Combination of Juvenile Papillomatosis, Juvenile Fibroadenoma and Intraductal Carcinoma of the Breast in a 15-Year-old Girl

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Abstract. The association of juvenile papillomatosis with carcinoma is proven, but very rare, as there exist several reported cases. Case Report: A 15-year-old girl with no family history of breast cancer presented with two masses in the left breast. The excisional biopsy on both lumps revealed juvenile fibroadenoma and juvenile papillomatosis epithelial proliferation multiple cystic expanded channels. In some of these channels, cytological features of intraductal carcinoma were observed. We performed a full immunohistochemical examination of the juvenile papillomatosis. The patient refused any further surgical or adjuvant treatment. There are no signs of recurrence in the 15 year follow-up. Discussion: This case is a diagnostic and therapeutic challenge, taking into account the patient’s age and the controversial treatment recommendations. Good collaboration between surgeons and pathologists is essential for an accurate diagnostic process and aims to avoid under- or overtreatment.

There exist few types of breast papillomas-solitary papillomas, juvenile papillomatosis (JP), and multiple papillomatosis (1). Juvenile papillomatosis (Swiss cheese disease) is usually a benign, localized mass without sharp borders (2). It appears as papillary proliferation of the ductal epithelium which partly fills-up smaller ducts and distends them to a degree. The histopathological criteria for diagnosis of this tumor were first described by Rosen in 1980 and are as follows: papillomatosis with or without a degree of epithelial atypia, apocrine and non-apocrine cysts, papillary apocrine hyperplasia, sclerosing adenosis and ductal stasis (2, 3, 4).

In their retrospective review of cases of JP from 2014 Ozerdem and Hoda describe it as a combination not only of multiple cysts of variable sizes (most with apocrine metaplasia) but also pronounced ductal stasis, with foci of papillary hyperplasia, and sclerosing adenosis. This constellation of findings is typical for the disease, and that is why it is too often mistaken for ‘fibrocystic changes’ (5).

JP occurs at a young age. It can be found in males and females, as the youngest reported patient that we found with this disease was a 7-month-old male infant (6). Usually it appears before the age of 30 years (7).

The association of JP with carcinoma is proven, as there exist several reported cases, but very rare. The risk of concurrent or subsequent development of breast cancer differs between multiple (more than 5) and non-multiple papillomas, centrally and peripherally placed papillomas, papillomas with and without associated atypia, and papillomas encountered in adults and adolescents (8).

The largest series of 180 reported cases of JP was collected by Rosen et al. in 1985 as part of the Juvenile Papillomatosis Registry. Out of all 180 patients, 50 (28%) reported that one or more relatives had had breast cancer. Fewer than 10% of patients for whom clinical findings were described had other lesions in the same breast. Mammography was only rarely performed because of the young age of the patients (mean of 23 years). Seven patients aged from 17 to 44 years (mean of 29 years) had breast carcinoma coincident with JP. Four of these patients were known to have a positive family history for breast carcinoma. Six patients underwent mastectomy. None were found to have axillary lymph node metastases. One patient with in situ lobular carcinoma in JP chose to have no further treatment and remained well one year after biopsy. One of the six patients treated by mastectomy later developed recurrent carcinoma (9).

In a case report of Nio et al., the authors performed immunohistochemical evaluation of multiple and recurrent JP. Immunohistochemistry demonstrated that the JP tumors...
were negative for estrogen receptor (ER), but positive for progesterone receptor (PR), epidermal growth factor receptor (EGFR) and HER-2. In addition, tumor suppressor proteins p53 and Rb-protein were negative. Immunohistochemical analysis suggested that an abnormality in estrogen receptor is important in the pathogenesis of JP, and that the patient had a relatively high risk of developing breast carcinoma since her JP was multi-centric and recurrent (10). The present report yet again suggests that immunohistochemical pathology may be beneficial in assessing the malignant potential of JP.

Case Report

This is a case of a 15-year-old girl, with no family history of breast cancer, who presented with two masses in the upper quadrants of the left breast. The ultrasound examination is shown in Figure 1. The excisional biopsy of both lumps revealed the first to be juvenile fibroadenoma (JF), 3 cm in diameter, and the second to be JP, 5 cm in its greatest dimension. Figure 2 shows the macroscopic appearance of the main lesion, with irregular shape and size of 5×4×1.5 cm, which represents a conglomerate of cavities (Swiss cheese type) with size from 0.1 cm to 0.5 cm and ductal stasis.

The microscopic examination showed JP with intraductal epithelial proliferation, apocrine metaplasia, myoepithelial hyperplasia and multiple cystic expanded channels. In some of these channels, the cytological features of intraductal carcinoma of micropapillary type without necrosis were observed, as shown in Figure 3. The Van Nuys Prognostic Index (VNPI) score (defined according to the index from 1996 was 5 (11).


Taking into account the patient’s age, tumor size, pathological and immunohistochemical findings, the multidisciplinary team recommended mastectomy or surgical excision to be followed by radiation therapy. Despite this fact, the patient and her family refused any further surgical or adjuvant treatment. The patient was followed-up with clinical and ultrasound examinations. One year and a half after operation, a mass between the two lower quadrants of the same breast was found on ultrasound examination. Excisional biopsy was performed and the histological examination showed new JF. There are no signs of recurrence of the intraductal carcinoma in the 15 years’ follow-up from the initial diagnosis.
Discussion

This case is a diagnostic and therapeutic challenge, taking into account the patient’s age and the controversial treatment recommendations. Juvenile or cellular fibroadenomas are an uncommon variant of fibroadenoma. JF are well-circumscribed lesions and, generally, surgical excision is advised for any rapidly growing mass in the adolescent breast, even if it has been previously characterized as benign by core biopsy (12). The surgical management of JP is a complete excision with histological confirmation. This process is usually effective, and incomplete excision invariably leads to recurrence (8). The concern should be greatest for women with a positive family history of breast cancer and recurrent bilateral JP (7).

There also exist cases with co-existence of an in situ lesion (13, 14). Treatment strategies for DCIS remain controversial. In a study of predictors of recurrence in patients with DCIS, patient age, race, tumor size, tumor histological subtype, and histopathological features were not associated with recurrence. The only association was found for higher tumor grade of DCIS on initial diagnosis (15). However, previous studies have found a relationship between young age and local recurrence, especially in the first 10 years after treatment (16).

The National Surgical Adjuvant Breast Project Protocol (NSABP) B-17 recommends breast irradiation for all conservatively treated patients with DCIS (17).

To define the risk of recurrence, we applied VNPI. The final VNPI score in this patient was 5. According to the original index from 1996, which was available at the time of our patient’s diagnosis, treatment recommendations for the intermediate risk group (patients with scores of 5, 6, or 7) are the most difficult. The VNPI recommends local excision with radiotherapy. The inter medium-risk group of patients experience a statistically significant local recurrence-free survival benefit when treated with radiation therapy (85% vs. 68%; p=0.017).

Two therapeutic options, mastectomy or surgical excision to be followed by radiation therapy, were offered to our patient in order to reduce the recurrence risk. She and her family refused further treatment during the whole follow-up period. The patient’s choice is crucial in the decision-making process. Good collaboration between surgeons and pathologists is essential for an accurate diagnostic process and aims to avoid under- or overtreatment.

References


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