

Case Report

Ductal Carcinoma In situ with Focal Invasion Arising in Fibroadenoma: A Case Report and Review of Literature

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Abstract

Fibroadenoma is the most commonly diagnosed benign tumor of the breast with highest occurrence in adolescent and young women. Its coexistence with invasive ductal carcinoma is extremely rare and infrequently reported. We report a case of 30-year-old female who was diagnosed with extensive ductal carcinoma *in situ* with focal invasion within fibroadenoma on lumpectomy. The carcinoma was detected incidentally on histopathological examination. Therefore a careful and extensive sampling of the tissue is required to prevent a false negative diagnosis by pathologists.

Keywords: Fibroadenoma; Ductal carcinoma *in situ*; Malignancy; Invasion

Introduction

Fibroadenoma is the most common benign breast neoplasm in females occurring most commonly in 2nd and 3rd decades of life [1]. Limited case reports and studies have shown that Fibroadenomas have a very rare chance of developing malignancy with reported incidences ranging from 0.002% to 0.125% [2]. They are usually found incidentally during pathologic examination. Carcinomas *in situ* are found to be more common than invasive carcinomas [3]. This progression is usually found in women over 40 years of age, which is nearly a decade older than those with the usual type of fibroadenoma. Due to rarity of this condition the consensus guidelines related to its management is controversial. Here, we report one such unusual case where extensive ductal carcinoma *in situ* with focal invasion developed in a fibroadenoma, presenting as a gradually progressive breast lump, in a young female.

Case Presentation

A 30 years old nulliparous lady presented with painless, slowly progressive right breast lump for 2 years with no history of nipple discharge. On examination the lump was firm, mobile, nontender. The overlying skin and nipple areola complex were normal with no evidence of any axillary lymphadenopathy. There was a negative family history for malignancy. Mammogram revealed a lobulated hypo echoic mass measuring 31x18 mm at 6 o'clock position. It showed well defined outline with long axis parallel to skin surface. These findings were consistent with BIRADS 2 and suggested a radiological diagnosis of fibroadenoma. In view of young age, possibly benign mammography and absence of any rapid increase in size, surgical excision (lumpectomy) was planned. Intraoperatively, an encapsulated lobulated mass was identified in right breast in the lower outer quadrant at 6 o'clock position (Figure 1).

Histopathological evaluation revealed a sclerosed fibroadenoma with extensive Ductal Carcinoma *In Situ* (DCIS) along with presence of an invasive component. Scant normal breast tissue was identified at the periphery and the surgical resection margins were clear. The tumor cells were positive for estrogen and progesterone receptor with allred score of 8 and 6 respectively. There was diffuse strong

complete membranous positivity for Her2 neu receptor as well. P63 immunostaining was performed to confirm *in situ* as well as invasive component. P63 was continuously positive at the periphery in DCIS component with absence in the central aspect. The invasive component was entirely negative for p63. The tumor cells also showed diffuse positivity for E cadherin excluding the possibility of lobular carcinoma *in situ* or lobular carcinoma. The tumor had high proliferative index with Ki-67 as 30%. Hence, the lesion was finally as "Fibroadenoma with extensive ductal carcinoma *in situ* and focal invasion.

Patient was referred to a higher centre and we evaluated her post lumpectomy which was done elsewhere. The above mentioned histopathological and immunohistochemical analysis was done in our department on the received blocks and slides. As the histology of the lumpectomy specimen was a surprise to clinicians, she was planned for further management to look for any residual lesion or recurrence.

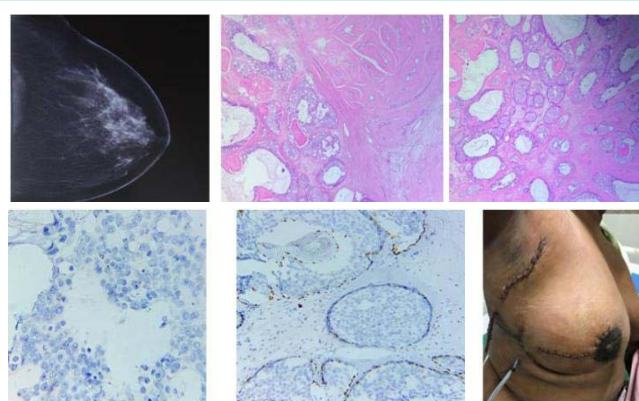


Figure 1: (a). Mammogram displaying a lobulated mass with well defined outline with long axis parallel to skin surface suggesting fibroadenoma (b). Extensive carcinoma in situ component in an old sclerosed fibroadenoma (Hematoxylin and eosin; 200X). (c). focal invasive component (Hematoxylin and eosin; 200X), (d). Absence of P63 in the invasive component (Immunohistochemistry; 400X); (e). P63 positivity at the periphery in the DCIS component (Immunohistochemistry; 400X); and (f) Lateral Intercostal Artery Perforator (LICAP) flap reconstruction (5th days post surgery).

