Case report

Dedifferentiation in adenoid cystic carcinoma of the breast – an unexpected intraoperative finding and a diagnostic challenge

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Adenoid cystic carcinoma (ACC) of the breast with high-grade transformation (dedifferentiation) is an extremely rare entity in the literature. Due to its potential to cause significant diagnostic challenges, recognition of this variant is clinically important. We report the case of a 58-year-old woman presenting with a 7 × 6 cm retroareolar breast mass. Core biopsy revealed features consistent with classic ACC; however, intraoperative frozen section of a sentinel lymph node demonstrated poorly differentiated carcinoma, showing no resemblance to the initial biopsy. This rare case is presented to contribute to the literature and raise awareness of this unusual phenomenon in breast tumors.

Key words: adenoid cystic carcinoma, breast, dedifferentiation.

Introduction

Adenoid cystic carcinoma (ACC) is an invasive malignancy composed of epithelial and myoepithelial cells, often embedded within a basophilic matrix [1]. The present case represents a high-grade transformation (dedifferentiation) of ACC occurring in the breast, an exceptionally rare entity. Given its rarity, this case is presented as a contribution to the existing literature.

Case report

A tru-cut biopsy was performed on a 58-year-old woman who presented with a 7 × 6 cm lobulated mass in the retroareolar region of the left breast, extending toward the outer quadrant. Needle biopsy revealed cell clusters forming tubular and, in some areas, trabecular structures within a hyalinized stroma, which appeared relatively well demarcated from the surrounding tissue. Based on the morphological features, the differential diagnosis primarily included ACC, as well as skin adnexal tumors and adenomyoepithelioma (AME). A mastectomy was subsequently planned for the patient, and the sentinel lymph node was submitted to the pathology department for intraoperative evaluation. Frozen section analysis revealed areas consistent with poorly differentiated carcinoma exhibiting a solid growth pattern within the lymph node sections. These findings showed no similarity to the tumor morphology observed in the initial needle biopsy. Macroscopic examination of the mastectomy specimen subsequently submitted revealed a 7 × 6 × 5 cm firm, cream-white tumor mass with focal hemorrhagic and necrotic areas. Microscopically, in addition to the well-differentiated tubular and trabecular components observed in the needle biopsy, the mastectomy specimen also revealed areas with a cribriform architecture, as well as solid regions composed of cells with marked cytological atypia and necrosis, consistent with high-grade (dedifferentiated) mor-

