Quiz Case

A rare type of breast carcinoma

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A 55-year-old postmenopausal female presented with painful breast mass for 1 year. The mass measured 2.5 cm × 2 cm and was located in the left upper quadrant. No axillary lymph nodes were palpable. Mammography showed an irregular mass with indistinct margins. Her medical and personal history was noncontributory. On palpation, the swelling was tender, mobile, and firm in consistency. Fine-needle aspiration cytology (FNAC) findings revealed the following findings [Figure 1a-d].

Figure 1: (a) Highly cellular smear-containing cellular tissue fragments with finger-like cords with a central core of homogenous basement membrane substance (Papanicolaou, ×10), (b) Pale, semitranslucent spherical globoid cluster consisting of homogenous basement membrane substance seen surrounded by loose epithelial cells usually devoid of cytoplasm (Papanicolaou, ×40), (c) cellular epithelial tissue fragment with a characteristic cup-shaped open at one end (Papanicolaou, ×40), (d) finger-like cord consisting of stromal material can be seen (Pap, ×40).

Q1. WHAT IS YOUR INTERPRETATION?

a. Collagen spherulosis
b. Adenoid cystic carcinoma (ACC)
c. Colloid carcinoma
d. Invasive cribriform carcinoma.

Please see the next page for answer and additional discussion on the topic.
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Answer

Q1: B

In ACC of the breast, the cytological pattern is identical as in other sites such as salivary glands and lungs. On FNAC, the smears are moderately cellular with two components: epithelial cells and acellular basement membrane material which appears as homogeneous spherical structures that are diagnostic and nearly unique to this tumor. The epithelial cells are relatively uniform with round-to-oval nuclei and have a coarse nuclear chromatin with prominent nucleoli. They are arranged in cohesive, often spherical or three-dimensional (3D) globoid clusters of various sizes surrounded by loose epithelial cells usually devoid of cytoplasm. The key to diagnosis is the identification of tumor cell clusters with central core of homogeneous basement membrane substance corresponding to the acellular component of the tumor.[1] Cellular tissue fragments with finger-like or beaded cords or strands of hyaline stroma may be seen. Multilayered dense cell clusters and cup-shaped fragments of tumor cells can be appreciated. However, hyaline stromal material may be absent in poorly differentiated tumors.

Collagenous spherulosis (CS) on fine-needle aspiration shows epithelial cells in clusters, scattered singly, with myoepithelial cells and spherules that appear magenta colored in May–Grunwald–Giemsa and light pink in hematoxylin and eosin-stained slides with numerous bare bipolar nuclei in the background.[2] The epithelial cells of CS are small and uniformly bland, whereas cells of ACC have a high N:C ratio and enlarged hyperchromatic nuclei and coarse chromatin with irregular nuclear membrane. Bipolar nuclei are absent in ACC of the breast. CS is usually associated with other benign lesions, such as ductal hyperplasia, proliferative breast lesions such as intraductal papilloma, papillary duct hyperplasia, atypical ductal hyperplasia, and sclerosing adenosis.[2]

In colloid carcinoma, abundant background mucin which can be recognized macroscopically is characteristic. Atypical cells in small solid aggregates and single intact epithelial cells can be seen. The cells have mild-to-moderate nuclear atypia. Chicken-wire blood vessels can be seen.

In invasive cribriform carcinoma of the breast, FNAC shows cohesive sheets and three dimensional (3D) cribriform clusters of bland-looking and mitotically inactive ductal cells. Scattered multinucleated, osteoclast-like giant cells can be seen.[3]

Q2. WHICH OF THE FOLLOWING IS TRUE ABOUT ADENOID CYSTIC CARCINOMA OF THE BREAST?

a. As compared to its salivary gland counterpart, ACC of the breast has a bad prognosis

b. ACC of the breast often metastasizes to lymph nodes

c. It accounts for 4% of all breast carcinomas

d. The secretions are periodic acid–Schiff (PAS) positive diastase resistant.

Q3. WHICH OF THE FOLLOWING IS FALSE ABOUT ADENOID CYSTIC CARCINOMA THE BREAST?

a. The most common site of metastasis is the lung

b. Perineural invasion is common

c. It stains positive for estrogen receptor and progesterone receptor

d. It can be associated with microglandular adenosis.

Q4. ADENOID CYSTIC CARCINOMA OF THE BREAST IS ASSOCIATED WITH WHICH OF THE FOLLOWING LESIONS?

a. Microglandular adenosis

b. Adenomyoepithelioma

c. Fibroadenoma

d. All of the above.

FOLLOW‑UP OF CASE

A wide excisional biopsy was done and sent for histopathology. It was well encapsulated, firm, and gray white in appearance. Multiple sections were taken and examined. On microscopy, the cells were arranged in a cribriform pattern [Figure 2]. Both true glandular spaces surrounded by luminal cells and pseudoluminal spaces surrounded by myoepithelial basal cells could be appreciated, thereby confirming the cytological diagnosis – ACC of the breast.

Figure 2: (a) Histological section showing cribriform pattern of adenoid cystic carcinoma with small dark, basal epithelial cell-lined cystic spaces filled with homogeneous material (H and E, ×10) (b) Higher power showing both true glandular spaces surrounded by luminal cells and pseudoluminal spaces surrounded by myoepithelial basal cells (H and E, ×40).
ANSWERS TO ADDITIONAL QUIZ QUESTIONS
Q2: D, Q3: C, Q4: D

A2: ACC of the breast is a rare tumor that represents about 0.1% of breast malignancies. It has a biological course that is slower than the extramammary ACC and does not present commonly with lymph node or distant metastases. Thus, it has got an excellent prognosis as compared to its salivary gland counterpart. It shows three different architectural patterns as the salivary analog: trabecular-tubular, cribriform, and solid. The solid variant is a rare high-grade variant that occasionally gives rise to metastatic disease and has a more aggressive clinical course both in the salivary glands and the breast.

