CASE REPORT

Infiltrating Ductal Carcinoma Arising in Fibroadenoma and Associated Proliferative Mammary Disease in a 38 Years Old Female -A Rare Case Report

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Abstract

Infiltrating ductal carcinoma arising in a fibroadenoma is a rare incidental finding. Incidence is 0.002-0.0125%. Women having proliferative disease without atypia have a twofold elevation in their risk for subsequent invasive breast cancer. We here present a case report in a 38 year female having fibroadenoma, intraductal papilloma and fibocystic disease of breast who subsequently developed invasive ductal carcinoma in the fibroadenoma. Thus these lesions can be considered to have increased risk of developing malignancy.

Keywords: Ductal Carcinoma, Fibroademoma, Proliferative, Mammary

Introduction:

Fibroadenoma is the most common benign tumor diagnosed in females of less than 30 years. They are classified into simple and complex fibroadenoma. In 50% of cases fibroadenomas are complex and associated with cysts more than 3mm, sclerosing adenosis, duct ectasia, apocrine metaplasia, epithelial calcifications, florid fibrocystic disease and duct papillomatosis. Malignancy is rarely encountered in fibroadenoma [1]. It is usually a secondary involvement. Carcinoma arising *de novo* in fibroadenoma is rare. We here report a case of malignancy developing in a fibroadenoma in a 38 year old female.

Case Report:

A 38 year old female presented with a lump in the right breast since one year in surgical outpatient department in our hospital. On examination, the lump was in lower outer quadrant, measured approximately 4 x 2.5cm, firm and mobile. Skin over the lump was unremarkable. There was no family history of breast or ovarian lesions in the past. On Fine Needle Aspiration Cytology (FNAC) benign duct epithelial cells seen were arranged in small sheets and groups in a background of few foamy macrophages. Considering the age of the patient, smears were reported as benign proliferative mammary lesion. Ultrasonography (USG) showed fibroadenoma with an intraductal papilloma. Her complete hemogram, ESR, blood sugar were within normal limits. On the basis of FNAC and USG report lumpectomy was done. Cut section of lumpectomy specimen revealed two grey white areas almost touching each other and measuring 1.5x1cm and 2x1cm respectively. Sections studied showed a fibroadenoma with an intracanalicular pattern. A part of fibroadenoma showed malignant cells lining the ducts (Fig. 1). The areas adjacent to these ducts showed necrosis of the stromal matrix of the fibroadenoma (Fig. 2). Just touching the fibroadenoma, the other grey white area revealed infiltrating ductal carcinoma (Fig. 3). The surrounding breast tissue revealed an intraductal papilloma (Fig. 4) and changes of fibrocystic disease (Fig. 5).

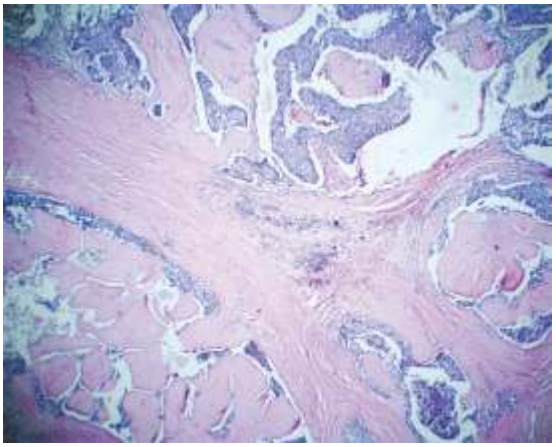

Fig. 1: Malignant Cells Lining the Ducts of Fibroadenoma (H&E Stain)

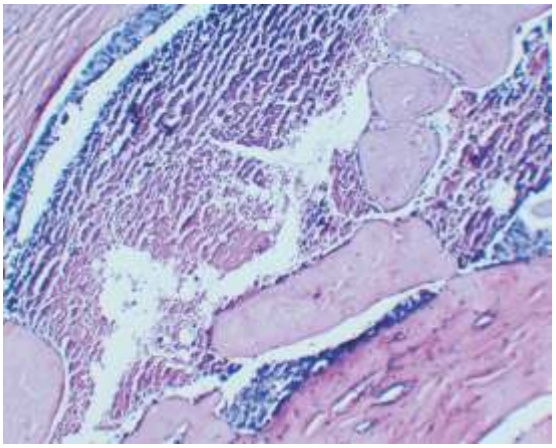

Fig. 2: Fibroadenoma showing Necrosis of Stromal Matrix (H&E Stain)

