

Massive Breast Intraductal Papilloma Undiagnosed After Several Core Needle Biopsies: A Case Report

Jiapaer P¹, Mengting D¹, Xiaofei L¹, Minjia Y¹, Ke J¹ and Jiayu S^{1*}

¹Department of Breast Diseases, Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine, China

*Corresponding author:

Sheng Jiayu,
Department of Breast Diseases, Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine, Shanghai, 110 Ganhe Road, Hongkou District, 200047 Shanghai, China, Tel: 13361990930; E-mail: sjy1983sh@126.com; pt2020pt@163.com

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1. Abstract

1.1. Background: Patients with breast Intraductal Papilloma (IDP) and atypical ductal hyperplasia have an increased risk for breast cancer. Core Needle Biopsy (CNB) plays a significant role in inchoate diagnosis of atypical IDP. However, the standard procedure of CNB may be unable to provide definite diagnosis of a complicated large mass. This is the first report of the largest case of peripheral atypical IDP with ductal epithelial atypical hyperplasia and hemorrhage necrosis. The mass grew larger, without a clear diagnosis. Herein, we documented our recommendations for the treatment of a large breast mass.

1.2. Case Summary: A 74-year-old Chinese female had a palpable left breast mass for two years, which was enlarging in the past one month. The patient had periodic breast check-ups in a reputed hospital. However, the ultrasound examination and four CNBs of the breast mass did not provide a clear diagnosis, besides non-lactating mastitis. However the mass was finally diagnosed as an atypical IDP after intraoperative pathology. The patient recovered well after the lumpectomy.

1.3. Conclusion: When obtaining the sample from cystic tissue during CNB, the needle should take the core of the mass as well as the surrounding wall of the cyst. Clear diagnosis is important for further treatment. Large breast IDP in elderly may develop into

breast cancer, so we recommend that lumpectomy is necessary rather than periodic check-ups for these patient.

2. Introduction

Intraductal Papilloma (IDP) is a benign breast papillary lesion derived from the epithelium of the lactiferous duct. The morphological changes of papillary lesions range from hyperplasia to atypical hyperplasia and carcinoma in situ [1]. Atypical ductal hyperplasia is considered to be a high-risk benign lesion, with an enhancement rate of 7.8% [2]. The Core Needle Biopsy (CNB) is crucial to determine whether to follow-up or excise the lesion [3]. However, premalignant tissue inside or adjacent to the papilloma may lead to missed diagnosis given the limited sample evaluated with CNB. Herein, we presented a case of a mass larger than 10 cm in the left breast, which had not been clearly diagnosed after repeated CNBs in the past two years until open surgical biopsy was performed. To the best of our knowledge, CNB failing to diagnose complicated large mass as atypical IDP of the breast with ductal epithelial hyperplasia and intraluminal hemorrhage necrosis has been rarely described.

3. Case Presentation

3.1. Timeline

The timelines of the occurrence of the illness and final diagnosis to treatment are shown in (Table 1).

Table 1

Time	Events
September 18, 2018	Patient was informed of left breast mass.
December 28, 2018	Patient's ultrasound and CNB examination revealed non-lactating mastitis and unclear breast nodule.
April 25, 2019	Patient's second CNB reported no evidence of malignancy.
August 26, 2020	The ultrasound examination showed that the previous mass was growing and also found other multiple nodules.
February 26, 2021	Patient felt pain in the left breast recently and the CNB revealed broken tissue and inflammation.
March 2, 2021	Patient's breast enhanced MRI revealed a cystic-solid mass, which was categorized as BI-RADS 4A-B.
March 5, 2021	The patient had a lumpectomy and the intraoperative pathology revealed that the mass was IDP with ductal epithelial atypical hyperplasia and hemorrhage necrosis.
March 10, 2021	The patient received routine postoperative care. The final pathological report supported the previous diagnosis.
After March 10, 2021	The patient was discharged from the hospital. She was advised to undergo breast check-ups every 3 month until next year

