

Original Article

Carcinoma in Situ Raised from Fibroadenoma: A Case Series of a Rare Combination

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Abstract

Introduction

Fibroadenomas are the most frequent cause of palpable breast lumps in young women. Although it's a benign lesion, malignancy can occur in extremely rare cases; this risk is higher in complex fibroadenomas and in patients with a family history of the disease. The aim of the current study is to report a case series of rare combination of two breast tumors (carcinoma in situ within fibroadenoma).

Methods

This is a retrospective case series study. The cases were managed in a single private center specific for breast diseases. They were evaluated and treated during the four previous years (January 2018-May 2022). It included all patients who had a fibroadenoma with malignant changes.

Results

The study included nine cases. The mean age was 41 years ranged from 31 to 51 years. Six cases were ductal carcinoma in situ within fibroadenoma and three cases were lobular carcinoma in situ.

Conclusion

Although fibroadenomas are the most common benign breast mass, it is rarely associated with malignant transformation.

1. Introduction

Fibroadenomas (FA) are the most frequent cause of palpable breast lumps in young women, with the majority appearing between the ages of 20 and 40 years [1]. Representing a

collection of hyperplastic breast lobules caused by disruption of organogenesis [2]. The tumor develops in response to elevated levels of estrogen and progesterone during breast feeding and pregnancy. However, it may experience atrophic changes during the postmenopausal period. [3]. Based on certain histological findings, FAs are classified into simple or complex [4]. Even

though it is a benign lesion, malignancy can occur in extremely rare cases. This risk is higher in patients with complex FA and a family history of the disease [5]. The incidence of FA harboring malignancy ranges from 0.002% to 0.125% [6].

The aim of the current study is to report a case series of a rare combination of two breast tumors (carcinoma in situ within FA).

2. Methods

2.1. Study design

This is a retrospective case series study of patients with a rare combination of two common disease of the breast. Patients were managed in a single private center. The cases were evaluated and treated during the four previous years (from January 2018 to May 2022).

2.2. Data collection

All data, including the patients' age, gender, marital status, past medical history, family history, ultrasound findings, mammography, fine needle aspiration (if available), and histopathological examination, were obtained from the center's database system.

Table 1. The demographic data and clinical characteristics of the cases

N. Case	Age (year), sex	Occupation	Marital status	Past medical history	Family history	Smoking	Chief complain	Ultrasound findings	Mammography finding
1	41, female	House wife	Married	Negative	Negative	Passive	Left breast mass for 2 years	Multicentric lesion, highly suggestive of malignancy (U5)	Left breast mass, BIRADS (M5), right breast mass BIRADS (M1)
2	51, female	House wife	Married	Negative	Negative	Non-smoker	Right breast mass	Right breast mass at subareolar region Solid mass toward three o'clock.	Right breast mass M4, left breast mass (M1)
3	33, female	House wife	Married	Negative	Negative	Non-smoker	Left breast mass for three months duration	Left breast solid mass of 38*15 mm in the inner quadrant at nine o'clock (U3)	None
4	43, female	House wife	Married	Negative	Negative	Non-smoker	Right breast mass	Right breast mass of 20*11.5 mm (U3) at 12 o'clock Right breast mass of 16*10 mm at 12 o'clock. From nipple root toward lower third (5-7 o'clock). Dilated ducts with tick internal echoes and adjacent heterogenous parenchyma with inflammation.	Right breast mass (M3)
5	37, female	House wife	Married	Negative	Negative	Non-smoker	Right breast pain for 6 years.	Right breast mass at 8-9 o'clock, appear circumscribed, oval mass, heterogenous hypochoic and moderate internal vascularity shows cystic changes with dots of calcification, The mass measuring (54*25 mm).	None
6	31, female	House wife	Married	Negative	Negative	Non-smoker	Right breast mass for three months	Right breast mass of 26*10 mm in the upper outer quadrant (U2)	None
7	43, female	House wife	Married	Thyroid disease	Breast cancer	Non-smoker	Bilateral breast mass for two years	None	Right breast mass, (M4)
8	50, female	House wife	Married	Renal cell carcinoma	Negative	Non-smoker	None	None	None
9	41, female	House wife	Married	Negative	Negative	Non-smoker	Left breast mass	Right breast mass of 1.7-2 mm (U2)	Right breast mass (M2)

2.3. Inclusion and exclusion criteria

The study included all patients with malignant changes within FA after confirmation by histopathological examination.

