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A Case of Unilateral Primary Adenoid Cystic Carcinoma with Invasive Ductal Carcinoma

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Abstract

Adenoid cystic carcinoma of the breast is a rare and specific type of breast cancer. Simultaneous primary adenoid cystic carcinoma and invasive ductal carcinoma of the unilateral breast are even rarer. We report a case of mammary associated cases in a 66-year-old woman. Pathological findings adenoid cystic carcinoma at 4 points in left breast. This is grade 3 infiltrating ductal carcinoma which is the molecular subtype basal-like in the left breast at 2 points. No cancer tissue was found at each incisal margin during intraoperative examination. The patient underwent breast conserving surgery on the left side and received postoperative chemotherapy. After 18 months of follow-up visits, there was no evidence of recurrence or new progress. By reviewing related disease literature, summarizing clinicopathological features, combining with characteristic morphological, immunophenotype and molecular genetic characteristics, identification of lesions similar to histomorphology and exploring experience in diagnosis and treatment.

Keywords: Breast cancer; Adenoid cystic carcinoma; Infiltrating ductal carcinoma

Case Presentation

The patient, a 66-year-old female, was admitted to the hospital as "left breast mass was found 20 days after physical examination". There was no redness, swelling and pain in the breast, no sunken nipple, no orange skin change, and no nipple discharge. Color Doppler ultrasound showed that there was a 16 mm × 11 mm × 12 mm hypoechoic nodules (BI-RADS Class of 4C) in the left breast at 2 points about 50 mm away from the nipple and 11mm away from the skin (Figure 1A). Hypoechoic nodules (BI-RADS Class of 3) about 6 mm × 5 mm × 5 mm in size can be seen at 4 points of the left breast (Figure 1B). Ultrasound-guided puncture biopsy is recommended. The patient was treated in the nail milk surgery department, and underwent molybdenum target and other preoperative examinations, followed by left unilateral mammary gland modified radical resection and left axillary lymphatic dissection, meanwhile conducting intraoperative rapid frozen pathological examination.

Pathological Examination

Intraoperative rapid freezing examination: (1) (4 points of the left breast) a piece of grayish yellow tissue, 2.0 cm × 1.5 cm × 1 cm in size, a gray nodule, 0.8 cm × 0.5 cm × 0.5 cm in size, was visible on the section, clearly demarcated from the surrounding tissue, medium texture and a piece was taken by freezing (Figure 2A). Intraoperative freezing diagnosis: Microscopic findings showed nodules with a size of 0.8 cm × 0.5 cm × 0.5 cm with clear boundaries, which were arranged in sieve shape and beam-tube shape (Figure 2B). The cells were consistent and mild, and the good and evil properties were hard to determine. The final result was to be reported by paraffi routine. (2) (Expanded specimen at 2-point position of left breast) A piece of grayish-yellow irregular tissue, 6.0 cm × 5.0 cm × 3.8 cm in size, marked with clinical quadrilateral line. The base bed has been opened, and a grayish-red gray nodule, about 1.5 cm × 1.3 cm × 1.2 cm in size, can be seen on the section surface, with unclear boundary with surrounding tissue, medium in quality and hard. The distance of the tumor from 1 online incisor, 2 external incisors, 3 offlin incisors and 4 internal incisors was about 1.4 cm, 0.8 cm, 1.4 cm and 2.0 cm, respectively (Figure 3). Intraoperative freezing diagnosis: Invasive breast cancer (expanded specimen at 2-point position of left breast), no cancer tissue was found at each incisal margin.

