled out.

Based on the above findings, the lesion was suspected to be breast cancer (T1aN0M0, Stage I, TNM Stage classification, General Rules for Clinical and Pathological Recording of Breast Cancer, The Japanese Breast Cancer Society). Accordingly, the patient was admitted to our department in March of 1996, and breast-conserving surgery with a level II lymph node dissection and subsequent frozen-section evaluation was performed.

Gross inspection of the resected specimen revealed a nodular, gray-white lesion, measuring

1.5 × 1.5 cm (Fig 5). Low magnification of the entire tumor showed a central nodule that appeared grossly circumscribed (Fig 6). Formalin-fixed paraffin-embedded tissue specimens were cut in serial sections and stained with H-E.

These sections revealed that the tumor cells formed various arrangements, such as cribriform, tubular, and solid nests. A variety of microscopic growth patterns were presented. They showed a "biphasic pattern" with myoepithelial cells intermixed with ductal epithelial cells. Epithelial cell nests permeated by numerous cylindric spaces, some of which were filled with eosinophilic mucous material predominated (Fig 7). Additionally, some infiltrating tumor cells were seen in the surrounding tissues. The pseudocyst lumen stained positively for Alcian blue, and the true duct contained PAS-staining mucous. Immunohistochemical studies were performed on the histologic sections. Glandular cells, composing the true ductules, stained positively for CEA (Immunotech, Marseille, France) and partially-positive for cytokeratin (Becton Dickinson, Mountain View, CA, USA), while the basaloid cells composing the pseudocysts were immunoreactive for Vimentin (Nichirei, Tokyo, Japan). The tumor showed intensive positivity for actin (Dako, Santa Barbara, CA, USA), but stained negatively for S-100 protein (Nichirei, Tokyo, Japan).

Histologically, this tumor was glandular type, histologic grade II (II: less than 30 percent solid) and nuclear grade 1 ACC. No evidence of perineural invasion was found in the lesion. The surgical margins were free of carcinoma and there were neither lymph node metastases nor vascular invasion. ER and PgR were both negative. The ER and PgR values were obtained by a sandwich enzyme immunoassay (EIA). The patient was well at the follow-up examination 4 years and 8 months after operation without radiotherapy and adjuvant therapy.

Discussion

ACC of the breast is a rare histologic form of breast cancer comprising about 0.1% of breast cancers[1,2,4-8]. The frequency of this tumor at our department is 0.16%. Since the tumor border is often clear on palpation and diagnostic imaging, it is hard to distinguish ACC from fibroadenoma of the breast.

ACC occurs predominantly in women whose average age is approximately 60 years, an average that is somewhat higher than in other breast cancers[1]. It is rarely bilateral and has no predilection with respect to laterality[4]. ACC typically presents as a sharply defined, firm, and smoothly bordered mass that is occasionally tender to palpation. The tumor is rarely fixed to the overlying skin, nipple, or pectoral muscles[3]. Although these tumors are most frequently subareolar lesions, nipple discharge is rarely present[4]. Most cases have been reported to be larger than 3 cm in diameter, and one case that has been reported was a slowly growing tumor observed throughout a 9-year period[9]. The growth of the tumor is thought to be slow[1]. Because ACC of the breast is not as malignant as that of salivary gland and very rarely involves the lymph nodes, spreads to other organs remotely, or relapses locally, it has been said to carry an eminently good prognosis[3,10]. Although our patient was a little older than the patients reported by other investigators, the prognosis was still considered excellent, as with many other reported cases [3, 10-14] without axillary lymph node invasion and distant metastases.

Estrogen and progesterone receptors were negative in our patient and have been reported to be negative in ACC[3, 4]. ER positive cases or lymph node positive cases of this type of tumor have been scarcely reported in the literature[1, 10-13].

