CASE REPORT

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Juvenile Papillomatosis of the Breast: a Report of Two Cases with Review of the literature

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ABSTRACT

Background: Juvenile papillomatosis (JP) of the breast is a rare and benign proliferative disorder affecting young women. The affected patients tend to have an increased risk of breast cancer development during follow-up. **Objective:** This article aims to highlight a rare entity of breast disease, that harbor risk of breast cancer. **Case Presentation:** Here, we present 2 cases of JP in young females; the first case is a 13 year-old presented with spontaneous nipple discharge, while the other patient is a 24 year-old presented with a right breast lump. Both patients had a total excision of the breast lesions, revealing JP at histology. Discussion: Juvenile Papillomatosis is considered a clinicopathological entity and is usually misdiagnosed as fibroadenoma clinically and radiologically, which requires histological correlation. The histologic findings are well-defined (hyperplasia, papillomatosis, and multiple cysts with foamy histiocytes).The controversy in management between surgery and observation is because of insufficient knowledge about the direct relationship between JP and subsequent cancer. **Conclusion:** Considering the risk of developing breast cancer in JP, enrolling patients and their families in a close follow-up and surveillance program is crucial.

Keywords: Juvenile Papillomatosis, breast cancer, fibroadenoma, immunoprofile.

1. BACKGROUND

Juvenile papillomatosis (JP) is a rare benign proliferative or hyperplastic ductal lesion of the breast. It typically affects females younger than 30 years (1, 2). It was first described in 1980 as a distinct clinicopathologic entity by Rosen et al. (3).

The clinical presentation varies from impalpable lesions to the presence of a mass mimicking fibroadenoma necessitating histopathological correlation. Spontaneous nipple discharge is a common presentation.

The histologic features are well defined as compared to the immune profile. The increased incidence of breast cancer observed in this group increases the need for regular follow up surveillance (1, 4, 5).

The challenging diagnosis and management of JP in these young age group triggered the presentation of this report.

2. OBJECTIVE

This article aims to highlight a rare entity of breast disease, that harbor risk of breast cancer.

3. CASE PRESENTATION

Case 1.

A thirteen years old Saudi female presented to the hospital with a one-year history of a right breast mass. Associated with cyclical pain, spontaneous, persistent brown nipple discharge. There were no associated other local or systemic symptoms. Menarche at the age of 10 years. Positive family history of breast cancer (maternal grandmother at the age of 40 years)

General examination was unremarkable. Local examination revealed obvious asymmetry. With a palpable breast mass occupying the lower quadrants of the right breast. No skin change or nipple changes. Both axillae were unremarkable. Ultrasonography (US) showed a large non-circumscribed cystic mass associated with multiple dilated ducts with nonvascular intraductal

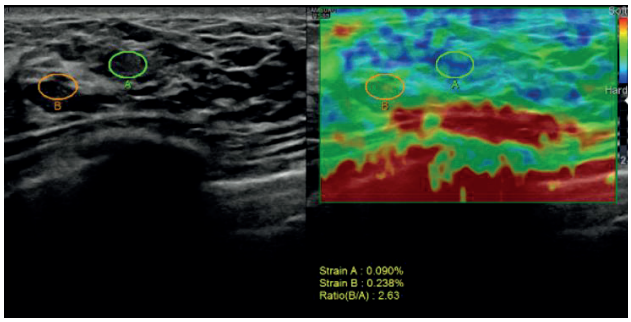

Figure. 1 Ultrasound Demonstrating extensive dilatation ductal system with multiple intraductal lesions

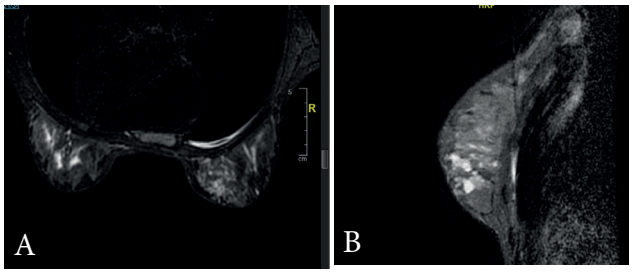

Figure. 2 (a,b) Both T1 an T2 showing dilatation of the ductal system with mass like formation occupying central and lower breast quadrants.