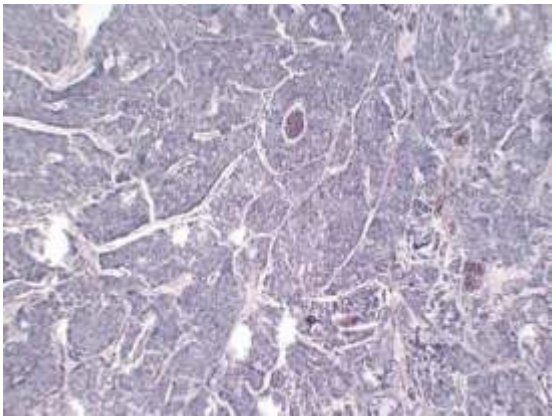

Fig. 3: Infiltrating Ductal Carcinoma (H&E Stain)

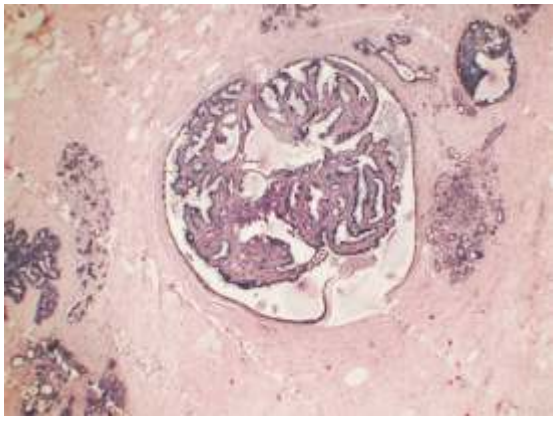

Fig. 4: Intraductal Papilloma (H&E Stain)

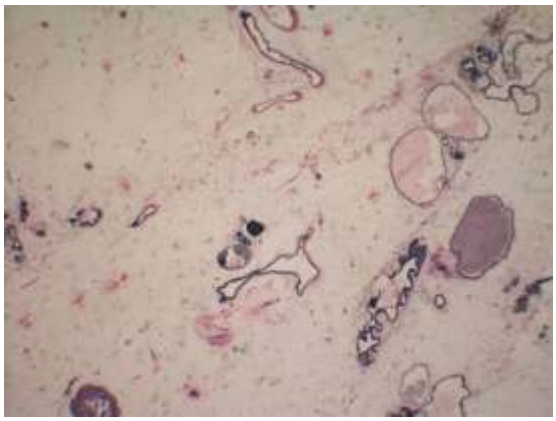

Fig. 5: Fibrocystic Disease of Breast (H&E Stain)

Discussion:

The development of carcinoma in fibroadenoma is a rare phenomenon with peak incidence at the age of 42 years. Azzopardi suggested that carcinoma involving a fibroadenoma might be due to one of the following: 1) Carcinoma arising in an adjacent breast tissue engulfing or infiltrating a fibroadenoma. 2) Carcinoma in the crevices of a fibroadenoma as well as in the adjacent breast tissue. 3) Carcinoma restricted entirely, or at least dominantly, to a fibroadenoma as well as in the adjacent breast tissue [2]. Incidence of a carcinoma evolving within a

fibroadenoma is reported to be 0.002-0.0125 [3]. Diaz *et al.* [4] in 1991 reported a largest series comprising of 105 patients though, over more than 200 cases have been reported [4].

There is a high prevalence of benign breast disease with fibroadenoma in one of every five women and one of every two women is affected by fibrocystic disease [5]. Epithelial hyperplasia within fibroadenomas and fibrocystic disease of breast is a common finding. Carter *et al*. found atypical hyperplasia in 0.81% of fibroadenomas [6]. This hyperplasia can be of ductal or lobular type.

