

# Adenoid cystic carcinoma of the breast

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## ABSTRACT

**Adenoid cystic carcinoma of the breast is a rare neoplasm that constitutes less than one percent of all mammary carcinomas. To date, there have been about 140 cases reported in the literature. It is a rare variant of adenocarcinoma that usually occurs in the salivary glands. In contrast to the aggressive nature of adenoid cystic carcinoma that occurs in the head and neck region, adenoid cystic carcinoma of the breast has a very favourable prognosis. Little has been published to date on its radiological features. We describe a 63-year-old woman with adenoid cystic carcinoma detected on mammography in our national breast screening programme, the radiological findings at presentation, the surgical management and a review of the literature.**

**Keywords:** adenoid cystic carcinoma, breast adenoid cystic carcinoma, breast tumour, mammography

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## INTRODUCTION

Adenoid cystic carcinoma of the breast is a rare neoplasm that accounts for only 0.1% of all mammary carcinomas. They are more commonly described in the salivary glands where they are usually associated with an aggressive course. In contrast to extramammary adenoid cystic carcinoma, those arising in the breast have an excellent prognosis. The incidence of lymph node metastasis is lower and distant metastases are uncommon.<sup>(1,2)</sup> Distant metastases, however, can occur without prior lymph node involvement. It is generally oestrogen (ER) and progesterone (PR) receptor negative. The cell of origin for adenoid cystic carcinoma of the breast is unclear. Evidence suggests that it may arise from ductal epithelium and myoepithelium.<sup>(3)</sup> Histologically, the tumour is composed of epithelial cells with variable degrees of glandular differentiation, myoepithelial cells and characteristic collections of acellular basement membrane material. It is important to distinguish this from other types of breast cancer as it has an excellent prognosis.

## CASE REPORT

A 63-year-old asymptomatic woman presented to our centre for a screen-detected abnormality seen on mammography. Her past medical history was significant for depression, for which she was treated with anti-

depressants. Family history was negative for breast and ovarian cancer. Menarche occurred at the age of 12 years and she attained menopause at the age of 50 years. She was placed on hormone replacement therapy postmenopausally for a period of less than five years. She was married with no children. She did not smoke or drink. Physical examination revealed a vaguely palpable 1 cm mass at the upper outer quadrant of the right breast. There were no skin changes nor was there nipple discharge. No palpable axillary adenopathy was detected.

Mammography revealed an asymmetric ill-defined mass in the upper outer quadrant of the right breast, approximately 5 cm from the nipple (Fig. 1). The patient was recalled for an assessment of the abnormal mammography finding through the breast screening programme. Ultrasonography confirmed an ill-defined hypoechoic mass measuring 14 mm × 9 mm in the upper outer quadrant of the right breast (Fig. 2). Ultrasound-guided 14 gauge core biopsy was performed with a BARD biopsy instrument. Histopathological evaluation of the five core biopsy specimens revealed a grade 1 invasive carcinoma composed of cribriform islands with epithelial cells featuring uniform dark nuclei (nuclear pleomorphism score 1 or nuclear grade 1), rimming luminal spaces containing a mucinous ground substance as well as basement membrane-like material, all features of adenoid cystic carcinoma (Fig. 3). The tubule score was 1 and there were hardly any mitoses (mitotic score 1). Immunohistochemistry for ER, PR and cerbB2 was negative, while p63 and 34βE12 decorated the tumour cells. The patient underwent definitive wide excision of the right breast lump with axillary clearance, followed by radiotherapy. Histopathology of the surgically-resected specimen confirmed the presence of a 1.8 cm × 1.4 cm × 1.3 cm tumour with histological features of adenoid cystic carcinoma. Lymph nodes were negative for tumour metastases. She remains well to date.