3.2. History of illness

A 74-year-old postmenopausal Chinese woman had a two-year history of painless left breast mass. She mentioned that the mass was growing rapidly, and became painful and uncomfortable in the last one month. The palpable mass was initially found during her annual health examination on September 2018, but she did not take it seriously since the mass exhibited no symptoms. For further examination, she visited the breast surgery department of a famous hospital in Shanghai on December 2018. The ultrasound examination revealed a hypoechoic mass measuring 2.5×1.7×2.4 cm on the outer side of the left breast, with relatively regular shape and edge, which was categorized as Breast Imaging-Reporting and Data System (BI-RADS) 4B (considered to be moderate suspicion for malignancy). Further evaluation with CNB revealed individual ductal dilation, local inflammatory cell infiltration and fibrous tissue hyperplasia, so the patient was diagnosed with a left breast non-lactating mastitis. In view of the non-lactating mastitis was a self-limited autoimmune disease, the surgeon suggested her to undergo periodic check-ups. In her third breast examination on August 2020, the ultrasound showed multiple nodules on the outer left nipple suspected to be an intraductal lesion, and the previous substantial mass had enlarged to 4.1×3.3×4.7 cm, both of which were classified as BI-RADS 4A. The CNB showed scattered tissue and inflammatory cells, with no evidence of malignancy. This result was similar to that of the second check-up on April 2019. Since February 2021, the patient felt that the mass was growing rapidly, with pressure pain. The fourth CNB was performed in the same hospital on February 26, 2021. The CNB presented left breast broken tissue, interstitial fibrous tissue hyperplasia, some areas of inflammatory cell infiltration and hemosiderosis. Since the mass was diagnosed as non-lactating mastitis, the surgeons advised the patient to regularly observe the mass, continue with periodic check-ups and have traditional Chinese herbal medicine. For further treatment, the patient visited our hospital on March 1, 2021, and received a complete breast examination. The patient had an unremarkable medical history. The patient was a non-smoker and

denied any personal or family history of breast or ovarian cancer.

A firm mass measuring 13×10 cm at 1 to 5 o'clock position of the left breast was palpable just near the nipple, without any skin changes (Figure 1). The patient reported pain in the left breast when we tried to check for nipple discharge. Bilateral nipple discharge was not found and no palpable axillary or supraclavicular lymphadenopathy was noted. She also had a normal right breast exam.



Figure 1: The range of the left breast mass was marked by the radiologist under ultrasound guidance, which accounted for the majority of outer side of the unilateral breast. No obvious epidermal change was demonstrated besides the bruise caused by latest CNB check.

Blood test on admission showed that carcinoembryonic antigen level was moderately elevated (8.61 ng/ml). Tumor markers and alpha fetoprotein were within normal range.

B-type ultrasound examination showed a mixed predominantly cystic mass in the left breast, classified as BI-RADS 3. The mass was increasing in size over time (Figure 2), but decreased to a lower BI-RADS category than before. The breast enhanced MRI revealed a cystic-solid mass in the upper outer quadrant of the left breast, which was categorized as BI-RADS 4A-B (Figure 3). Sur-

gical treatment was recommended. In addition, bilateral breast fibroadenoma, fibrous cystic disease and bilateral mammary gland degeneration were also reported.

Based on the results of the examinations, we decided to perform a breast lumpectomy on the patient on March 5, 2021. A spindle incision was made on the outer side of the left breast and a giant lump was excised (Figure 4), while preserving the nipple. The intraoperative pathology of the resected tissue indicated IDP with ductal epithelial atypical hyperplasia and hemorrhage necrosis. Thereafter, a drainage tube was placed and the incision was sutured. Following surgery, the patient was given routine postop-

erative care. The drainage tube was removed four days after the surgery. Section view showed that the lump was 14.0×10.0 cm and had a cyst with necrosis, solid tissue inside and surrounding firm wall (Figure 5).

The final pathological diagnosis was peripheral atypical IDP with ductal epithelial atypical hyperplasia and hemorrhage necrosis. The excised skin showed no obvious abnormality (Figure 6A-F). Immunohistochemically studies showed that the estrogen and progesterone receptors were strongly positive, HER2 receptors were negative, and low (less than 10%) proliferation index (Figure 6G-H). The wound healed well and after 2 month of follow-up, the patient had a good prognosis with no clinical symptoms.

