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Case Presentation of Breast Adenoid Cystic Carcinoma

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ABSTRACT

Adenoid cystic carcinoma (ACC) of the breast represents a rare basal-like subtype that can exhibit cribriform, solid, tubular, or trabecular architectural features. Histologically, breast ACC exhibits a unique arrangement consisting of both epithelial and myoepithelial cells, mirroring the structure seen in its salivary gland counterpart. This report highlights an unusual presentation of breast ACC characterized by a cribriform and trabecular growth pattern. Although imaging techniques are valuable tools for preliminary evaluation and guiding clinical management, their utility may be limited due to the diverse imaging manifestations of ACC. Definitive diagnosis relies on histopathological evaluation, which remains the diagnostic gold standard. Despite ongoing debates regarding the pathological subclassification of ACC, it plays a pivotal role in shaping treatment strategies. Surgical intervention is widely recognized as the primary treatment modality for breast ACC. However, due to the rarity of this malignancy, there are no standardized surgical protocols, which often leads to inconsistent treatment approaches.

Keywords: Screening, Adenoid cystic carcinoma, Pathological, Breast, Tumor

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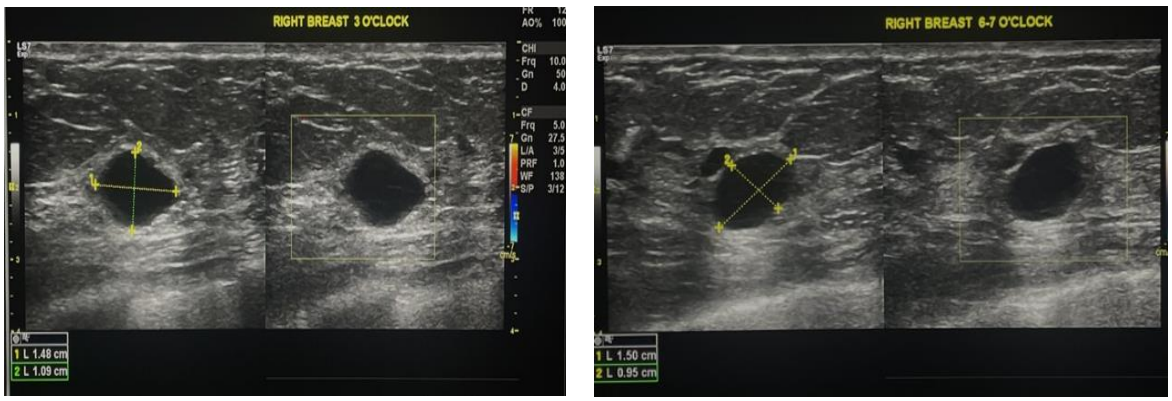
Introduction

Adenoid cystic carcinoma (ACC) is categorized as a basal-like subtype that exhibits cribriform, solid, trabecular, or tubular architectural features within the breast [1, 2]. Histologically, ACC of the breast is marked by a dual-cell population comprising epithelial and myoepithelial components, mirroring the characteristics of the identically named tumor found in the salivary gland [3, 4]. Recent studies have prompted a re-evaluation of cribriform-patterned carcinomas in organs such as the prostate, colon, lung, and stomach, now recognizing them as more aggressive than previously believed [5, 6]. This shift has implications for clinicians, especially in prognosis and therapeutic planning, due to the diagnostic significance of cribriform morphology [7, 8]. Invasive cribriform carcinoma remains an infrequent histological variant of breast cancer, accounting for fewer than 4% of all cases [9-11]. We report an unusual presentation of adenoid cystic carcinoma of the breast demonstrating a trabecular and cribriform growth configuration.