Two types of spaces are present in ACC. The first type contains myxoid stroma or collagen fibers. The second type is composed of glands that contain a granular secretion of diastase-resistant PAS-positive neutral mucosubstances. Thus, it has secretions which are PAS-positive and diastase resistant.

A3: As explained above, mammary ACC rarely involves the axillary lymph nodes. However, it can spread to distant sites without first involving local axillary lymph nodes. Distant metastases though uncommon most commonly involve the lungs. Perineural invasion is also rare, unlike salivary ACC and has been reported in up to 8% of cases. It is a basaloid tumor and is hormone (estrogen and progesterone) receptor negative. It is negative for human epidermal growth factor receptor 2 (Her2) and expresses one or more basal/myoepithelial cell markers (CKs 5, 5/6, 14 and 17). ACC of the breast is associated with microglandular adenosis.

A4: ACC of the breast has been associated with various benign lesions, including microglandular adenosis, tubular adenosis, adenomyoepithelioma, and fibroadenoma. It has been suggested that ACC of the breast may arise in a background of and in continuity with microglandular adenosis. A morphological spectrum of lesions has been described with a trend of progression, encompassing microglandular adenosis, “atypical microglandular adenosis” (also described as “ACC in situ”), and invasive ACC. In fact, ACC can coexist with other invasive ductal carcinoma breast, no special type.

BRIEF REVIEW OF THE TOPIC

ACC of the breast is a rare tumor that represents about 0.1% of breast malignancies. It was first termed as “cylindroma” by Billroth in 1856. Geschickter and Copeland referred it as adenocystic basal cell cancer of the breast in 1945 and acknowledged its eccrine gland origin and slow growth. It occurs in several areas of the body: tracheobronchial tree, nasopharynx, maxillary sinus, salivary glands, Bartholin’s gland, and uterine cervix. However, in these locations, it is associated with a poor prognosis.

Although ACC of the breast can occur between 30 and 90 years of age, it is more common in women in their fifth or sixth decade. It is rarely bilateral and has no predilection for any particular sides. It most frequently presents as a tender breast mass, often in the subareolar area. Nipple discharge is uncommon, even though it most commonly presents as subareolar mass. It has a more favorable prognosis as compared to other types of breast cancers as lymph node involvement and distant metastasis are rare.

Mammographically, these tumors may appear as asymmetric densities or irregular masses. Sonographically, they appear as well-defined, irregular, heterogeneous, or hypoechoic masses. The radiographic findings are nonspecific and can be misdiagnosed with benign lesions.

Histologically, it consists of a dual cell population of luminal and myoepithelial-basal cells which may be arranged in one or more of three architectural patterns: tubular-trabecular, cribriform, and solid basaloid. There are two types of structures lined by these two different types of cells: true glandular spaces and pseudolumina. Luminal cells which are characterized by round nuclei and eosinophilic cytoplasm surround true gland lumina containing periodic acid–Schiff-positive neutral mucin. Immunohistochemically, they are positive for CK7, CK8/18, epithelial membrane antigen, and CD117 (c-Kit).

On the other hand, the myoepithelial-basal cells exhibit central oval nuclei and scant cytoplasm and form pseudolumina, which result from intraluminal invaginations of the stroma. They are immunoreactive for basal cytokeratins (CK5, CK5/6, CK14, and CK17), myoepithelial markers (p63, actin, calponin, and S-100 protein), vimentin, and EGFR.

It has been classified into three grades based on the solid component: Grade 1, completely glandular and cystic; Grade 2, <30% solid component; and Grade 3, >30% of solid components. All Grade 3 tumors appear to behave like high-grade ductal breast cancer.

As compared to its salivary analog, this tumor has an excellent prognosis. The 10-year survival rate is 90%–100%, and lymph node metastasis is rare, as well as distant metastases, which affect mainly visceral organs.

Based on its indolent clinical course and favorable outcome, the ACC of the breast is generally cured by breast-conserving surgery such as wide excision or quadrantectomy with or without radiotherapy. Mastectomy is recommended for invasive lesions when a cosmetically satisfactory excision is not possible, especially when the tumor has a high-grade pattern.

SUMMARY

ACC is a rare breast tumor with an excellent prognosis as compared to its counterpart in other sites of the body. Most commonly, it presents as a painful subareolar mass. CS is
an important differential and should be kept in mind while reporting ACC of the breast.

COMPETING INTERESTS STATEMENT BY ALL AUTHORS
The authors declare that they have no competing interests.

AUTHORSHIP STATEMENT BY ALL AUTHORS
Each author has participated sufficiently in the work and takes public responsibility for appropriate portions of the content of this article. All authors read and approved the final manuscript. Each author acknowledges that this final version was read and approved.

ETHICS STATEMENT BY ALL AUTHORS
As this is case without identifiers, our institution does not require approval from the Institutional Review Board (IRB) (or its equivalent).

LIST OF ABBREVIATIONS (In alphabetic order)
ACC: Adenoid cystic carcinoma
CS: Collagenous spherulosis
FNAC: Fine-needle aspiration cytology.

EDITORIAL/PEER-REVIEW STATEMENT
To ensure the integrity and highest quality of CytoJournal publications, the review process of this manuscript was conducted under a double-blind model (authors are blinded for reviewers and vice versa) through automatic online system.

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