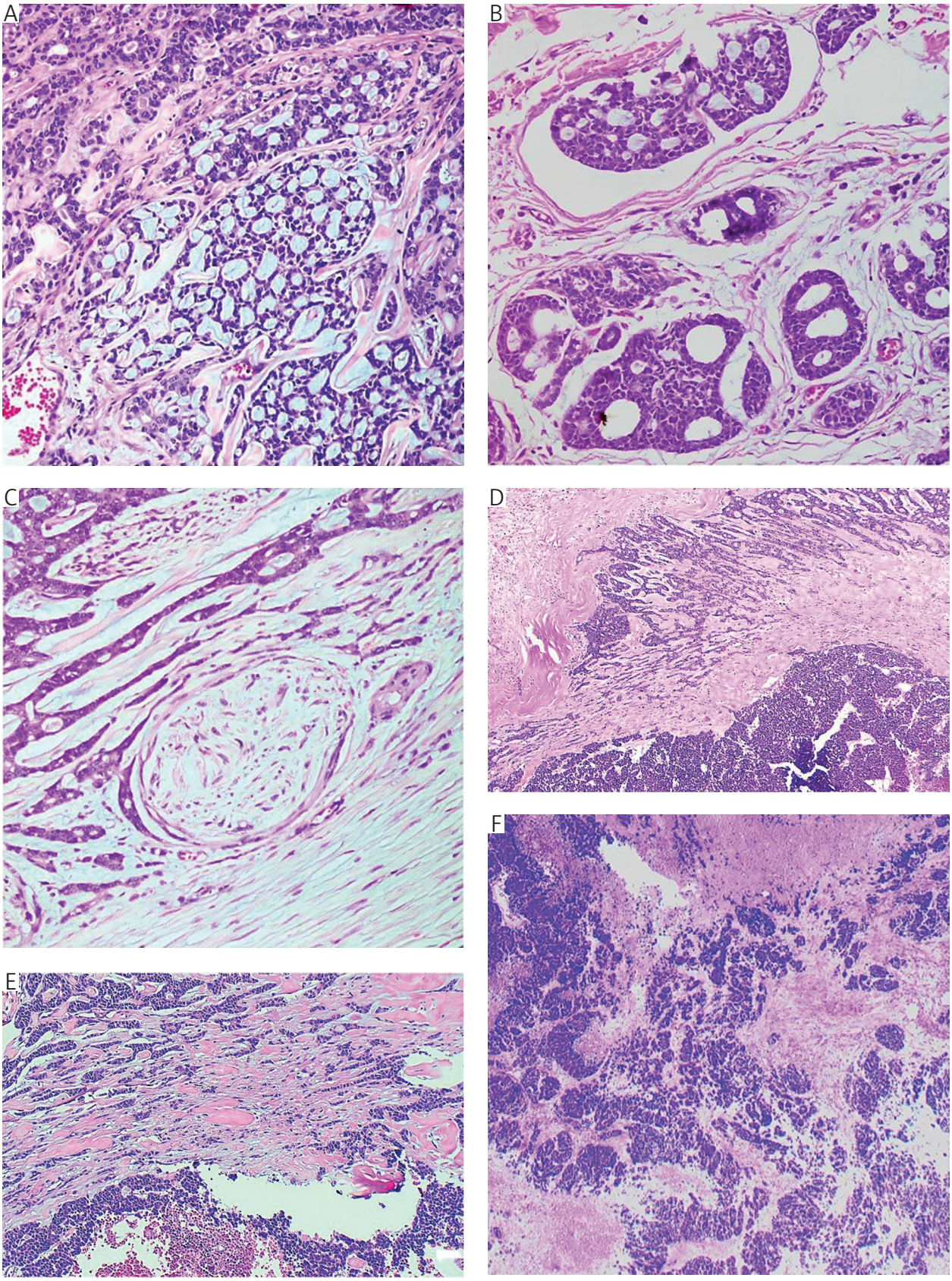

Figure 1. **A, B**) Widespread cribriform architecture observed in the classic component (HE 100×, 200×, respectively). **C**) Perineural invasion in the classic component (HE 400×). **D, E**) Intermixed classic component and high-grade regions (HE 40×, 100×, respectively). **F**) Zones of high-grade transformation with necrosis (HE 40×). **G, H**) Images showing high-grade transformation (HE 200×, HE 400×, respectively)

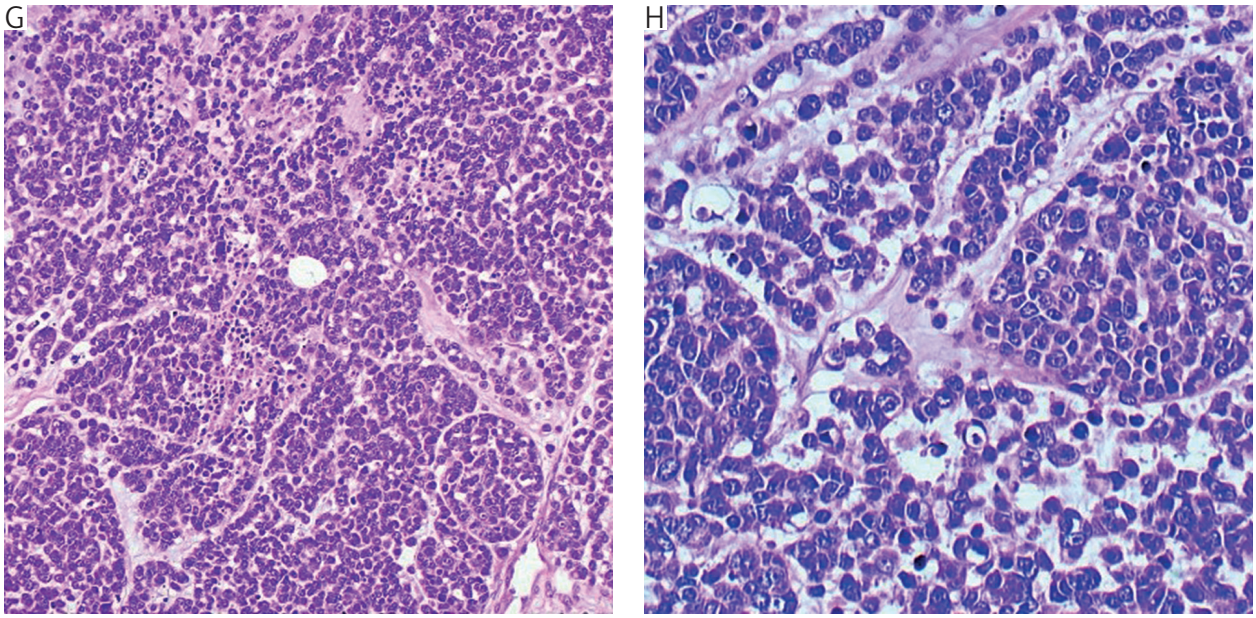

Figure 1. Cont. G, H) Images showing high-grade transformation (HE 200×, HE 400×, respectively)