Although malignant transformation in a fibroadenoma is rare, there is a high suspicion index in middle aged women with proliferative diseases. Women having proliferative disease without atypia have a two-fold elevation in their risk for subsequent invasive breast cancer compared with women without proliferative disease and women with proliferative disease with atypia have a fourfold elevation in relative risk of breast cancer. Seven studies have attempted to confirm the breast cancer risk associated with fibroadenomas. Dupont *et al*. and McDivitt *et al*. showed that the relative risk for excised fibroadenomas without hyperplasia ranges from 1.48–1.7 that for fibroadenomas with hyperplasia is 3.47–3.7, and that for fibroadenomas with hyperplasia and atypia is 6.9–7.29, persisting for more than 20 years [7, 8]. The other studies by Levi *et al*. [9], Ciatto *et al*. [10], and Carter *et al*. [6] are considered to provide weaker evidence although; they showed similar results [1, 9]

The overall risk of invasive breast cancer is 2.17 times higher among patients with complex fibroadenomas than among controls [95% Confidence Interval (CI), 1.5 to 3.2]. The relative risk increases to 3.10 among patients with complex fibroadenomas (95% CI, 1.9 to 5.1) and remains elevated for decades after diagnosis [1].

Atypical lobular hyperplasia is associated with the greatest risk, approximately 5-fold and especially, high relative risk of developing premenopausal breast cancer. Atypical ductal hyperplasia is associated with 2.4-fold risk [11].

It is not well understood whether the lesions are precursors of breast cancer or only indication of increased risk, for most types of lesions the chance of developing breast cancer is nearly the same in the affected and unaffected breast (side) indicating only coincidence of risk factors [12].

Therefore, clinicians, radiologists and pathologists should be aware of the possible yet uncommon stepwise progression capabilities of fibroadenomas. Fibroadenomas have been found to contain both in-situ and invasive malignancies. In 66% of the reported cases of carcinomas occurring in a fibroadenoma, the malignancy has been an in-situ lesion, in 34% of cases, the cancer is invasive. In 65% of patients with an in-situ lesion in a fibroadenoma, the lesion is lobular carcinoma-*in-situ*. About two-thirds of the carcinomas arising within a fibroadenoma have lobular morphology; the rest are ductal or mixed ductal and lobular [13].

In this case the changes of conversion or development of malignancy is visible microscopically. To start with the duct epithelial cells become neoplastic. As they proliferate the surrounding stromal tissue undergo necrosis and gradually the space is occupied completely by malignant cells.

In our case, the patient had fibroadenoma, intraductal papilloma and fibrocystic disease in the breast along with invasive ductal carcinoma. There was no family history of any breast lesion in the family. BRCA mutation could not be evaluated as the patient was of low socioeconomic strata.

The development of malignancy is because of association of proliferative disease or because of long standing lump may be of which the patient was unaware for long time. It is only when the lesion is palpable or when it pains the patient notices it. The most important factor in development of intraepithelial neoplasm is to attain heterozygosity with passage of time.

In our case, the surgeon performed lumpectomy because the mammography and FNAC was reported as benign epithelial lesion. Difference between benign and malignant neoplasm is not possible on mammography. Detection of malignancy in a fibroadenoma is difficult on imaging techniques since characteristic radiological signs are usually not evident until a breach occurs in the false capsule. Changes such as increase of color flow signals in Doppler study suggest morphological changes like epithelial hyperplasia, atypia or carcinoma in a fibroadenoma [14]. Unequivocal mammographic features of carcinoma originating within fibroadenoma include indistinct margins and clustered microcalcifications. The age of a lump is usually reflected by calcifications, popcorn-like large (>2 mm) calcifications may be considered "benign-looking", whereas small, branching type and heterogeneous calcifications can express foci of carcinoma-*in-situ* [15].

To summarize, all breast lesions should undergo triple test comprising of FNAC, core biopsy and radio-imaging techniques such as ultrasound and mammogram. In previous reported cases, one of the tests was at least possible which helped the surgeon in correct management. In our case the patient had to undergo radical mastectomy after lumpectomy. Therefore to avoid this, triple test should be mandatory in all cases above 30 years when the risk of proliferative breast lesions increase. More caution should be taken in cases where family history is positive for breast or ovarian lesions. Not always the diagnosis given on FNAC would reflect the lesion of concern/ importance. During FNAC, the cytologist makes passes with a needle into few areas and quite often only the surrounding area is sampled and the lesional areas remain untouched.

To conclude, this case report highlights the need for extensive tissue sampling of fibroadenoma in patients above 30 years and especially in patients with positive family history and to undergo molecular studies to further increase knowledge in mutations leading to development of carcinoma.

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