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Papillary Lesion of the Breast in a Young Girl Suspicious to Juvenile Papillomatosis, Clinical Decision Making in a Multi-disciplinary Team and Review of the Literature

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ABSTRACT

Background: Papillary lesions of the breast are a heterogeneous group of neoplasms, the diagnosis and treatment of which is challenging. Typically surgical excision is recommended for papillary lesions after core needle biopsy (CNB) to rule out concurrent malignancy when a diagnosis of papilloma with atypia is yielded on CNB. For papilloma without atypia, however, making a decision about excision versus observation is challenging.

Case Presentation: A 14-year-old female with nipple discharge, and a 2 cm mass in the right breast, with the pathology of intra-ductal papilloma without atypia on CNB presented. The question to be answered by multi-disciplinary team was the best management of this papillary lesion and whether the follow up was adequate or excision was mandatory.

Question: What is the best plan for management of the young patient according to the primary pathology report of Juvenile Papillomatosis?

Conclusion: Histoathology review of CNB specimen in rare and high risk lesions may have some advantages. On the other hand, in high risk circumstances, the excision of the lesion is recommended. Thus, in this case, the multi-disciplinary team recommended excision of the lesion.

Introduction

Papillary lesions (PL) of the breast are a heterogeneous group of neoplasms, which include intra-ductal papilloma (IDP), IDP with usual ductal hyperplasia, IDP with atypical ductal hyperplasia, as well as IDP with ductal carcinoma in situ (DCIS), papillary DCIS and papillary carcinoma (encapsulated papillary carcinoma and solid-papillary carcinoma). These lesions demonstrate papillary morphology.[1]

IDP is a benign, circumscribed, intra-ductal proliferation consisting of fibro-vascular cores covered by benign myoepithelial and outer epithelial layer. IDPs can be generally categorized into two types: central IDPs which involve large, central lactiferous ducts, and peripheral IDPs which involve the terminal duct lobular units. Central IDPs are mostly solitary, and peripheral IDPs tend to be multiple. Although multiple peripheral IDPs have been sometimes referred to as papillomatosis, this appellation is discouraged because of its inconsistent usage for different types of lesions. Clinically, central IDPs have variable sizes and present with

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nipple discharge that is often bloody. Peripheral IDPs are most frequently identified as small masses or densities on mammography. Both lesions may have micro-calcifications because of infarction and/or sclerosis followed by dystrophic calcium deposition.[2-4]

Papillary lesions are challenging to diagnose and treat. PLs are usually identified by mammography and ultrasonography and subsequently diagnosed by core needle biopsy and/or vacuum-assisted biopsy.[5] Imaging-guided core needle biopsy (CNB) provides reliable diagnosis of breast lesions, but papillary lesions detected at percutaneous biopsy may be difficult to interpret histologically.[6] In addition, limited material and sampling error at CNB may lead to neglecting the presence of atypia or malignancy within or adjacent to the lesion.[7]

Surgical excision is often conducted for papillary lesions after CNB to rule out concurrent malignancy when a diagnosis of papilloma with atypia is yielded at CNB.[8] However, for PLs without atypia, making a decision about excision versus observation is a dilemma for the surgeon.

Case presentation

The patient was a 14-year-old female presented with right breast spontaneous nipple discharge and mass. She had nipple discharge in the last 18 months, which was bloody in the beginning and then turned to serous discharge. She did not take any medication and had no family history of breast cancer. On physical examination, there was no distinct mass but a 2 x 2 cm thickening area was noted under the nipple-areolar complex. There was no spontaneous nipple discharge though a single duct serous discharge was detected on compression.

Ultrasonography revealed a 27 x 15 x 24 mm iso-echoic mass with lobulated margin in the right breast retro-areolar region (BIRADS 4b). Because of the young age of the patient, MRI was requested, which showed a 30 x 12 x 18 mm sub-areolar mass with irregular margins, there was an iso to hyper-intensity and heterogeneous enhancement pattern with rapid washout kinetics in right retro-areolar area in T2 (BIRADS 4b). She underwent core needle biopsy, and the pathology diagnosis of florid papillary hyperplasia (compatible with juvenile papillomatosis) was reported. There was no sign of atypia or malignancy.

Question

The best management of the disease in a 14-year-old female patient with a symptomatic papillary breast lesion (surgical excision vs. follow up) was the main concern faced by the Multi-disciplinary Team(MDT).

Discussion

Juvenile papillomatosis of breast or Swiss cheese disease is a rare lesion, which is more common in adolescence and young people (with mean age under 23). The disease typically presents with painless mass that, on physical examination, is circumscribed, easily movable, and most often considered to be a fibroadenoma. These lesions appear to be well-circumscribed but they are not encapsulated.[9] Patients usually present with mass; however, hemorrhagic discharge and pain are rarely seen.[10] Our patient had nipple discharge which was not bloody. The size of juvenile papillomatosis reportedly ranges between 1 and 8 cm, but the lesion was 3 cm in our patient.