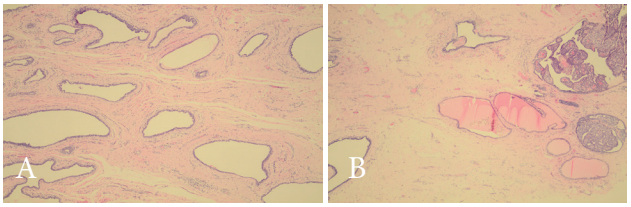

Figure.3 (a,b) Variable sized cysts lined by both epithelial and myoepithelial layers and surrounded by loose fibrotic stroma with intraductal lesions

components involving the right lower quadrants. The elastogram train ratio of 2.63 It was reported as BI-RAD 4.(Figure.1)

MRI Both T1 and T2 images demonstrated extensive dilatation of the ductal system with intraductal lesions (Figure.2). Core needle biopsy reported as multiple intraductal papillary lesions.

Considering the age of the patient and the size of the mass. The case was discussed in a multidisciplinary team (MDT) meeting, and the consensus was wide local excision in two stages six weeks apart. Surgical pathology of both excisions confirmed the diagnosis of multiple papillomatosis, negative for malignancy. (Figure 3 and Figure 4).

Regular follow up intervals has shown full recovery with no active complaints. Final US at 6 months follow up has reported interval regression of right lower inner retro-areolar cyst. No suspicious lesion BI-RAD (2).

Case 2.

A twenty-four-year-old female presented with right non-cyclical breast pain associated with a progressively increasing breast mass noticed few months prior to presentation. There were a no nipple or skin changes. She gave history of bilateral lumpectomies reported as tubular adenoma and fibroadenoma, with loss of follow up

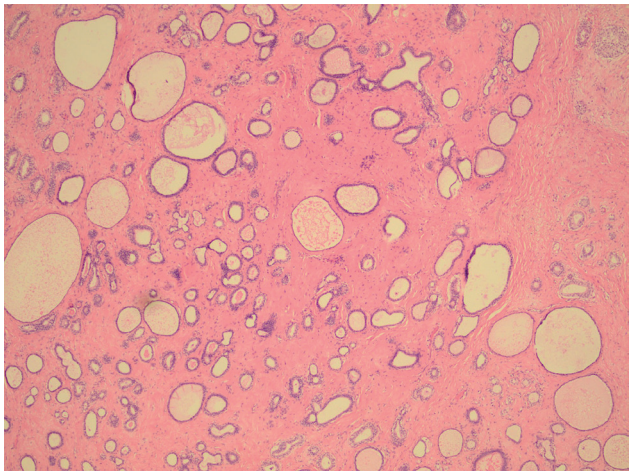

Figure 4. CK5,6 shows positive staining of both epithelial and myoepithelial layers.

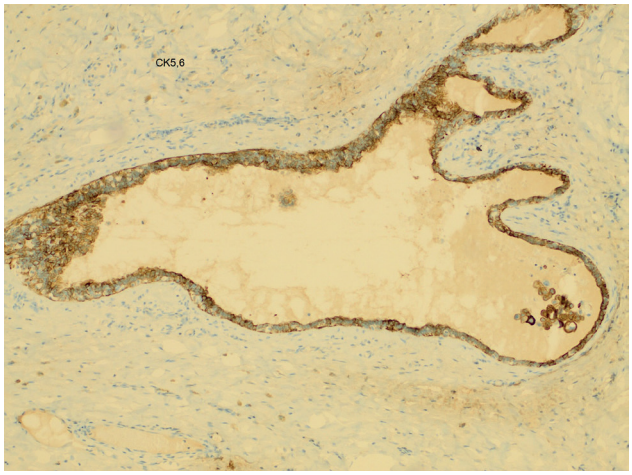

Figure 5. Classic Swiss-Cheese appearance of JP.

for two years. She had her menarche at the age of 14 years, with a regular menstrual cycle. No family history of breast cancer.

Systemic examination and the vital signs were within normal limits. Breast examination revealed a 3x2cm right breast mass at 12 o'clock. No nipple nor skin changes with unremarkable axillae bilaterally. Ultrasound demonstrated right upper posterior mass at 12:00 Elastic strain 1.5 with interval increase in size and change in texture, reported as BI-RADS 4B.