phology (Figure 1). Immunohistochemical analysis demonstrated positivity for CD117, Keratin 7, and Keratin 5/6 in the classic component. In the high-grade (dedifferentiated) areas, CD117 exhibited weak cytoplasmic positivity in a small subset of cells, whereas Keratin 7 expression was diffuse but less intense compared with the classic component. Strong and diffuse nuclear positivity for p53 was observed, and the Ki-67 proliferation index was markedly elevated (> 90%) (Figure 2). No immunoreactivity for estrogen receptor, progesterone receptor, HER2, synaptophysin, or chromogranin was detected in either component. Based on these findings, the lesion was diagnosed as ACC with high-grade transformation (dedifferentiation).

Discussion

Adenoid cystic carcinoma is a rare tumor of the breast. According to the latest World Health Organization (WHO) classification, three subtypes are recognized: the classic type, the solid-basaloid type, and the high-grade transformation type. The previously obtained tru-cut biopsy specimen from our case contained areas that raised the differential diagnosis of ACC, AME, or adnexal-type tumors. In contrast, the sections from the sentinel lymph node submitted for intraoperative consultation exhibited a distinctly different morphology, composed of highly cellular areas with marked nuclear pleomorphism, numerous atypical mitoses, and extensive necrosis. This morphologic divergence was entirely unexpected during intraoperative consultation. Diagnostic coherence was achieved only after examination of the mastectomy specimen, which demonstrated the full histologic spectrum of the tumor. In this context, it is evident that, although extremely rare, these high-grade areas which lose their morphological differentiation in breast biopsies and are also immunohistochemically triple-negative, may pose significant diagnostic challenges.

Among the possible differential diagnoses, the most important consideration is AME. In contrast to AME, the classic component of the present case exhibited widespread cribriform and microcystic areas. The presence of prominent desmoplastic stromal reaction, thick basement membrane–like hyalinized material associated with cribriform structures, and perineural invasion are findings that favor ACC. Immunohistochemically, diffuse CD117 positivity was observed, which is a characteristic feature of ACC. Furthermore, spindle-shaped myoepithelial proliferation, which can be seen in AME, was not identified in our case. Although MYB rearrangement analysis could not be performed, the overall morphological and immunohistochemical features are consistent with a diagnosis of dedifferentiated (high-grade transformed) adenoid cystic carcinoma.

The phenomenon of dedifferentiation in ACC was first described in 1999 by Cheuk *et al*. [2] in a salivary gland tumor. This phenomenon has been well characterized ACC arising from the salivary glands [1]. Outside of the head and neck region, a case of ACC with high-grade transformation has been reported in the Bartholin gland [3]. This transformation of ACC in the breast has been reported in association with various other tumors, including invasive ductal carcinoma and malignant AME [1, 4, 5].

A review of the English-language literature revealed that, according to the latest WHO classifica-

