



## Lobular Carcinoma *In Situ* within Fibroadenoma: A Case Report and Literature Review

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### Abstract

Breast fibroadenoma is the most common tumor with benign biological behavior in women. However, the imaging and clinical features of carcinoma *in situ* within a fibroadenoma are often similar to those of a fibroadenoma. This study aimed to report the case of a 38-year-old young woman with a regular painless mass in her right breast for 6 years. This tumor had a clear boundary and was composed of epithelial and mesenchymal cells. Most of the area comprised the so-called fibroadenoma structure, besides swelling and proliferation in a small part of the terminal duct and no expression of E-cadherin protein. The histological morphology and immunohistochemistry confirmed the diagnosis of a fibroadenoma with lobular carcinoma *in situ*. We need to be careful of malignant transformation within fibroadenomas and improve the understanding of lobular carcinoma *in situ* within fibroadenoma.

**Keywords:** Lobular carcinoma *in situ*; Fibroadenoma; Differential diagnosis

### Introduction

Breast fibroadenoma is a benign tumor confined to the terminal ductal lobular unit; it consists of bidirectional hyperplasia of epithelial and mesenchymal components [1,2]. Fibroadenoma is a common tumor in young women, especially women of childbearing age, which is often diagnosed initially by color Doppler ultrasound [3]. Besides, it also occurs in adolescents and older women. Fibroadenoma is usually a painless, well-defined, and solitary solid mass [4]. The diagnosis of breast fibroadenoma mainly depends on histopathological characteristics. Different groups of people adopt different methods to manage fibroadenomas, that is, asymptomatic small fibroadenomas can be followed up for observation. The surgical resection of larger ones is the most common treatment for fibroadenomas [5]. Most fibroadenomas after resection have a good prognosis.

However, in a small part of the fibroadenoma in the present case, carcinoma *in situ* coexisted, including lobular carcinoma *in situ*, ductal carcinoma, and mixed carcinoma of the two. Studies have shown that fibroadenoma combined with lobular carcinoma *in situ* is the most common [6]. Compared with fibroadenoma, fibroadenoma with lobular carcinoma *in situ* has no special clinical and imaging features. In addition, no agreement exists on its management. This study was performed to report a case and review the literature to strengthen the understanding of the clinical characteristics of lobular carcinoma *in situ* in breast fibroadenoma and discuss its management plan.

### Case Presentation

A 38-year-old woman presented with a painless mass in her right breast for 6 years. Since the discovery of the mass, the patient had been rechecked using breast color ultrasound every year, and no significant enlargement of the mass was found. However, color Doppler ultrasound showed that the mass was enlarged, that is, a hypoechoic area of 2 cm × 1.5 cm × 1 cm was observed in the upper right breast quadrant, with regular morphology and clear boundaries in December 2020. The Breast Imaging Reporting and Data System (BI-RADS) was classified as Category IV.

The doctor performed a fine-needle aspiration biopsy on the patient to clarify the nature of the mass. Then, hematoxylin eosin-stained pathological sections were made, and the tissue morphology was observed under a microscope. The components of fibroadenoma, namely, epithelial and mesenchymal hyperplasia comprising mesenchymal cells, grew around the ducts of the breast, and

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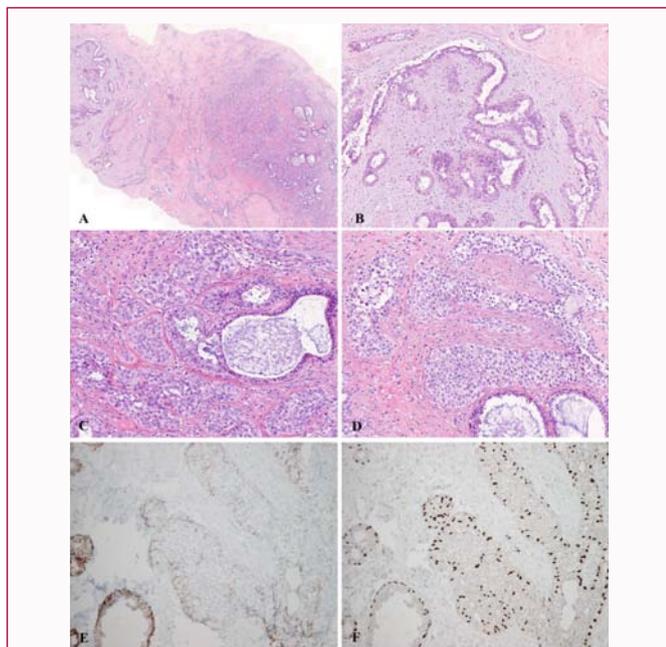
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**Figure 1:** (A) At low magnification, a breast fibroadenoma was found on the left side, while the right side had a large number of cells and deep staining. (B) Epithelial component of the fibroadenoma area had a peripheral growth pattern, with mucinous changes in the interstitium. (C) At a high magnification of the hyperchromatic area, the acinar swelling around the duct was found to be filled with round and uniformly sized cells, that is, lobular carcinoma *in situ*. (D) Lobular carcinoma *in situ* involved the terminal duct. The results of immunohistochemistry showed that the cells in the terminal duct were negative for E-cadherin (E), while the outer myoepithelial cells were positive for p63 (F).

