

# An elderly woman with multilobulated breast mass presenting as a diagnostic dilemma: A rare case report

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### ABSTRACT

A breast mass in women often presents a diagnostic challenge due to the diversity in the diagnosis. We herein report a rare variant of breast carcinoma, an invasive apocrine carcinoma (AC), in an elderly woman where the breast mass clinically mimicked phyllodes tumour. Immunohistochemistry (IHC) showed the tumour as triple-negative and also negative for androgen receptor (AR). Gross cystic disease fluid protein (GCDFP-15) was strongly and diffusely positive. It is an exceptional finding. It implies its significance as a diagnostic marker of AC of the breast. The accurate diagnostic criteria of AC are still lacking. Patients with breast lumps offer unique challenges and enormous responsibility to primary and family care physicians.

**Keywords:** Apocrine carcinoma, GCDFP-15, phyllodes tumour

### Introduction

Krompecher in 1916 first described the malignant transformation of apocrine cells. Apocrine differentiation is seen in benign as well as some *in situ* or invasive carcinoma of the breast.<sup>[1]</sup> AC usually presents in older age patients with smaller tumour sizes.<sup>[2]</sup> The reported frequency is 0.3–4%, as the accurate diagnostic criteria of AC are still lacking. Both morphological and immunohistochemistry (IHC) criteria have been proposed to make a definitive diagnosis of pure invasive AC.<sup>[3]</sup> Morphologically, AC presents with large granular and foamy cells of the epithelium in more than 90% of the tumour cells.<sup>[4]</sup> The molecular apocrine (MA) definition is based on the immunohistochemistry features of estrogen receptor/progesterone receptor (ER/PR)–ve and AR +ve. It resembles a basal-like triple-negative phenotype, but clinically it behaves differently from basal-like triple negative breast cancer (TNBC) with a good prognosis.<sup>[5,6]</sup> TNBC with AR +ve is very often observed in

intraductal carcinoma and is more variable in invasive carcinoma.<sup>[6]</sup> GCDFP-15 glycoprotein is not expressed in normal ductal or lobular epithelium of the breast, however, it is almost always present in cells with apocrine differentiation and its expression is more often linked with the AR expression.<sup>[7]</sup> The case presented herein posed a diagnostic dilemma, both clinically and immunohistochemically.

### Case History

A 65-year-old multiparous woman with no known comorbid conditions presented with a 3-year history of a painless, progressively enlarging multilobulated mass in her right breast. She stated that the mass initially started deep to the nipple with associated intermittent serosanguinous discharge, the amount of which gradually diminished with the inversion of the nipple as the mass showed rapid growth in the last 6 months. She denied any history of carcinoma breast, ovary or other malignancy in her family. Physical examination showed the right breast enlarged and deformed with multilobulated mass, shiny overlying skin and slit-like complete inversion of the nipple. The mass was non-tender, firm, free from skin and underlying fascia. The axilla, opposite breast, neck and systemic examination was unremarkable [Figure 1].

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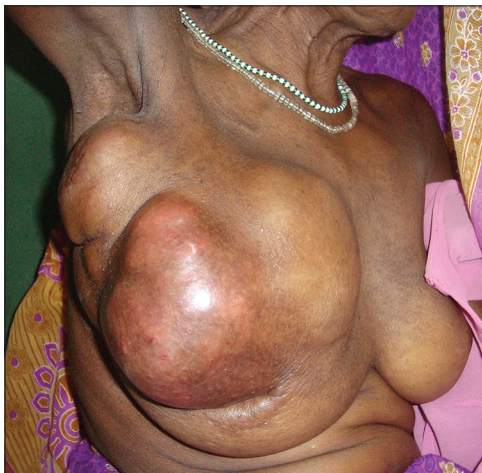
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Routine laboratory reports were within the normal range. Sonomammography showed heterogeneous mass lesions. Computed tomography (CT) of the breast demonstrated multilobulated, isodense mass lesion measuring 17.1 cm × 8.6 cm × 14.4 cm size with internal septations and amorphous calcifications with evidence of internal necrosis. There was no evidence of axillary lymphadenopathy. The imaging features suggested a malignant pathology. Fine-needle aspiration cytology (FNAC) of the mass suggested borderline/malignant phyllodes tumour with cystic degeneration or malignant fibrous histiocytoma. Core-needle biopsy revealed moderately differentiated, invasive intraductal carcinoma featuring large granular and foamy cells representing over 90% of the tumour cells, consistent with a rare apocrine morphological variant with Modified Bloom-Richardson score of 2 + 2 + 1 = 5 and histological grade 1. The immunohistochemistry reports were negative for ER, PR, herceptin receptor (HER)-2 and AR. However, another biomarker, gross cystic disease fluid protein (GCDFP-15) was strongly and diffusely positive [Figure 2]. Ki-67 was 5%. After complete metastatic workup and with consent, a right total mastectomy with sentinel lymph node biopsy (SLNB) was performed. Histopathological examination of the dissected specimens confirmed the biopsy finding. SLNB was negative for tumours. The postoperative period was uneventful. No adjuvant chemotherapy and/or radiotherapy was advised by the tumour board. The patient was asymptomatic on follow-up till 3 years and showed no sign of local recurrence or metastasis.