## DISCUSSION

Adenoid cystic carcinoma of the breast is a rare and slow-growing neoplasm, accounting for 0.1% of all breast neoplasms. It is of interest due to its favourable prognosis, as lymph node involvement and distant metastases are uncommon. Adenoid cystic carcinoma of the breast was first termed “cylindroma” by Billroth.<sup>(4)</sup> This tumour occurs predominantly in women with a mean age of 50–64 years. It is rarely bilateral and has no predilection with respect to laterality.<sup>(5)</sup> The most frequent presenting symptom is that of a tender

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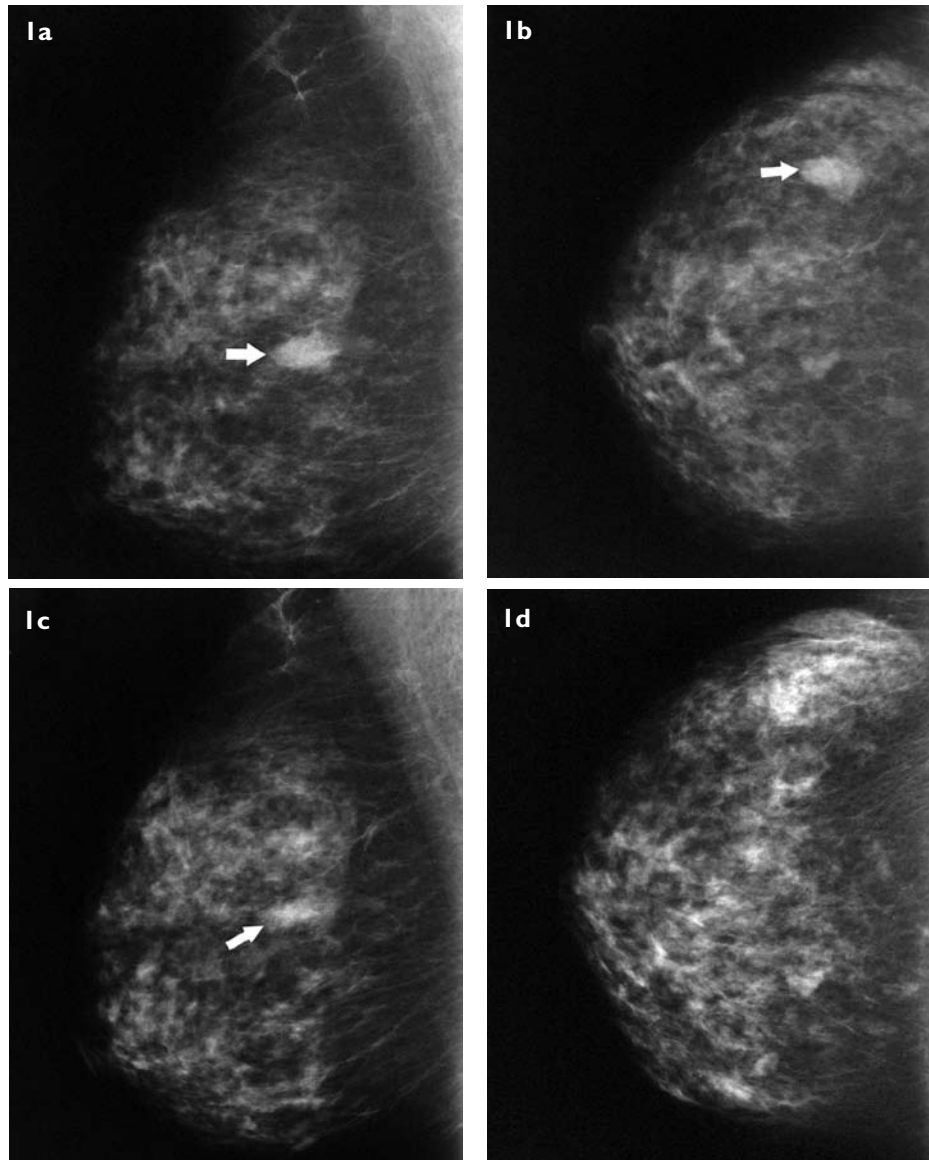
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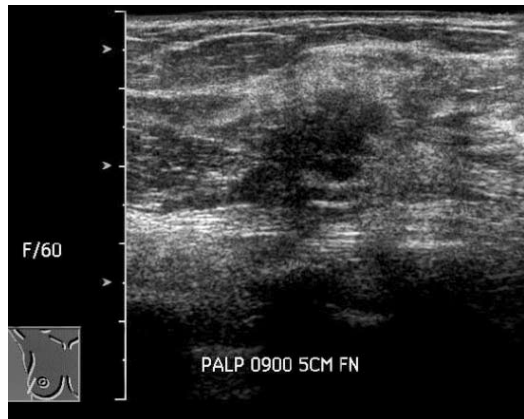


**Fig. 1** Mediolateral oblique (MLO) and craniocaudal (CC) view mammograms of the right breast performed in March 2006 (a & b) and February 2004 (c & d). Evolving density (arrow) is detected in the upper and outer quadrant of the right breast. Corresponding density is not seen in the earlier CC view.