Case description

A 48-year-old premenopausal woman (gravida 5, para 5), without any underlying medical conditions, presented to our hospital in 2016 with complaints of pain localized to the right breast. Her personal and family histories were negative for any form of cancer, including breast malignancies. On physical examination, no masses or lymphadenopathy were detected, and the skin over the breast showed no abnormalities. Gentle pressure on the right nipple revealed a slight serous discharge, but no other notable clinical signs were evident **(Figure 1)**.



a) b)

Figure 1. Ultrasonographic imaging of the right breast revealed several cystic formations, the largest measuring approximately 1.5 by 1 cm; these cysts exhibited sharply demarcated margins and thin walls; a number of them contained fluid with visible debris layering, though no internal mural nodules were observed within any of the lesions.

The patient was advised to return for regular yearly check-ups but missed these visits. She presented again in January 2023, reporting the same issue. Upon examination, a painful lump, measuring 2 x 1 cm, was identified in the upper outer region of the right breast. Imaging through mammography and ultrasound revealed a BI-RADS-4 classification, as depicted in **Figures 2 and 3**, prompting the recommendation for a tissue diagnosis via ultrasound-guided core biopsy.

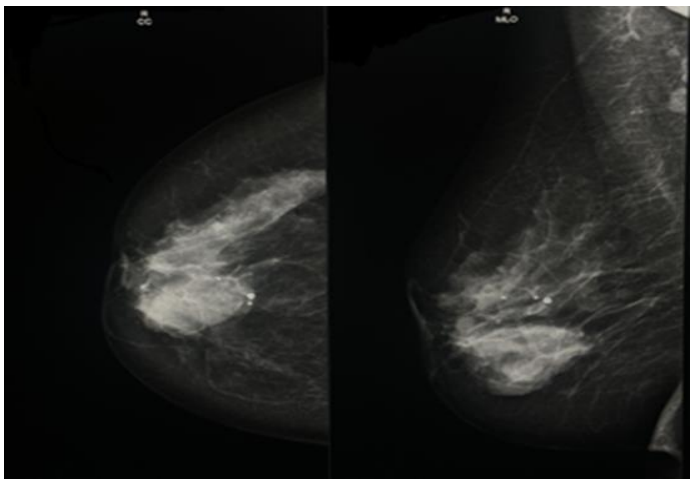
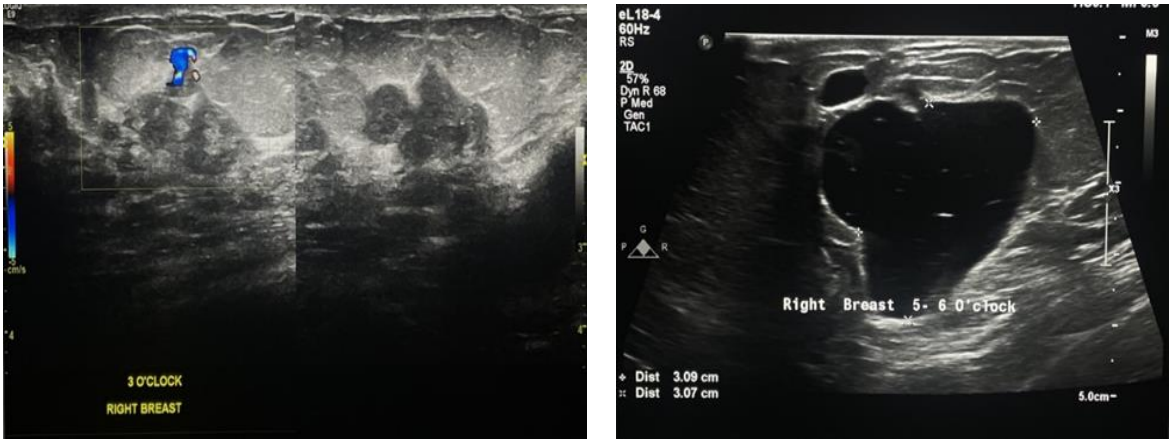


Figure 2. The mammogram revealed a partially obscured lesion with low density located near the nipple at approximately the 3 o'clock position, without any suspicious microcalcifications; additionally, a large, well-defined dense mass was observed in the lower inner quadrant of the right breast.