Following the histopathological report, post-operative mammogram was performed which showed an area of architectural distortion in the right upper outer quadrant at 9 o'clock position 3.4 cm from the nipple.

It measured approximately 20x29x17 mm. No microcalcification was seen. Finding were suggestive of radial scar, however malignancy could not be ruled out and was reported as BIRADS 4b (suspicious for malignancy). HRUSG also suggested subtle architectural distortion with hypoechoic lesion seen extending from skin up to the mammary zone. Bilateral benign axillary lymph node were seen with central lucent hilum. Further surgical exploration was planned for wide local excision and axillary lymph node dissection along with Lateral Intercostal Artery Perforator (LICAP) flap reconstruction. The histopathological evaluation showed no evidence of malignancy or metastatic tumor deposits in the lymph nodes. The postoperative period was uneventful and the patient is still in follow up.

Discussion

Fibroadenoma is a benign fibroepithelial neoplasm mostly seen in young female in 2nd or 3rd decade of life. The overall incidence is about 2.2%, however they represent ~68% of all breast masses. They are solitary lesion in approximately two third of the cases but may present as multiple lumps in 10-25% of these patients [1]. It is very unusual for a carcinoma of the breast to arise within a fibroadenoma with most studies reporting an incidence of less than 1% [3,4]. Cheatle and Cutler defined carcinoma developing from fibroadenoma in 1931 for the first time [5] and since then limited cases and studies have been reported in literature. Cases of breast carcinoma within a fibroadenoma typically occur at an older age as compared to conventional fibroadenoma and are usually diagnosed in female older than 40 years [3,4,6]. However in our case the female was only 30 yrs, old suggesting that malignancy is not limited to older age group rather can arise at an early age group mandating a proper evaluation.

Dupont et al., in their study documented that the relative risk of invasive breast cancer was 2.17 times higher for patients with FA than for matched controls. This risk increased to 3.10 for women with complex FAs and remained elevated for more than 20 years after diagnosis [7]. Twenty year later, Nassar et al., suggested that Complex FA does not confer increased risk of breast cancer beyond that of other established histologic features such as proliferative disease with atypia and atypical hyperplasia [8].

The mammographic features of malignancy arising in a fibroadenoma include clustered micro-calcification and indistinct margin but these features are not always present, as seen in our case. It may be difficult to suspect the malignant transformation, as the clinical and radiological signs may be masked until breach of the false capsule and hence the diagnosis is invariably reached on histopathological examination of the tumor thereby mandating a high suspicion index [9-10]. In the present case the malignant transformation was revealed on histopathological examination of the lump, which was radiologically, and clinically suggestive of fibroadenoma. The pathological evaluation revealed that the changes were confined within the lump without any breach of the capsule. Studies in the past have shown malignant transformation in fibroadenomas were mainly carcinomas *in situ* (66.9% LCIS and 12.4% DCIS), followed

by invasive carcinoma (11% IDC and 3.4% ILC) [11,12]. In 2014, Yu-Ting Wu in a collective case analysis documented that the major histological type was IDC (53.3%), followed by DCIS (23.3%), LCIS (16.7%) and ILC (13.3%). These findings are not consistent with previous reports which suggest that lobular are more common.

Owing to rarity of malignancy arising in fibroadenoma, the management guidelines are not well defined. It is unknown whether such patients should be treated similarly to those with breast cancer or differently. Lumpectomy is the treatment of choice for benign fibroadenoma [1]. According to the collective analysis of case reports by Yu-Ting Wu et al published in 2014, breast conservative surgery was the most common surgery performed in this scenario [3]. Tumorectomy or lumpectomy may alone be sufficient, if the initial resection margin is free of cancer or only LCIS is inside the fibroadenoma. Further wide local excision may be required if the tumor is close to or involve the resection margin. Large size, multifocal lesion and central location may be an indication of mastectomy.

The use of radiotherapy is debatable and chemotherapy is preferred in cases with nodal metastasis. Certain studies also state that breast cancer in fibroadenoma behaves like breast cancer at the same stage and that therefore the treatment should follow the same modality [13]. To conclude, this case highlights that malignancy may arise in fibroadenoma at younger age and required through clinical and histopathological evaluation. Ductal carcinoma *in situ* or invasive ductal carcinoma may commonly arise. Therefore a careful and extensive sampling of the tissue is required to prevent a false negative diagnosis by pathologists. The management is controversial, however breast conservative surgery with or without radiotherapy is still the treatment of choice.

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