Juvenile papillomatosis is a clinicopathological entity, first described by Rosen et al. Pathologic examination demonstrates a constellation of benign lesions and proliferations including dilation of ducts, multiple intraductal papillomas, usual ductal

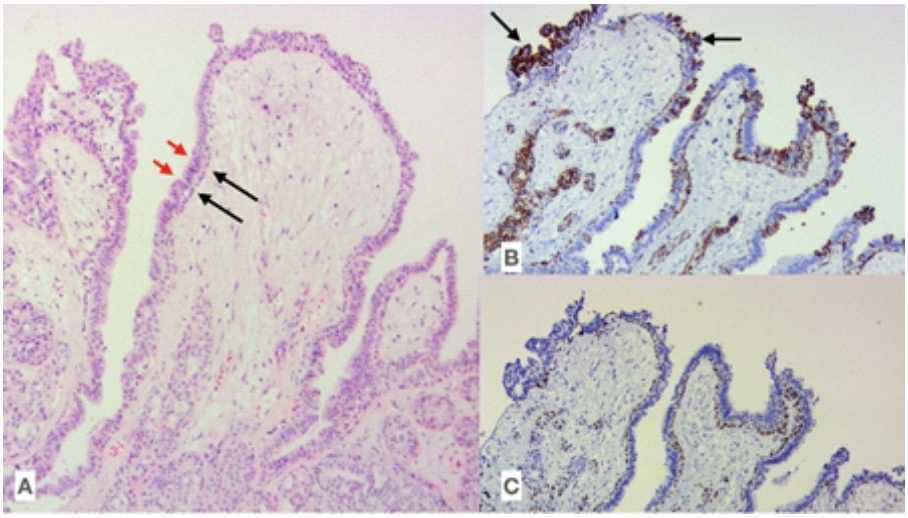

Figure1. Intra-ductal papilloma. A. Papillary fronds lined by a continuous layer of cuboidal myopepithelial cells (long black arrows) underlying a layer of columnar epithelial cells (short red arrows). H&E, 200x. B. Cytokeratin 5/6 highlights myoepithelial cells. Some epithelial cells are also stained (arrows). CK5/6 immunostain, 200x. C. P63 shows positive nuclear reaction in myoepithelial cells. P63 immunostain, 200x.

hyperplasia, cystic changes, apocrine metaplasia, fibroadenomatoid hyperplasia and sclerosing adenosis.[11]

Ultrasonography is an optimal tool for diagnosis. MRI also aids in diagnosis by showing small internal cyst on T2.[12] In our patient ultrasonography and MRI revealed an irregular mass in retro-areolar region, which was not compatible with the pathology of juvenile papillomatosis. Therefore, the MDT recommended the review of the patient's slides. Subsequently, a diagnosis of intraductal papilloma with usual ductal hyperplasia was rendered.

In some situation, surgical excision is recommended for papillary lesions following CNB to rule out concurrent malignancy when a diagnosis of papilloma with atypia is yielded at CNB.[8] However, for the papillary lesions without atypia, decision-making regarding excision versus observation are conflicting. In fact, as 17-24% of the lesions can be underestimated by CNB,[13] some authoroties prefer to remove the lesions surgically. Others, however, support follow-up with repeated imaging owing to the low rate of malignancy of benign papillomas.[14] Different studies reported a malignancy risk of 2-7% associated with benign papillary lesions. The rate of upstaging of the lesions in surgical excision is quite variable among published studies. There is a risk of 7.5% for the upstaging of papillary lesions without atypia. This risk rises to more than 30% in papillary lesions with atypia.[15] Recently, there has been a tendency toward risk stratification instead of a uniform surgical approach for papillary lesions without atypia. According to previous studies, low-risk situations that could be followed are listed in Table 1.[15,16] If there was a high-risk circumstance, excision of the lesion is prudent.

Our patient had two high-risk factors, the first being the size of mass which was about 3 cm and secondly the observation that she experienced nipple discharge.

The patient's concern about malignancy is an important point that should be considered in decision-making. Patients should be informed about the low risk of malignancy in cases with benign papillary lesions without atypia, and should be part of the decision-making process.[16] Our patient and her family were concerned about malignancy.

MDT recommendations

After imaging review, the lesion in MRI was found to be a BIRADS 4a lesion, and the MDT decided to review the CNB specimen histopathology result for precise interpretation due to the discrepancy between imaging and pathology. Pathology review demonstrated "intra-ductal papilloma with usual ductal hyperplasia." The MDT recommended the excision of the lesion because it was symptomatic and the lesion was about 3 cm in size which made her follow up with a higher risk of missing an underlying malignancy. As the patient and her family were concerned about follow-up too, she underwent excisional biopsy. Postoperative pathology examination illustrated dilated ducts, intra-ductal papilloma with complex intricate branching fronds with well-developed stroma, two cell types without cytological atypia but florid epithelial hyperplasia in some foci in favor of intra-ductal papilloma with florid usual ductal hyperplasia" as can be seen in Figure 1. Then the patient went under routine follow up.

Table 1: Low risk situations which could be considered for follow-up with imaging

Size less than 1 cm
Age under 50-55 years
Lesions discovered incidentally
Imaging concordance
Low BIRADS
Central papilloma (located less than 5 cm from the nipple)
Asymptomatic lesions

In conclusion, it seems that it is better to review the CNB specimen when the primary report is among rare diseases of the breast and the patient is in high-risk group for papillomas. Surgical excision is recommended for the latter group

Conflict of Interest

None.

Ethical Consideration

The written consent was signed by the patient and her parents.

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