3. Results

There were a total of nine cases in this study. The mean age was 41 years, with a range of 31-51 years. Eight (88.9%) of them were housewives, and just one (11.1%) was a teacher. The patients were all married. Just one (11.1%) of them was a smoker, and one (11.1%) had a family history of breast cancer. Breast mass was the most common presentation in eight (88.9%) cases, followed by breast discomfort in one (11.1%) case (Table 1). In seven (77.8%) cases, a lumpectomy with wide local excision was performed, and in two (22.2%) cases, a mastectomy with axillary lymph node dissection was conducted. Six (66.7%) of them had ductal carcinoma in situ (DCIS) in FA, whereas the other three (33.3%) had lobular carcinoma in situ (LCIS) in FA (Table 2).

4. Discussion

Fibroadenoma is a fibroepithelial tumor that commonly affects young females. It accounts for nearly 68% of breast tumors and 2.2% of the general population. Most commonly (70%) it appears as a single mass and about 10–25% may be present as multiple masses [7]. Although FA is not a known risk for breast malignancy, malignant transformations have been reported rarely within it [5]. Some of the recent reports explain that malignant changes are more frequent in complex FA than in simple FA. However, other studies state that the risk is strongly related to the amount of epithelial proliferation inside the FA rather than the existence of FA [5]. Patients with malignant changes within FA are typically older (42–44 years) than patients with pure FA (20–30 years) [4]. The mean age of the cases in the current study was 44.4 years. The reported incidence of different cancers arising within FA differs from the normal incidence of cancer subtypes. LCIS (50%) is the most common malignant change, followed by DCIS, invasive ductal carcinoma (IDC) (20%), and invasive lobular carcinoma (ILC) (5%). Other forms of breast cancer are extremely rare.

Table 2. Core needle biopsy, treatment, and histopathological result of each case.

N. Case	Core needle biopsy	Operation	Histopathological Finding	Follow up
1	IDC, grade III	Left radical mastectomy + axillary lymph node dissection level 1 and 2	Invasive ductal carcinoma of no specific type with extensive high grade ductal carcinoma in situ arising from fibroadenoma (Figure 2)	Sent for oncologist. Received five session of chemotherapy and 15 sessions of radiotherapy and putted on tamoxifen. No sign of recurrence in 60-month follow-up
2	None	Right breast lumpectomy	Low-grade ductal carcinoma in situ without invasion arising within complex fibroadenoma (Figure 3)	Sent for oncologist for follow up. received tamoxifen. No sign of recurrences in 24-month follow-up.
3	None	Left breast lumpectomy	Proliferative breast changes with intraductal papilloma and classical lobular carcinoma in situ (Figure 4)	Sent for oncologist for follow up with imaging.
4	Proliferative fibrocystic disease	Right breast Lumpectomy with wide local excision	Complex fibroadenoma with suspicious area of atypical ductal hyperplasia/low grade ductal carcinoma in situ	Sent for oncologist for follow up. There were no signs of recurrence in 33 month follow up.
5	None	Right breast Lumpectomy with wide local excision	Extensive high-grade ductal carcinoma in situ without invasion arising within a complex fibroadenoma	Sent for oncologist for follow up. receiving radiotherapy. Now on tamoxifen. No sign of recurrences during 12-month follow-up
6	None	Right breast Lumpectomy	Lobular carcinoma in situ, classical type raised within a complex fibroadenoma, no invasion is seen	Sent for oncologist for follow up. no sign of recurrence during 24-month follow-up
7	None	Right breast Lumpectomy with wide local excision	Lobular carcinoma in situ, pleomorphic and florid type raised within a complex fibroadenoma, no invasion is seen (Figure 5)	Sent for oncologist for follow up. no sign of recurrence during 20 month follows up.
8	None	Right mastectomy with axillary lymph node dissection	Focal low grade ductal carcinoma in situ, no invasion seen arising from fibroadenoma	Sent for oncologist for follow up. there was no sign of recurrence during 24-month years follow up.
9	IDC, grade III	Left breast Lumpectomy	High-grade ductal carcinoma in situ without invasion arising within complex fibroadenoma	Referred to oncologist