Mammography most often discloses a circumscribed, lobulated nodule, usually in the upper quadrants or in the periareolar region. The mammographic features of adenoid cystic carcinoma of the breast, to the author's knowledge, have not been previously described. Few reports are available concerning the specific features on diagnostic imaging of ACC lesions[15, 16]. Mammographic and ultrasonographic findings vary widely, and it has even been reported that the shadow of a tumor can be hard to find on mammography[9]. In the present case, although we could find the breast tumor on palpation, mammography showed neither tumor nor microcalcifications. The lesion had some features suggestive of a fibroadenoma on both palpitation and ultrasonography, but retrospectively, the tumor margin was partially indistinct by ultrasonography. This is the sole clinical finding that suggested an underlying malignant tumor. Tsuboi *et al*[16] recently reported that by performing dynamic MR imaging, ACC of the breast can be considered in the differential diagnosis, which also includes breast cancer with

a cribriform pattern, but our patient was suspected to have a benign neoplasm by MR mammography. Therefore, we think that it is difficult correctly diagnose ACC of the breast preoperatively by various diagnostic imaging studies.

Cytologic features of ACC of the breast by ABC have been reported to consist of small and round tumor cells surrounding amorphous mucous material[10]. There are some reports[14, 17-19] that the diagnosis of ACC was established by ABC. In our patient, however, the lesion was classified as suspicious of malignancy even before the second ABC. Although breast cancer was suspected, no definite histologic type could be determined by ABC.

ACC has two prominent histological features, one being cribriform structures of varying size and the other being a pseudocyst without polarity with respect to the true ducts or the lumen. Varying degrees of these two features seem to account for a variety of histologic findings of ACC[10, 14, 20, 21].

Histologically, two diagnostic requirements restrict the recognition of ACC of the breast: (1) intercellular cystic spaces lined by basement membrane material, and (2) biphasic cellularity with myoepithelial cells intermixed with another cell type[20, 21].

Lamovec *et al*[22], who stained ACC immunohistochemically, demonstrated ductule cells staining with CEA, EMA, and keratin. Matsuyama *et al*[23] reported that CEA and EMA were present in the true duct, and that the cells mainly comprising the pseudocysts and myoepithelial cells were reactive to vimentin. In our case, the tumor histologically showed a biphasic cellular pattern[21], the pseudocyst lumen stained with Alcian blue, and the true duct contained PAS-staining mucous material, so the diagnosis of ACC was straightforward. The epithelial cells forming the true duct were reactive to CEA and cytokeratin, while the epithelial cells of the pseudocyst stained with Vimentin and actin. S-100 protein was negative in this tumor. These results reconfirmed that immunohistochemical analyses are helpful for the diagnosis of ACC.

Santamarìa *et al*[9] compared the histologic subtypes, defined according to a system previously documented for ACC of the salivary gland, with the mammographic findings. They reported that tumors appearing on mammography as poorly- or partially poorly-defined masses were of either glandular or tubular types, and that the case corresponding to solid-type ACC appeared as a focal asymmetric density on mammography. Szant *et al*[24] and Ro *et al*[25] proposed stratifying ACC into three grades on the basis of the proportion of solid growth within the lesion (I: no solid elements; II: less than 30 percent solid; III: more than 30 percent solid). Kleer *et al*[26] graded the tumor cell nuclei from nuclear grade 1 to 3, and proposed that an appropriate surgical method be selected based upon this stratification. The tumor in our case corresponded to the glandular type, histologic grade II, and nuclear grade 1. The breast conserving surgery selected for this patient can therefore be considered appropriate[26, 27], except for the fact that there was no need for axillary dissection. In this respect, further investigation involving many cases is warranted.

We performed ABC suitably and followed our patients carefully, such that we found this case. The results obtained in this case suggest the importance of following up and/or cytopathological examination for patients diagnosed with fibroadenoma by diagnostic imaging studies, because some of these cases may actually be ACC, even though ACC of the breast is an extremely rare neoplasm.

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