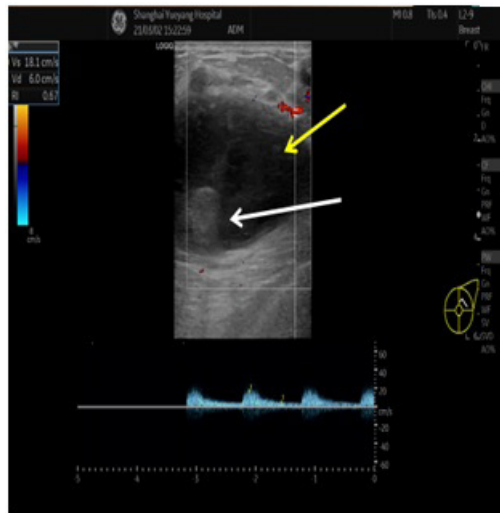


Figure 2: Ultrasound image presented a hypoechoic area with uneven echo inside and clear boundary in the outer upper quadrant of left breast, the size was 5.2×4.2×5.0 cm (yellow arrow), and a fine floating echo signal with several weak hypoechoic lumps located outside that area. Among them, the largest was 2.0×1.6×1.8 cm (white arrow). The RI indicated blood supply equaled 0.67.

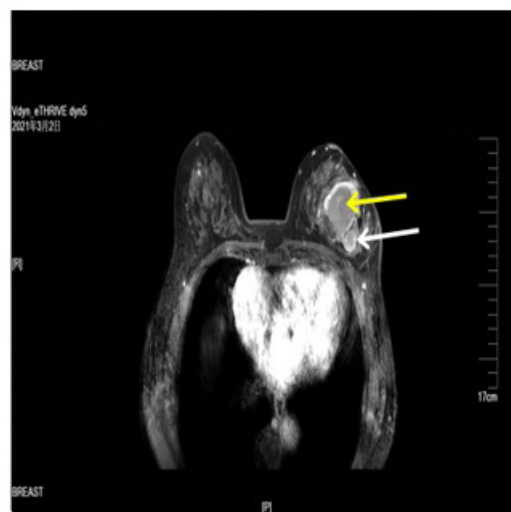


Figure 3: The enhanced MRI showed a cystic lesion with unclear boundary in the left breast upper outer quadrant, the size was 5.4×5.0 cm (yellow arrow) and inside with a solid space-occupying (white arrow). Bilateral breast fibroadenomas were reported.

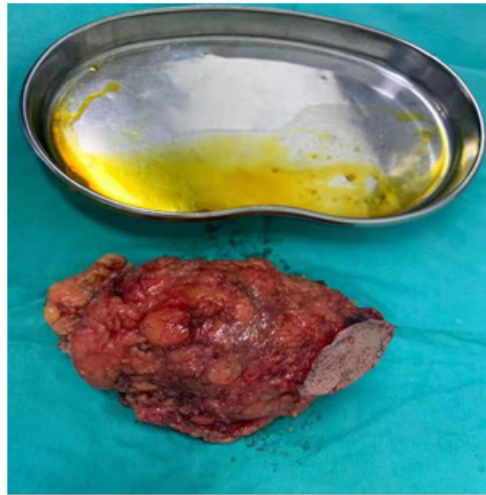


Figure 4: The image of the removed lump.

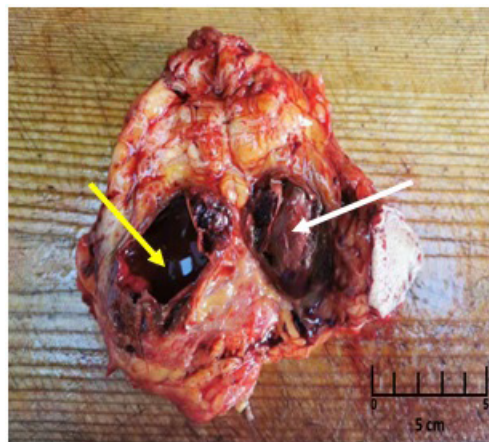


Figure 5: The sectional view of the mass measuring 12.0×10.0×5.0 cm, with focal skin of 6.0×2.5×2.0 cm under epidermis, a cystic lumina of 4.0×3.0×4.0 cm was visible, including taupe and kermesinus necrotic substance (yellow arrow). Solid wall surrounded the cystic lumina, breast tissue around that was off-white or infarctate. In addition, multiple nodules were present with diameter of 0.9-1.0 cm (white arrow), solid structure, medium texture and clear boundary