Routine pathological examination and immunohistochemistry: (1) (4-point mass of the left breast) the central region of the tumor was arranged in ethmoid shape and solid sheet, and

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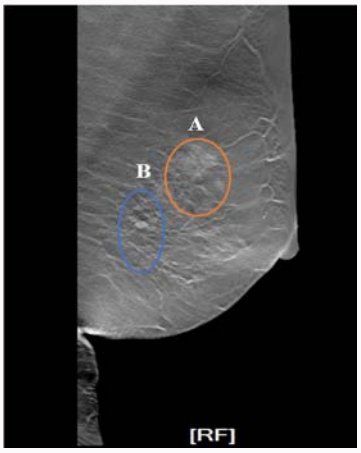

Figure 1: Color ultrasound image of patient's breast.
A. In the red circle at 2 points, BI-RADS 4C mass was observed, with lobules and burr shadows at the edges, high signal on DWI, and unclear boundary.
B. In the blue circle at 4 points, BI-RADS 3 mass was observed, with high density shadows and clear boundaries.

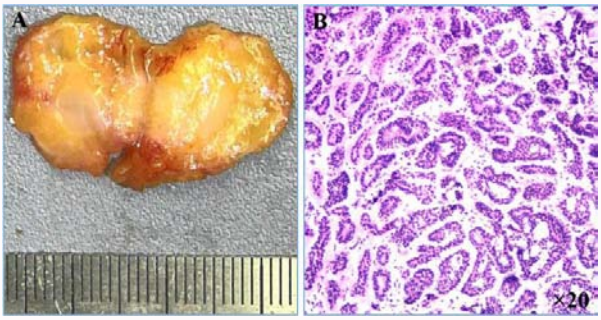

Figure 2: 4 - point surgical specimen and HE staining image.
A. The section of the 4-point surgical specimen showed a nodule with clear gray boundary.
B. Frozen section showed that the tumor cells were arranged in the shape of sieve and tube, and the cells were consistent and mild.

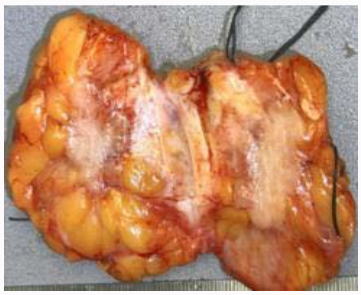

Figure 3: Section of a 2-point surgical specimen.
The section of the 2-point surgical specimen showed an irregular grayish-red nodule with unclear boundary with the surrounding tissue.

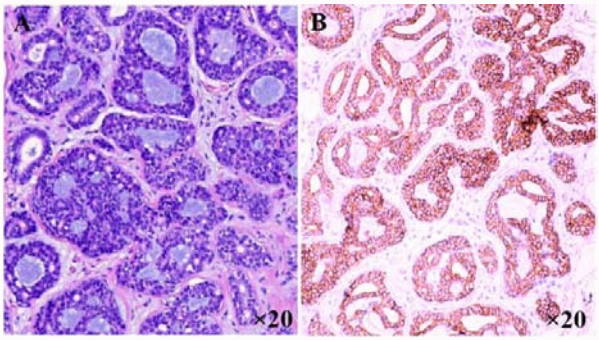

Figure 4: HE staining and Immunohistochemical staining images of left breast 4-point tumor.
A. HE staining showed that the tumors were arranged in a sieve shaped pattern, and the lumen was filled with a light blue-stained mucoid matrix.
B. Immunohistochemical staining showed that both basal like cells and glandular epithelial cells expressed CD117.

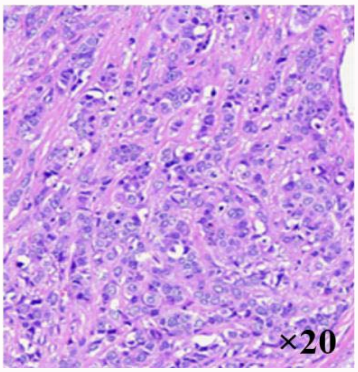

Figure 5: HE staining image of left breast 2-point enlarged specimen.
The tumor cells are arranged in a strip like and trabecular shape, with aggressive growth in the fibrous stroma, marked cell heterogeneity, and easy to see nuclear division.