Ultrasound revealed a hypoechoic mass with an irregular shape and lobulated edges situated near the 3 o'clock position, approximately one centimeter from the nipple. Another large cystic formation with internal echoes and a lobulated structure was observed at the 5-6 o'clock area **(Figure 3)**.



a) b)

Figure 3. a) the ultrasound examination identified a hypoechoic, irregular solid mass at the 3 o'clock position, located 1 centimeter from the nipple, this mass had lobulated borders, an echogenic rim, posterior acoustic shadowing, and peripheral blood flow, with measurements of 1.7 x 1.1 cm, prompting classification as BI-RAD-4, indicating the need for biopsy, and b) a large cystic lesion, also lobulated, was detected at the 5-6 o'clock area, exhibiting multiple internal echoes, and measured 3.1 x 3.1 cm.

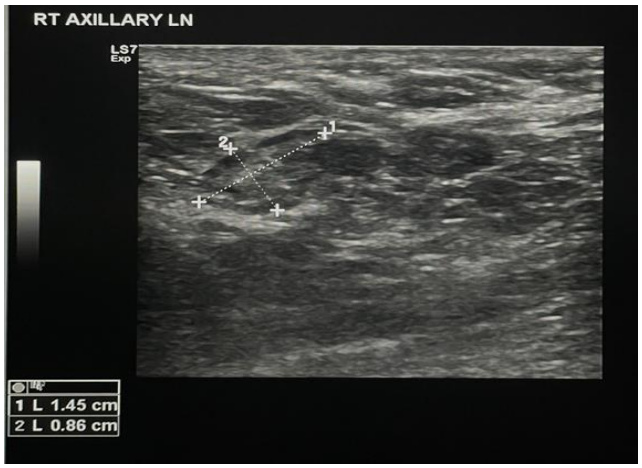
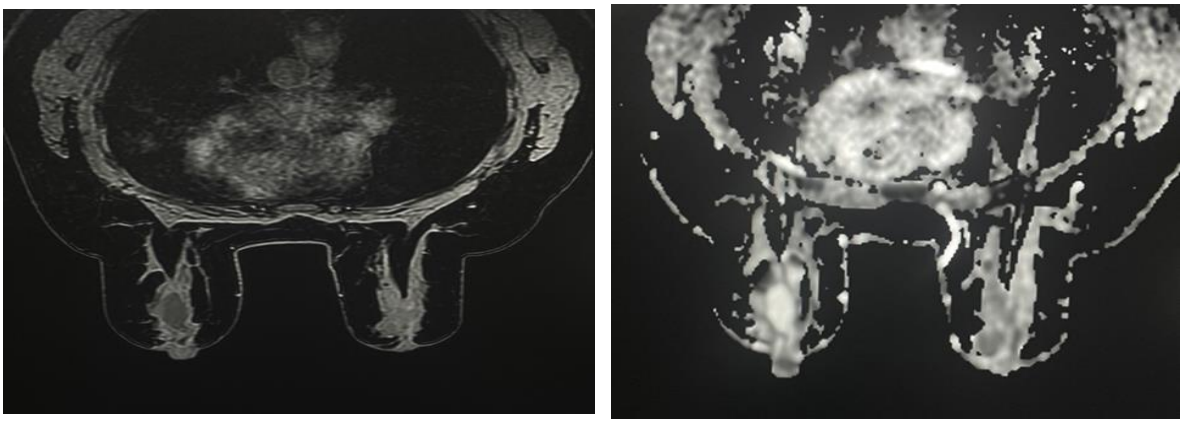


Figure 4. The right axillary lymph nodes displayed intact fatty hilum.

The right axillary lymph nodes, maintaining their fatty hilum, are also visible in **Figure 4**. For the biopsy, a tru-cut procedure was conducted on the solid mass lesion at the 3 o'clock position, using local anesthesia and following proper aseptic techniques.