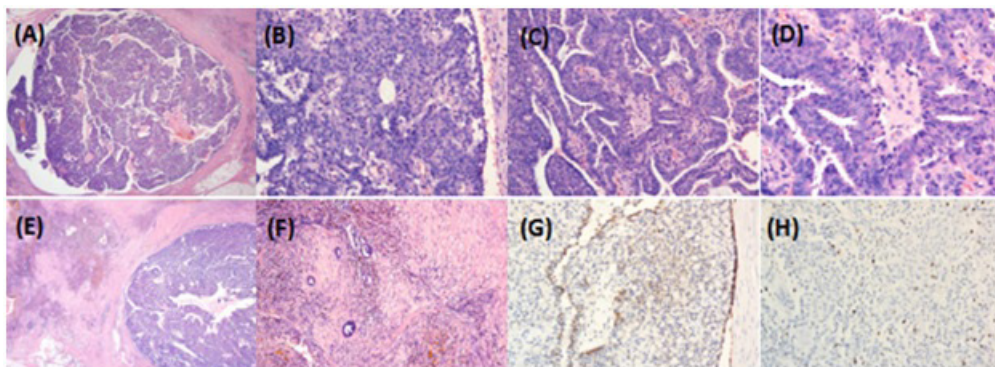


Figure 6: Microscopic appearance of the removed breast mass. (A) Intraductal papilloma with manual fracture around the tumor [hematoxylin & eosin (H&E) stain, ×40]. (B) Intraductal papilloma that demonstrated the tumor inside the duct (H&E, ×200). (C) The tumor consisted of glandular epithelium and myoepithelium cells, and the axis of fibrous vessels was visible (H&E, ×200). (D) High-power view of picture C, the glandular epithelium was apparently abnormal. The myoepithelium around the axis of fibrous vessels was clearly visible (H&E, ×400). (E) Fibrous tissue proliferation around intraductal papilloma and a wide range of inflammatory granulation tissue (left) (H&E, ×40). (F) Vast chronic inflammatory cells, old bleeding and remaining gland were seen in fibrous connective tissue (H&E, ×100). (G) With CK5/6 immunohistochemical staining, numerous positive cells were seen inside the ducts and tumor (×200). (H) With Ki67 immunohistochemical staining, a few sporadic positive cells were observed (×200).

4. Discussion

Ultrasound-guided CNB can provide histological diagnosis by inserting a needle of variable length into the core of the target tissue and obtaining the sample [4]. It is necessary to sample the nuclei of the nodule for identifying the propensity of malignancy. CNB is the preferred approach for the diagnosis of breast cancer or other high-risk breast diseases [5]. Therefore, CNB is frequently used for suspicious tumors.

IDP does not have a pathognomonic appearance on conventional imaging, ultrasound and mammography, although it could be benign or malignant [6]. CNB plays an important role in the diagnosis of papillary diseases and has replaced open surgical biopsy as an initial diagnostic tool [3]. CNB shows similar results as resection specimens in terms of histological features and receptor status of breast diseases [7]. However, the patient in this case was not diagnosed after repeated CNBs. Atypical IDP with solid cystic mass might be diagnosed by sampling the solid part of the cyst, instead of the core of the lump alone, which might be filled with necrotic tissue.

A previous study indicated that the risk factors for malignant transformation of IDP were older age, larger lesion size and distance from the nipple [8]. A literature review revealed that most IDPs were less than 2 cm, the largest reported IDP was 10.5×6.0×5.0 cm on MRI, and massive size was a predisposing factor for the development of complications [9].

5. Conclusion

The diagnosis of IDP by CNB needs to include the sample from the core of the target mass as well as the solid wall around the tissue. In case of enlarging breast mass without evidence of malignancy, the patient may be advised to undergo routine periodic check-ups. However, elderly patients without serious diseases should undergo surgical treatment to prevent growth of the mass.

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