However, adenoid cystic and mucinous carcinomas developing within FA have been reported [8]. In the current study, 62.5% of cases (5 cases) were diagnosed as having DCIS in FA and 37.5% (3 cases) were diagnosed as having LCIS in FA. Rarely, a mixture of both invasive and in situ cancers may arise from FA [9]. In this study, one case had both invasive ductal carcinoma and DCIS in FA (Figure 2). An increase in the age, size, and thickness of the tumor is one of the most important indications of malignant changes in FA [10].

of each of the included cases (Table 1). Although it is hard to diagnose malignant changes within FA by mammography, it may reveal alarming signs of malignant changes [2]. Microcalcification appearing on mammography is an important indicator of malignant changes [14]. Irregular contours, ill-defined spiculated borders, or pleomorphic/linear microcalcifications should all be considered as hallmarks of cancer [12]. Ooe et al presented a case of DCIS emerging within a FA with a well-circumscribed, polygonal, moderately iso-

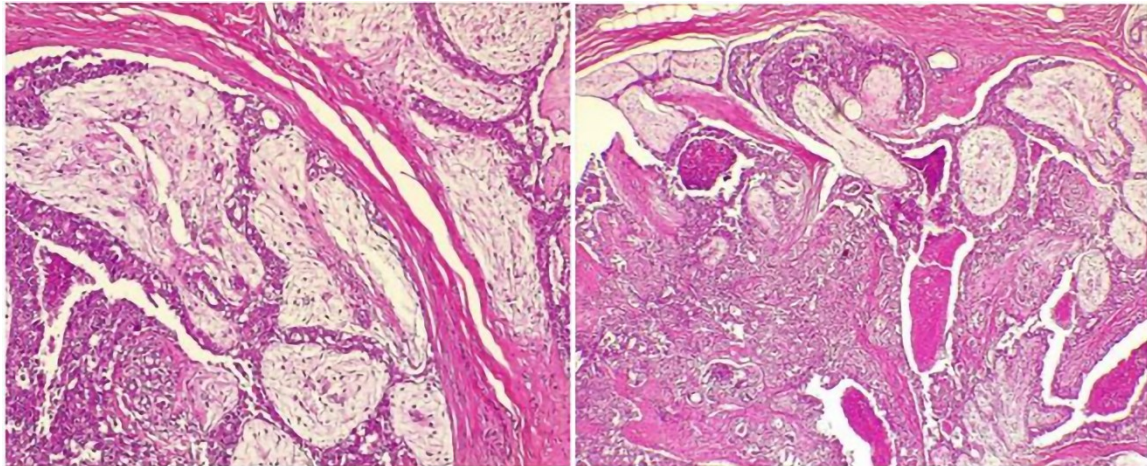


Figure 1. Invasive ductal carcinoma with high grade DCIS raised within a pre-existing FA of breast.