## Discussion

We have reported an exceedingly rare case of invasive AC breast that posed a unique challenge. The tumour was exceptional mainly for two reasons. First, multilobulated large breast mass mimicked a phyllodes tumour clinically. AC is often indistinguishable clinically from other breast lumps and needs to be differentiated from a benign condition like giant fibroadenoma, fibrocystic disease and apocrine metaplasia which are common in young, premenopausal women, unlike our case of the elderly woman.<sup>[8]</sup> A breast mass



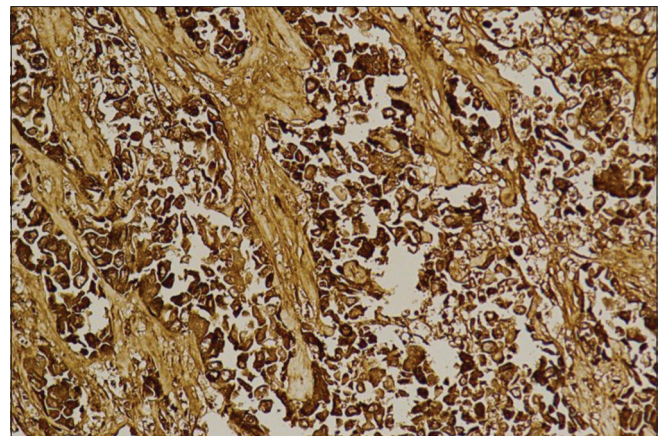
**Figure 1:** Photomicrograph depicting multilobulated right breast mass with unremarkable axilla

could be a hydatid cyst in the endemic area,<sup>[9]</sup> chest-wall abscess or chronic inflammatory pathology.<sup>[10]</sup> A Schwannoma, lymphoma, angiosarcoma or metastasis should also be kept in mind while making a differential.<sup>[10-13]</sup> In our case, FNAC indicated the borderline phyllodes tumour, however, the demonstration of apocrine morphology with invasive ductal carcinoma on core-needle biopsy confirmed the diagnosis of AC.<sup>[2]</sup>

Second, the tumour expressed GCDFP-15 in the absence of AR. GCDFP-15 expression is seen in approximately 50% of all breast cancers. It is more commonly associated with breast tumours expressing AR and MA variants. It is said that AR controls the GCDFP-15 production, and hence, is effectively controlled by antiandrogens.<sup>[13]</sup> GCDFP-15 positive AC are less aggressive, rarely spread to lymph nodes and have a good prognosis. In the advanced cases of AC, however, the GCDFP-15 level is reported to be decreased, hence, GCDFP-15/AR positivity is not a consistent feature of AC.<sup>[14]</sup> Therefore, a composite molecular and IHC signature for a better definition of MA breast carcinoma is suggested using their qualitative reverse transcriptase polymerase chain reaction (qRT-PCR)-AR profile rather than AR-IHC in ER-ve breast cancer. It was found that HER +ve and GCDFP-15 expression are more specific markers to differentiate MA from basal-like. Search for markers for accurate diagnosis and treatment options is needed. Ki-67 expression, CK5/6, B-cell lymphoma-2 (BCL 2), mammaglobin, P53 and other metabolism-related genes may have potential therapeutic implications.<sup>[15]</sup>

For the patient with triple negative apocrine carcinoma (TNAC) with GCDFP-15 expression, a better survival outcome was noted with surgery alone compared to other TNBC.<sup>[16]</sup> The role of chemotherapy was reported to be marginal in such cases.<sup>[17]</sup> In cases with other cutaneous swelling showing apocrine morphology, the breast lumps need to be examined and excluded as a possible primary.<sup>[18]</sup>

Patients with breast lumps like other illnesses report mostly to the primary care or family care physician first. They offer unique challenges and enormous responsibility on them as they have



**Figure 2:** Immunohistochemistry of apocrine carcinoma (AC) showing strong and diffusely positive gross cystic disease fluid protein (GCDFP-15)

to coordinate various activities like initial care, timely diagnosis, appropriate referral and subsequent follow-up care in addition to educating patients and spreading awareness about the disease and its prevention. Therefore, awareness and knowledge of the entity are imperative.

### Key messages

1. Invasive apocrine carcinoma of the breast is a very rare type of breast carcinoma showing typical morphologic, immunohistochemical and molecular features with a good survival rate.
2. GCDFFP-15 biomarker needs to be recommended to establish a correct diagnosis.
3. Primary and family care physicians can play a crucial role in the management of a patient with a breast lump.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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