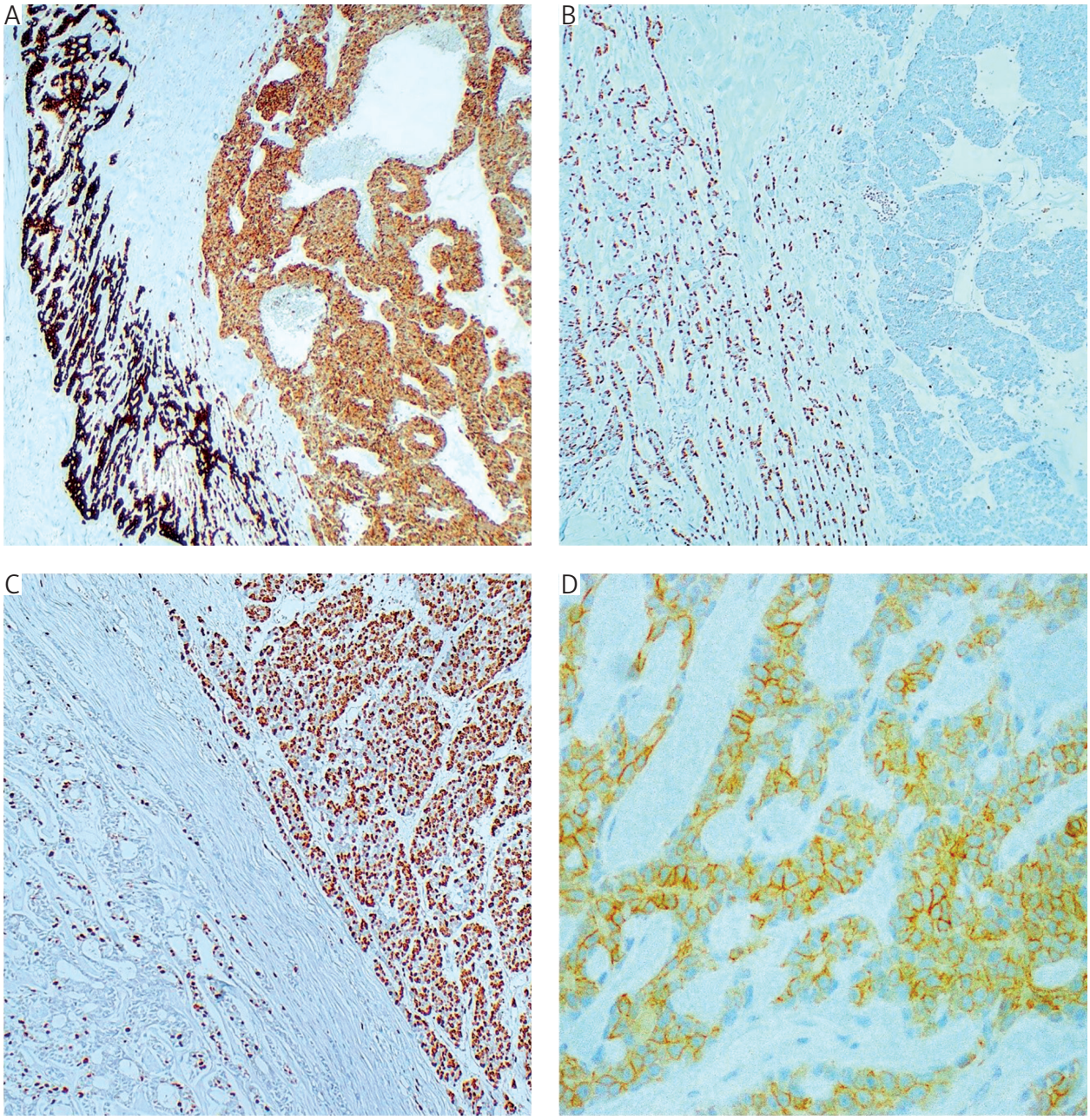

Figure 2. **A**) Keratin 7 immunostaining shows diffuse, strong expression in the classic component and reduced staining intensity in the high-grade area (40×). **B**) p63 immunostaining is positive in myoepithelial cells of the classic component and negative in the high-grade area (40×). **C**) Ki-67 proliferation index is markedly higher in the high-grade area compared with the classic component (100×). **D**) CD117 immunostaining is positive in the classic component (400×)

A–C) Classic component (left) and high-grade transformation area (right) in panels.

tion, only a single previously reported case of ACC of the breast exhibiting high-grade transformation in the form of dedifferentiation has been identified [6]. This case, therefore, represents an exceptionally rare tumor of the breast and, to the best of our knowledge, the second reported case of breast ACC exhibiting dedifferentiation. There is insufficient information regarding the prognosis and survival of such patients, and given that these tumors may comprise heterogeneous components, no standardized treatment protocol has been established to date. During follow-up, approximately 30 months after the initial diagnosis, a 1.5-cm mass lesion abutting the pleura in the upper lobe of the left lung, along with pleural effusion, was detected. Cytological evaluation of material obtained from the mass revealed a high-grade malignant epithelial tumor, considered likely to represent the high-grade component of the primary neoplasm. The pa-

tient died approximately 48 months after the initial diagnosis.

Conclusions

Although ACC of the breast is a well-characterized tumor, it should be kept in mind that dedifferentiation may occur, particularly posing diagnostic challenges in tru-cut biopsies. This rare case is presented to contribute to the existing literature and to raise awareness of this unusual phenomenon in the breast.

Disclosures

1. Institutional review board statement: Not applicable.
2. Assistance with the article: None.
3. Financial support and sponsorship: None.
4. Conflicts of interest: None.

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