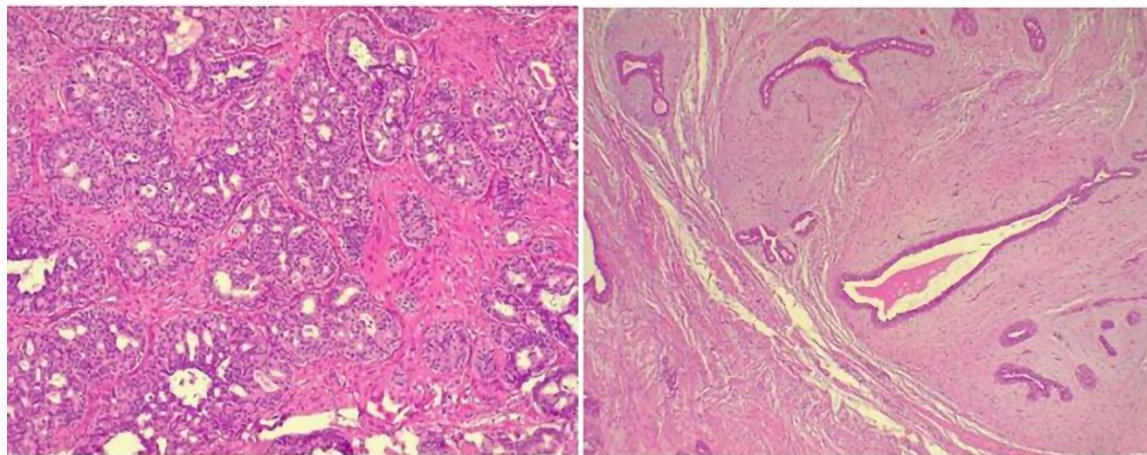


Figure 2. Low grade DCIS in fibroadenoma

The majority of FAs with malignant changes are found by accident during pathological examinations [5]. One study revealed that FAs with foci of cancer in situ might be indistinguishable on imaging from benign lesions [11]. However, according to other studies, radiological examinations may reveal alarming signs suggesting the existence of malignant changes within FA. In ultrasound examination of FA, the appearance of irregular border and shape, extensive hypoechoic shadowing with an echogenic halo, and distortion of surrounding tissue are considered to be significant indicators of malignancy [12]. Ultrasound is better for evaluating tumor size because it provides high-resolution images [10]. A focal rise in color flow signals around the mass on color doppler ultrasound suggests the possibility of malignancy [13]. Table one revealed the ultrasound appearance

dense mass and free of microcalcifications [15]. On magnetic resonance imaging (MRI), FAs usually appear as round or oval-shaped tumors with smooth borders. It may have varying degrees of enhancement; nevertheless, enhancement generally lasts until the delayed phase [16]. In dynamic contrast-enhanced breast MRI (DCE-b MRI), the malignant changes within FA appear as a mass with an early peak enhancement in the core and a delayed rim enhancement in the margin [16]. Other studies reported that the area of carcinoma within FA on DCE-b MRI appeared as a rapid initial enhancement and washout kinetics [16]. Benign FAs and DCIS/IDC can be distinguished using dynamic MRI based on vascularity [16].

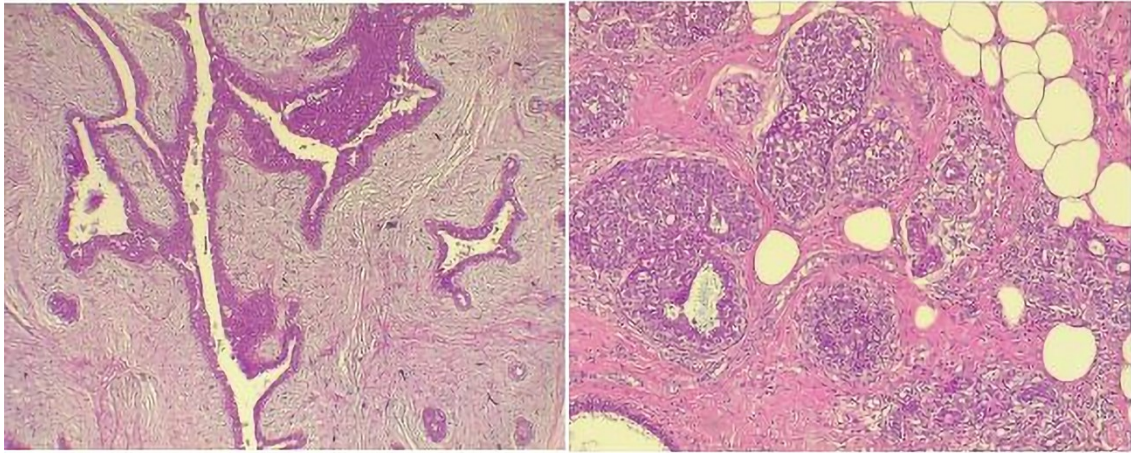


Figure 3. Fibroadenoma with LCS in situ.