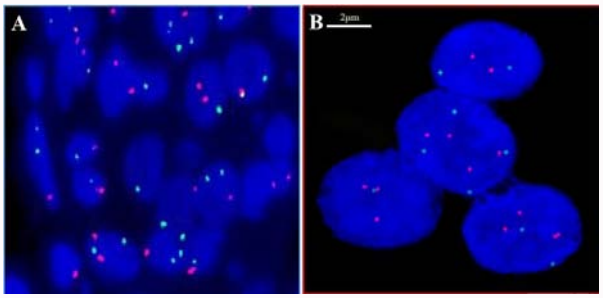

Figure 6: Fluorescence in situ hybridization results.
A. MYB/NFIB fusion gene detection. 200 tumor cells were analyzed, the red and green fluorescence probe signal expression was normal, but no MYB/NFIB fusion gene was detected.
B. HER2 amplification assay. HER2/CEP17 <2.0 and the mean copy number of HER2 <4.0 were judged as negative for HER2.

the surrounding local tubular structure was dominant, and the ethmoid and tubular spaces were filled with light blue mucous matrix (Figure 4A). Immunohistochemical results showed that p63, CK5/6, Calponin, CD117, E-cadherin and P120 were expressed in tumor cells, but ER, PR and HER-2 were not expressed (Figure 4B). (2) (Expanded specimen at 2-point position of left breast) The tumor cells were arranged in strips, clusters and trabecula's with locally aggressive growth of adenoid structures in the fibrous adipose tissue (Figure 5). Immunohistochemical results showed that the tumor cells expressed E-cadherin, P120 (membrane +), HER-2 (2+), Ki-67 (50%-60%), but did not express ER, PR, p63, CK5/6 and Calponin.

Molecular pathological examination by fluorescence in situ hybridization was performed and the following results were obtained: (1) (4-point mass of left breast) MYB-NFIB gene fusion was detected by FISH, 200 interphase cells were analyzed, and the signal patterns were as follows: 2G2R 35.5%, 1G1R1F 1.5%, 2G1R 19.0%, 1G2R 18.0%, 1G1R 24.0%, 1R1F 2.0%, the results showed that no

MYB/NFIB fusion gene was detected (Figure 6A). (2) (2-point mass of left breast) The amplification results of HER2 gene were as follows: The average copy number of HER2 was 3.55, the value of HER2/CEP17 was 1.51, and the results showed that HER2 amplification was negative (Figure 6B).

Pathological diagnosis

(1) The diagnosis of the 4-point mass in the left breast was adenoid cystic carcinoma; (2) The diagnosis of the left breast 2-point enlarged specimen was invasive ductal carcinoma grade III, and the molecular typing was basal like subtype.

Follow up

The patient was admitted to hospital for surgery in June 2020, and generally in good condition after surgery. He received 8 cycles of AC-T chemotherapy in the early stage of triple negative invasive ductal carcinoma, followed by local radiotherapy. Follow up until June 2022 showed no tumor recurrence or metastasis.

Discussion

Adenoid cystic carcinoma of breast is a rare and special type of breast cancer [1], the incidence of which accounts for about 0.1% of all breast malignancies [2], and the patients are mostly elderly women [3]. In 2012, WHO classification of breast tumors was defined as breast cancer with low malignant potential, morphologically similar to adenoid cystic carcinoma occurring in salivary glands, which can be cured by simple mastectomy [4]. Adenoid cystic carcinoma was classified into rare tumors and salivary gland tumors in the fift edition of WHO classification of breast tumors published in 2019, and its diagnosis was consistent with that of adenoid cystic carcinoma of the salivary gland [5-7]. Invasive ductal carcinoma is the most common type of invasive breast cancer without specific types [7]. It is extremely rare for both of them to be independently and originally from unilateral breast cancer. In the process of domestic literature review, only a case of bilateral primary breast cancer with unilateral adenoid cystic carcinoma reported by Xiao Xuewen et al. was found [8], and a case of mixed adenoid cystic carcinoma and ductal carcinoma of breast cancer reported by Kontos et al. was found in foreign literature search [9]. In addition, individual cases of adenoid cystic carcinoma mixed with small cell carcinoma [10] and spindle cell melanoma [11] were reviewed and analyzed. Independent primary adenoid cystic carcinoma and invasive ductal carcinoma of the same breast were rarely reported.