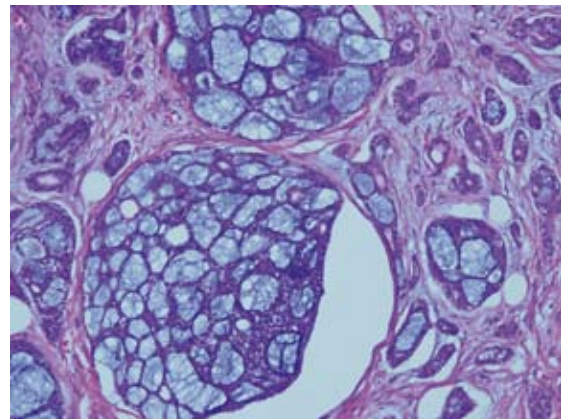
breast mass, which was absent in our patient. Although it is commonly located in the area of the nipple and areola, nipple discharge is an uncommon symptom. Pain is a symptom of adenoid cystic carcinoma of the salivary gland, the cause being attributed to perineural invasion by the tumour. However, perineural invasion in adenoid cystic carcinoma of the breast is rare, though it is commonly seen in adenoid cystic carcinoma of the salivary glands. It is uncertain why tenderness is a predominant symptom in patients with adenoid cystic carcinoma of the breast. Perineural invasion and pain were absent in our patient.

The tumour usually presents symptomatically, with only a few cases detected incidentally in asymptomatic patients. In a described series, only four out of 22

patients with adenoid cystic carcinoma were detected radiologically; the rest were investigated for breast lump and pain.<sup>(5)</sup> As such, the imaging features of this tumour have rarely been described. A review of the literature shows that its radiological appearances are generally non-specific and it can present as a benign-appearing, smooth, round or lobulated density or as an irregular mass. In a review of mammographical appearances with pathological correlation by Santamaria et al, mammography most often disclosed a circumscribed lobulated nodule, usually in the upper quadrant or in a peri-areolar location.<sup>(6)</sup> They also found that masses that appeared ill-defined or partially ill-defined on mammography could usually be correlated with tumours showing microscopic invasion. This was,



**Fig. 2** Ultrasonographical image of the right breast shows an irregular hypoechoic mass measuring 14 mm × 9 mm in the upper and outer quadrant of the right breast.



**Fig. 3** Photomicrograph of the specimen obtained from an ultrasound-guided core biopsy shows adenoid cystic carcinoma composed of cribriform islands of cells with dark nuclei and luminal spaces containing pale mucinous secretions on light microscopy. Several irregular tubules are also noted (Haematoxylin and eosin, × 200).

however, not the case in our patient who, despite having had an ill-defined mass on mammography, did not have lymphovascular or perineural invasion, although there was a microscopically invasive front. Calcifications may also be associated with this tumour, but these are usually seen on histology and only rarely detected on mammography. As the tumour in our patient has an ill-defined appearance mammographically and ultrasonographically, the radiological differential diagnosis for adenoid cystic carcinoma includes invasive ductal carcinoma.