The areola, retroareolar regions, and both axillae appeared unremarkable. US-guided biopsy of the index lesion was consistent with normal mammary parenchyma No malignancy.

Based on the discrepancy between the pathology and the clinical-radiologic findings, wide local excision was performed. The final surgical pathology report showed JP and fibroadenoma, with the lesion extending to the surgical margin (Figure 5). The postoperative follow-up revealed that the patient was in good condition, with no active complaint.

4. DISCUSSION

Juvenile Papillomatosis is considered a clinicopathological entity. It is frequently misdiagnosed both clinically and radiologically as fibroadenoma (3). The his-

tologic findings are described as cellular hyperplasia, papillomatosis, and multiple cysts with foamy histiocytes. They have no distinctive characteristics in the immune-histo-chemistry profile.

Clinically, most of the patients present with breast masses that occupy the upper outer quadrant, but nipple discharge has been reported in some cases (1, 2, 5). The reported association between JP and breast cancer is estimated that around 10%. It has been documented that the risk rises with recurrent and bilateral disease and a positive family history of breast cancer (6). The estimated positive family history of breast cancer associated with JP is 26 - 58% (4, 7). Association with the rare subtype of low-grade, translocation-associated invasive breast carcinoma known as secretory carcinoma has been alsoreported (8, 9).

The possibly of a documented link with between JP and breast carcinoma has suggested the possible underlying genetic relation and/or hormonal disturbance (10).

US and magnetic resonance imaging (MRI) are the best modalities for assessment and follow-up rather than mammography, as most JP patients are young with dense breasts. Reported ultrasonographic features are well or poorly-demarcated lesions, echo-poor, heterogeneous internal patterns with multiple anechoic foci (11). Alternatively, MRI is preferred for patients with small breasts or highly dense breast tissue (12).

Typical histological features include florid hyperplasia, papillomatosis, and multiple cysts with foamy histiocytes. In some cases, sclerosing adenosis, apocrine metaplasia, atypical hyperplasia, and necrosis has been reported (3, 5).

The main histologic differential diagnosis of JP with classical similarities is cystic hypersecretory hyperplasia. The hormonal receptors are commonly positive but can be negative, and the androgen receptor (AR) can show positivity. Basal-like carcinoma markers like EGFR and CK5, along with HER2/neu, are likely to be negative in this cancer (13, 14).

The immune histo chemistry is not yet a proven tool for diagnosis. Both of our cases revealed positivity for ER, PR, AR, c-kit (CD117), high molecular weight cytokeratin (CK5/6), and focally for S-100 protein, while the reaction was negative for epidermal growth factor receptor (EGFR) and human epidermal growth factor receptor 2 (HER2). These results may distinguish JP from the cystic hypersecretory hyperplasia but not the cystic hypersecretory ductal carcinoma in situ.

The controversy in management between surgery and observation is mainly due insufficient reports linking JP to subsequent cancer.

Observation is suggested in the absence of cellular atypia. Surgery on the other hand is preferred due to the likelihood of upstaging of 7.5% in post surgical cases in the absence of atypia as compared to 30% cancer risk in cases of atypia (5, 15-16).

5. CONCLUSION

JP is a rare proliferative ductal lesion with a challenging diagnosis. The reported risk of breast cancer should not be underestimated. Surgical excision is advised in JP.

- **Patient Consent Form**: All participants were informed about subject of the study.
- **Ethical approval**: IRB approval are not needed for Case reports in our center
- **Consent for publication**: Informed written consent was taken for the publication of this paper.
- **Data Availability**: The text contains all the data supporting the findings of these case reports.
- **Author's Contributions**: Mariam Mohammed Al-Qurashi: written the manuscript, reviewing and editing. Arwa Hanafie Ibrahim: literature review, written the manuscript, reviewing and editing. Tarek M. ElSharkawy: reviewing and editing. Prof. Areej Al Nemer: written the manuscript, reviewing and editing. Hiyam Alhaddad: reviewing. Maha Abdel Hadi. Reviewing and modifying manuscript and images
- **Conflicts of interest**: There are no conflicts of interest.
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