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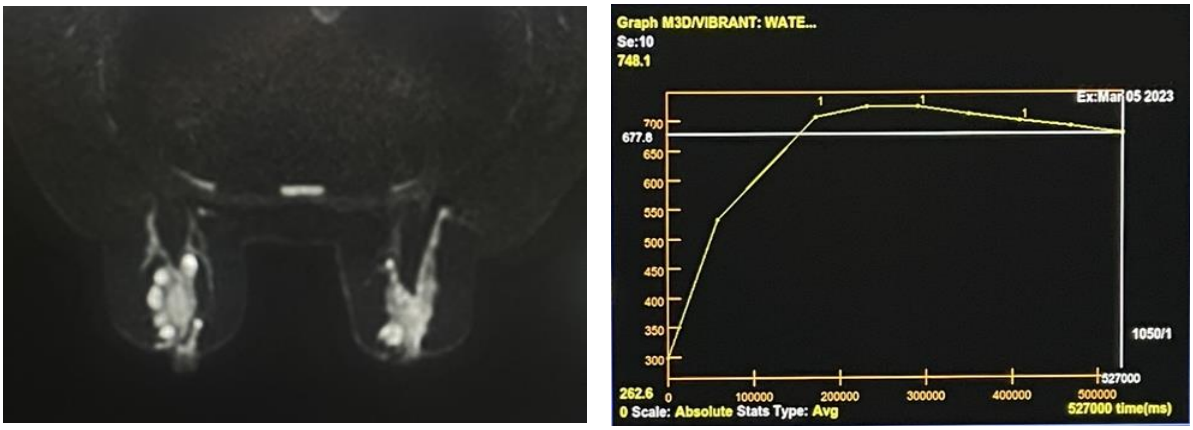
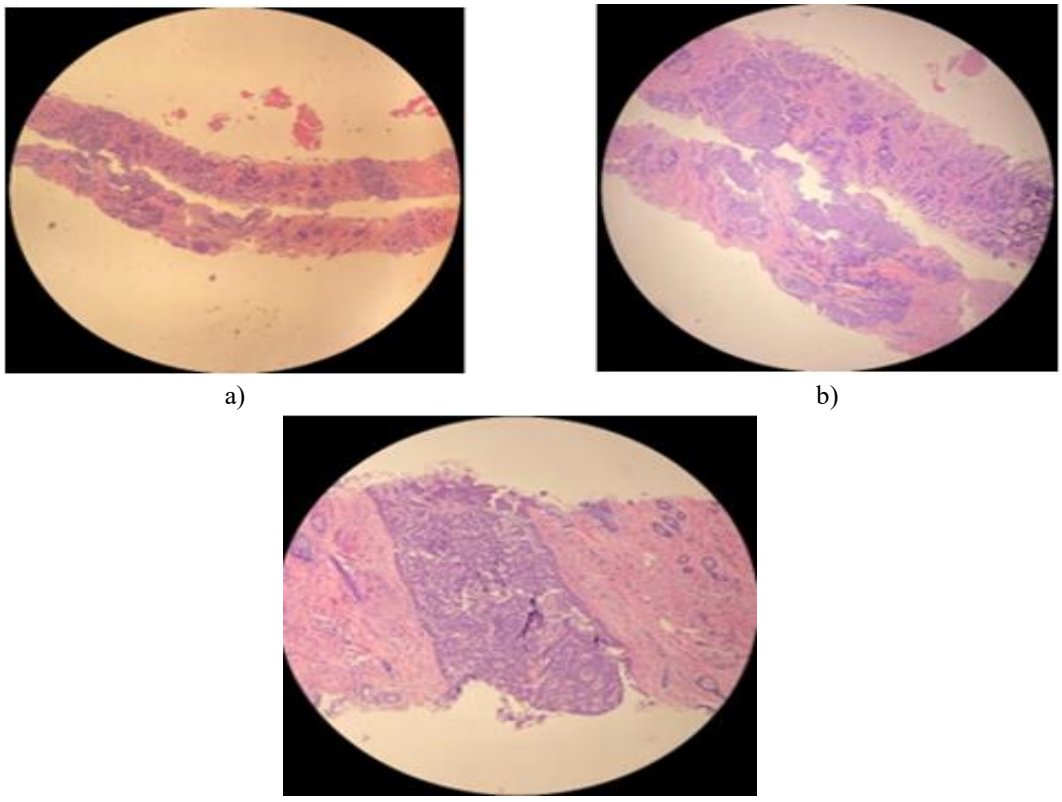


c) d)