Malignant changes that originate within a FA behave similarly to those that arise separately, therefore, therapy should be the same. The controversy over which therapeutic technique to use in a case of in situ carcinoma within a FA reflects the discussion regarding standard treatments of LCIS and DCIS [13]. The treatment of FA varies depending on the patient's age. Those under the age of 35 year should consider additional follow-up until the mass has declined and disappeared entirely. If the mass

two cases (one with both IDC and DCIS and one with only DCIS) underwent radical mastectomy and axillary lymph node dissection. The other six cases underwent breast conserving therapy. All patients were sent to an oncologist and there were no signs of recurrences during follow up. remains stable after 6-12 months of follow-up, excision is recommended. If, on the other hand, the mass has grown, an immediate excision is undertaken [11].

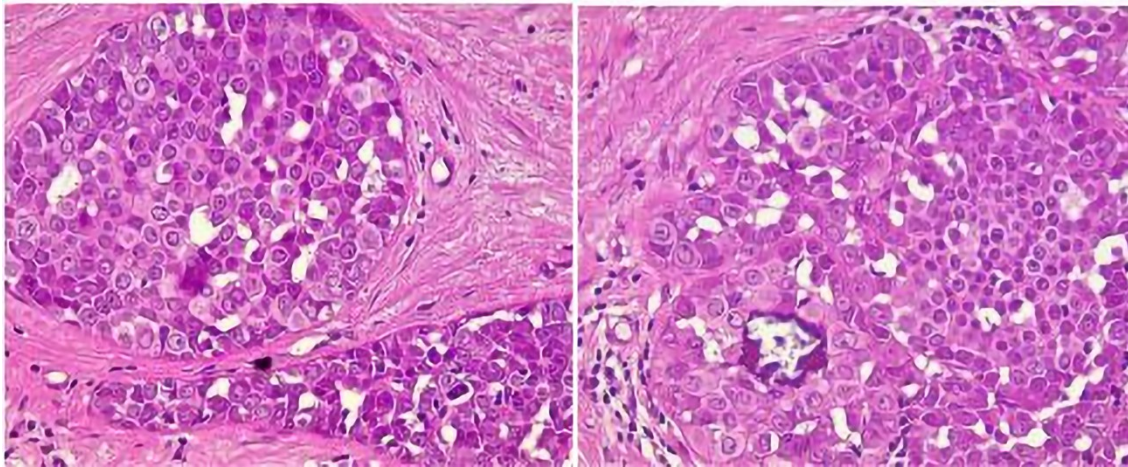


Figure 4. Florid LCIS with calcification in this case.

Excision is recommended if the age is over 35 years and the FA is stable or growing after a 6–12-month follow-up; nonetheless, the complex FA should be excised surgically [5]. Most women with DCIS within FA will definitely benefit from breast conservation therapy, but most women with LCIS within FA will benefit from close observation following wide local excision and biopsy. Although preventive mastectomy can cure LCIS, the surgery is generally regarded as excessively invasive for most women [13]. Lumpectomy may be adequate if the surgical margin is cancer free. However, wide local excision may be required if the resection margin is close or involved [12]. In the current study,

5. Conclusion

Although FAs are the most common benign breast mass, they are rarely associated with malignant transformation. Therefore, the risk of malignant changes within FA should always be suspected, particularly at older ages.

Declarations

Conflicts of interest: The author(s) have no conflicts of interest to disclose.

Ethical approval: Ethical approval was obtained from the ethics committee of university of Sulaimani prior to data collection. Informed consent was obtained from all study participants.

Patient consent (participation and publication): Written informed consent was obtained from all participants of this study.

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Role of Fonder: The funder has no role in the design of the study, data analysis, drafting of the manuscript, or conclusion.

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Authors' contributions: AMS was a major contributor to the conception of the study, as well as in the literature search for related studies. MNH, BAA and FHK were involved in the literature review, in the writing of the manuscript, and in the examination and interpretation of the patient's data. HOA, HMR, and SHM were involved in the literature review, the design of the study, the critical revision of the manuscript. FHK and SHM confirm the authenticity of all the raw data. AJQ and LRP were the radiologists who performed the assessment of the case. AMA was the pathologist who performed the specimen. All authors have read and approved the final manuscript.

Data availability statement: Not applicable.

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