Pathologically, various growth patterns have been described in adenoid cystic carcinoma of the breast. The patterns can be described as glandular (cribriform), tubular and solid (basaloid) types. The differential diagnosis of the glandular and tubular subtypes includes cribriform intraductal carcinoma (ductal carcinoma *in situ* [DCIS]), invasive cribriform and tubular carcinoma. Cribriform DCIS can be distinguished from adenoid cystic carcinoma by the absence of basement membrane-like material found in the lumens of the latter, and the presence of ER and PR expression in cribriform DCIS. Invasive cribriform carcinoma, similar to cribriform DCIS, also expresses ER and PR, but lacks myoepithelial cells related to its invasive nature. A benign histological mimic is collagenous spherulosis typified by the pink spherules and accompanying usual type epithelial hyperplasia. Adenoid cystic carcinoma of the solid type can resemble ordinary ductal carcinoma.<sup>(7)</sup> Studies attempting to investigate the possible correlation between the histologic grade and prognosis have been published. Ro et al suggested that adenoid cystic carcinoma of the breast can be graded on the proportion of solid growth of the tumour which correlated with prognosis.<sup>(8)</sup> Grades

1–3 were assigned according to the proportion of solid elements. Grade 1 (no solid element), Grade 2 (< 30% solid elements) and Grade 3 (> 30% solid elements) were found to have a possible bearing on treatment. Their proposed treatment was local excision for grade 1 tumours, simple mastectomy for grade 2 tumours and mastectomy with axillary clearance for grade 3 tumours. However, axillary lymph node metastases are rare in adenoid cystic carcinoma of the breast. Arpino et al noted that nodal metastases only occurred in less than ten reported cases in the literature.<sup>(9)</sup> Distant metastases are uncommon and they can occur without prior lymph node involvement. Tumours with a higher proportion of solid elements tended to be larger, with a higher risk of recurrences, and have a more aggressive clinical course.<sup>(6,8)</sup>

Arpino et al reviewed the molecular markers in adenoid cystic carcinoma of the breast, the treatment and clinical outcome in a group of 28 patients.<sup>(9)</sup> They analysed the DNA content of the tumours and found that 92% of their patients were DNA diploid, whereas the frequency of DNA aneuploidy in invasive breast carcinomas is approximately 60%–65%. Adenoid cystic carcinoma also showed low proliferative activity and were usually ER and PR negative. Compared with infiltrating ductal carcinomas of the breast, adenoid cystic carcinomas were far more likely to be DNA diploid and have low proliferative activity. They concluded that adenoid cystic carcinoma of the breast has favourable biological characteristics, consistent with the favourable phenotype.

There is no consensus on optimal treatment for patients with adenoid cystic carcinoma of the breast as this is such a rare diagnosis. Reported surgical treatment modalities range from a simple lumpectomy

with radiotherapy to radical mastectomy. Due to the reported low incidence of nodal metastasis, McClenathan and de la Roza suggested that even limited lymph node dissection is not warranted.<sup>(10)</sup> Little has been published to date on the role of adjuvant systemic therapy for this diagnosis. Finding the optimum treatment regime will require prospective clinical trials to compare the different treatment options, but this will be difficult to conduct in such a rare neoplasm. A review of the literature by Santamaria et al revealed 14 cases of local recurrences from 182 reported cases, of which 11 occurred after local excision, one after simple mastectomy and two after radical or modified mastectomy.<sup>(6)</sup> High rates of local recurrence have been reported following local excision. Sumpio et al found that among eight cases of local recurrences, six had local excision.<sup>(7)</sup> Leeming et al showed that nine out of 24 patients (37%) had local recurrence after local excision.<sup>(3)</sup> In a recent case report, local recurrence of adenoid cystic carcinoma in the breast after successful treatment by lumpectomy and adjuvant chemotherapy and radiotherapy was described.<sup>(11)</sup> The patient presented with localised tenderness in the peri-areolar aspect of the ipsilateral breast on follow-up. Initial mammographic and ultrasonographic investigations at the tender area were negative. Subsequent ultrasonography six months later, done because of increased tenderness, revealed a mass, which proved to be recurrent tumour. Despite its excellent prognosis, local recurrence and distant metastasis that occur long after initial treatment have been reported in the published literature. While the lungs are the predominant site of metastasis, other reported sites of metastasis include the liver, kidneys, lymph nodes and brain.<sup>(9)</sup> Therefore, close follow-up

with clinical examination to exclude local recurrence and chest radiography for screening of metastases is prudent. In particular, patients with a prior history of adenoid cystic carcinoma who present with recurrent mastalgia should be investigated for recurrent disease and closely followed-up, even if initial investigations yield negative results.

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