The histological characteristics of breast adenoid cystic carcinoma in frozen sections are often not obvious, and due to the limitations of frozen material extraction and production, it is often difficul to distinguish it from other benign and malignant breast tumors, leading to misdiagnosis. Among the 8 cases of adenoid cystic carcinoma of the breast reported by Liu Yufei et al. [12], 5 cases underwent intraoperative rapid freezing examination, and only 1 case was clearly diagnosed. This case of intraoperative freezing was also a tumor with a descriptive cribriform and trabecular tubular arrangement, which was not clearly diagnosed; when the tumor mainly presents as a sieve-like structure, the following types need to be identified: (1) Invasive sieve-like carcinoma: An invasive carcinoma with a significant sieve-like structure, often accompanied by tubular carcinoma components, with mucoprotein secretions and dead bodies visible in the sieve pores. The tumor cells lack neoplastic myoepithelial cells, mainly glandular epithelial cells, with immunohistochemical ER and PR positive, and CD117 and myoepithelial markers negative. Adenoid cystic carcinoma exhibits invasive growth and heterogeneous tissue structure. Tubular, trabecular, and ethmoidal structures, as well as basement membrane like or mucoid substances in the lumen, are important clues for diagnosis. Morphological glandular epithelial cells are mixed with myoepithelial and basal like cells, with typical immunohistochemical ER and PR negative, and positive staining for CD117, myoepithelial Calponin, and p63 are helpful for differential diagnosis; (2) Sieve shaped ductal carcinoma *in situ*: Intraductal lesions in which the glandular epithelium exhibits a sieve shaped neoplastic proliferation. The tumor cells are relatively consistent and both ER and PR are diffusely positive. Myoepithelial cells exist around the duct, and myoepithelial cells such as p63, Calponin, and SMA are positive, while CD117 is negative, which is helpful for differential diagnosis.

The main diseases that need to be differentiated from invasive ductal carcinoma include (1) sclerosing adenopathy: A tubular adenopathy with lobular hyperplasia accompanied by fibrosis and sclerotic interstitial hyperplasia that constitutes a pathological change in the conscience, but its gland/tubule compression is obvious, making it difficul to identify the double layer cellular structure, and its growth pattern is similar to nerve invasion, especially in intraoperative rapid freezing and biopsy of small specimens, which is difficul to distinguish. Diagnosis needs to be very careful, and can be made with the help of calponin immunohistochemical staining of muscle epithelium such as p63 was used to label the remaining lobular structures on the muscle epithelia to assist in diagnosis. (2) Invasive lobular carcinoma: The classic type often presents a private-like or target circular arrangement, and the atypical morphology of the two often overlaps, making it difficul to distinguish. Immunohistochemistry P120 and E-cadherin can be used to assist in the differential diagnosis: Both invasive ductal carcinomas are positive for cell membrane; the cytoplasm of lobular carcinoma P120 was positive, while E-cadherin was negative.

In differential diagnosis, it can be seen that immunohistochemical CD117 can be specifically expressed in adenoid cystic carcinoma, mainly related to regulatory genes. Research has found that C-KIT is one of the downstream genes regulated by MYB, and C-KIT mutations can be detected in adenoid cystic carcinoma at different sites such as salivary gland and breast, and their protein products express CD117 [13]. At the same time, the literature suggests that about half of adenoid cystic carcinoma is accompanied by the MYB-NFIB fusion gene, but the use of the C-KIT targeted drug imatinib has poor efficac in treating adenoid cystic carcinoma [14], so the treatment is still primarily surgical. The treatment of invasive ductal carcinoma has shifted from surgery+hormone+neoadjuvant treatment to neoadjuvant treatment+surgical treatment, provided that HER2 testing is positive and trastuzumab can be used for targeted treatment.

In summary, simultaneous independent primary adenoid cystic carcinoma and invasive ductal carcinoma of the unilateral breast are extremely rare, with unique histomorphology, immunohistochemical characteristics, and biological behavior. It is necessary to accumulate case summary diagnosis and treatment experience.

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