Figure 5. a-c) MRI images reveal a well-defined, circular mass, and d) The lesion demonstrates rapid enhancement followed by a slower washout pattern (type 3 on the kinetic curve), which is concerning for malignancy.

The histopathological examination reveals a predominant cribriform and trabecular growth arrangement, with a few areas showing spaces filled with pink or mucoid-like substances **(Figure 5)**. The tumor cells are characterized by round to oval nuclei, exhibiting clumped chromatin and occasional nucleoli that are not prominent, with the cytoplasm being unclear. A few angular tubular formations are also identified. Mitotic figures are rare. The tumor shows weak positivity for estrogen receptors (ER), but both progesterone receptors (PR) and HER2 are negative. The Ki67 index for cellular proliferation is estimated to be between 15–20%.



a) b)

c)

Figure 6. Histopathological analysis, a-c) reveals a mainly cribriform and trabecular growth arrangement, with several formed spaces filled with pink or mucoid-like substances; the tumor cells display round to oval-shaped nuclei, with clumped chromatin and nucleoli that are either faint or occasionally prominent, accompanied by indistinct cytoplasm; among the cells, there are also a few angular tubular glandular structures observed.

The patient had a right mastectomy, along with the removal of axillary and sentinel lymph nodes **(Figure 6)**. Fresh frozen section analysis of the sentinel lymph nodes revealed no signs of malignancy.

Results and Discussion

ACC of the breast represents fewer than 0.1% of all primary breast cancers, making it an exceptionally rare form of invasive carcinoma [12]. The age of diagnosis for this rare subtype ranges between 38 and 81 years, with the median age being around 60 years [12]. While it predominantly affects women, there have been rare instances in men as well [10, 13].

In histological terms, tumors that display a development pattern consisting of tightly packed glands with irregularly sized lumens and without intervening stroma are classified as cribriform (from the Latin term "cribrum," meaning sieve) [7]. Cribriform neoplasms are found in a variety of organs, including the lung, prostate, stomach, and colon, and have recently been recognized as more aggressive than previously thought [6, 10]. This recognition is crucial for pathologists and oncologists as the cribriform pattern can influence prognosis and treatment strategies [7]. Invasive cribriform carcinomas make up less than 4% of all invasive breast cancers, making them a rare subtype [10]. This subtype is characterized by clusters of epithelial cells arranged in a sieve-like formation, surrounded by fibrosclerotic stroma, and composed of cells with mild to moderate atypia [10]. In the case presented here, histopathology showed a predominance of a cribriform and trabecular growth pattern, along with a few areas containing pink or mucoid secretions. The tumor cells were round to oval, with clustered chromatin, occasional prominent nucleoli, and indistinct cytoplasm. Scattered angulated tubular glands were also identified. Although mitotic figures are generally infrequent in cribriform carcinoma, our patient's tumor exhibited rare mitoses. Importantly, microcalcifications, which are often seen in other cribriform carcinomas, were absent in this case.

Typically, invasive breast carcinomas with a cribriform pattern test positive for cytokeratins, estrogen receptors (ER), and progesterone receptors (PR), while showing a lack of myoepithelial markers such as p63 and smooth muscle actin [14]. In contrast, the tumor in our case showed only faint ER positivity and was negative for both PR and human epidermal growth factor receptor 2 (HER2).

There are three recognized subtypes of invasive cribriform carcinoma: pure invasive (where more than 90% of the tumor shows a cribriform pattern), invasive (when the cribriform pattern is mixed with tubular carcinoma components in equal measure), and mixed (where 10-49% of the carcinoma exhibits a histological type other than tubular) [10]. Our case falls under the "pure invasive" category, as the cribriform pattern was dominant with only a few tubular structures present.

ACC can occur in either breast, and both breasts are equally affected. Lesions typically arise in any of the four breast quadrants, although about 50% of cases are found near the areola [15]. The primary presentation of ACC is often a palpable mass, and cases involving multiple masses are uncommon. In Alis *et al*. study, all seven patients had a solitary tumor, five of which were located in the superior lateral quadrant [16]. In our case, one tumor was located close to the areola measuring 1 cm, while the other was situated in the superior lateral quadrant. The average tumor size in published cases is about 3 cm, ranging from 0.7 cm to 12 cm [17]. The size of the lesion in our study (3x3 cm) was consistent with this average.

The classification of ACC tumors remains debated [14]. Tumors composed solely of tubular or cribriform cells are classified as grade I, those with 30-70% solid components as grade II, and those with more than 70% solid components as grade III. Prognosis worsens as the proportion of solid elements increases [18].

The imaging features of ACC can vary significantly. When an irregular mass with poorly defined margins is observed, ACC should be differentiated from other carcinomas. To ensure accurate diagnosis, radiologists may categorize such lesions as BI-RADS-4 and recommend biopsy for further evaluation [19]. In our case, ultrasound imaging revealed an irregular, hypoechoic mass with lobulated edges, accompanied by a larger cystic lesion with internal echoes, prompting us to categorize the lesion as BI-RADS-4 and proceed with an ultrasound-guided core biopsy.

In some instances, ACC can present as a well-circumscribed mass with defined margins. In a report by Agafonoff *et al*. the mammographic findings in their patient indicated BI-RADS-2, with no clear indications of malignancy, possibly due to dense breast tissue [20, 21]. As a result, an MRI was performed to further evaluate the tumor. Although there is no uniform pattern for MRI, larger lesions often show T2 hyperintensity, and smaller lesions are typically T2 iso-intense. MRI tends to be more sensitive than mammography and ultrasound when it comes to

assessing tumor size and extent. In our case, the ultrasound findings were similar, showing a hypoechoic or heterogeneous mass with minimal vascularity. MRI revealed rapid enhancement followed by delayed washout, indicating malignancy, in line with findings from Tang *et al*. study on mammary ACC [22]. Their report described dynamic contrast enhancement patterns with different kinetic curves, consistent with our observations.

While imaging plays a critical role in screening and management, it can sometimes lead to misinterpretation due to the heterogeneous nature of ACC's imaging characteristics. Ultimately, histopathological examination remains the gold standard for accurate diagnosis.

The primary treatment for ACC of the breast remains surgical. However, due to its rarity, no standardized surgical protocol exists, leading to variations in treatment practices. According to Ro *et al*. [23], the surgical approach should depend on the tumor grade: grade I tumors are treated with lumpectomy, grade II tumors with mastectomy, and grade III tumors with mastectomy and lymph node dissection.

In our case, the tumor exhibited solid components and was classified as grade III, prompting the decision to perform a right mastectomy with axillary and sentinel lymph node excision. Fortunately, fresh frozen section analysis of the sentinel lymph nodes showed no evidence of malignancy.

Conclusion

This report describes an exceptional case of adenoid cystic carcinoma (ACC) of the breast, exhibiting a cribriform and trabecular growth pattern. While imaging plays an important role in the screening and management of ACC, its usefulness can be limited due to the varied imaging appearances of this carcinoma. Ultimately, pathological examination remains the definitive method for diagnosis. Although the classification of ACC remains debated, it is crucial for determining appropriate treatment strategies. Currently, surgical intervention is considered the primary treatment approach for breast ACC. Given the rarity of this tumor type, there is no standardized protocol for surgical treatment, leading to differences in therapeutic approaches.

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