the ducts were squeezed into cracks or an open lumen (Figure 1A, 1B). In addition, some swollen terminal ductal lobular units were found in the fibroadenoma, and the acini were filled with uniform and deep-stained round cells, that is, lobular carcinoma *in situ* (Figure 1C). The hyperchromatic and uniform round cells involved the ducts of the breast (Figure 1D). These deeply stained cells were negative for E-cadherin (Figure 1E), while myoepithelial cells surrounding acini were positive for p63 (Figure 1F). Subsequently, the tumor was resected. The lobular carcinoma *in situ* was present only in the fibroadenoma, with no involvement of the surrounding margins.

## Discussion

Breast fibroadenoma is the most common fibroepithelial tumor comprising both epithelial and mesenchymal components. Although ductal epithelial hyperplasia or metaplasia is common in fibroadenomas, malignant transformation in fibroadenoma is very rare. Cheatele in 1931 first reported carcinoma within fibroadenoma was first reported; subsequently, people gradually increased their understanding, and different types of intra-fibroadenoma carcinoma were reported successively [1,2,7]. The types of intra-fibroadenoma carcinoma include lobular carcinoma *in situ*, ductal carcinoma *in situ*, and invasive breast cancer. This study focused on the clinical features, pathological characteristics, differential diagnosis, therapy, and prognosis of lobular carcinoma *in situ* within fibroadenoma.

Fibroadenomas are often painless, isolated, and slow-growing nodules. However, breast carcinoma within a fibroadenoma may be accompanied by a rapid increase in mass in a short period. The radiology showed clear nodules with occasional calcification. Studies have shown that one should be vigilant against the occurrence of

tumors with fuzzy edges or microcalcifications. Many studies have reported that fibroadenoma is the most common type of benign tumor in women aged less than 35 years. In addition, older age is considered a risk transformation of factor for malignant fibroadenoma [8]. In fact, no clear difference exists between intra-fibroadenoma carcinoma and fibroadenoma in terms of clinical and radiological manifestations. Malignancy is rarely suspected even during gross examination, and the final diagnosis depends on pathology. As reported in this case, the patient was a 38-year-old relatively young woman who had no special clinical and imaging findings but was diagnosed with lobular carcinoma *in situ* within fibroadenoma. Therefore, we must be careful of not only the malignant transformation of old or suddenly enlarged fibroadenoma, especially lobular carcinoma *in situ*, but also young and symptomatic fibroadenoma.

Breast fibroadenoma is a common benign fibrous and epithelial tumor. The latest edition of the World Health Organization of the breast divides fibroadenoma into four types, namely classic type, juvenile type, complex type, and cell-rich type [4]. The risk of breast cancer in complex fibroadenoma is increased compared with that in other types of fibroadenoma [9]. The fibroadenoma mainly presents a growth pattern in and around the tube, with no dysplasia of interstitial cells. Epithelial components are often accompanied by common ductal hyperplasia, myoepithelial hyperplasia, sclerosing adenopathy, fibrocystic degeneration, or apocrine metaplasia. Moreover, atypical ductal or lobular hyperplasia, ductal or lobular carcinoma *in situ*, and invasive carcinoma are occasionally seen in fibroadenoma.

Carcinomas within fibroadenoma refer to the cancerous transformation of epithelial components into fibroadenoma; the cancerous tissue is limited to fibroadenoma or accompanied by small infiltration. Carcinomas within fibroadenoma include lobular carcinoma *in situ*, ductal carcinoma, and invasive carcinoma. The literature reports showed that the occurrence of lobular carcinoma *in situ* was the most common. Other types of cancer, such as mucus carcinoma, metaplastic carcinoma, and adenoid cystic carcinoma, are rarely reported. Lobular carcinoma within fibroadenoma needs to be differentiated from the following diseases. (1) Ductal carcinoma *in situ* within fibroadenoma: It has uniformly packed cells in the lumen, but lobular carcinoma *in situ* loses adhesion and is negative for E-cadherin. (2) Common ductal epithelial hyperplasia in fibroadenoma: It also involves the terminal ductal lobular unit, but the cells are disorderly or with the flow-like arrangement, and cell size is inconsistent. In addition, immunohistochemical markers show a mixed phenotype of the myoepithelial and glandular epithelium; Estrogen Receptor (ER) and Progesterone Receptor (PR) are expressed unevenly. (3) Carcinoma within phyllode tumors: Sometimes, it is difficult to distinguish between fibroadenomas and phyllode tumors. The latter often forms distinct phyllode-like structures; mesenchymal spindle cells are also significantly proliferated and even atypical. (4) Lobular carcinoma: It should be differentiated from invasive carcinoma in fibroadenoma. The main body of invasive cancer is often absent in fibroadenoma and infiltrates into fibroadenoma. Cell atypia of the invasive cancer is obvious, mitosis is easily seen, and negative for p63.

Managing cancer in fibroadenomas often adopts corresponding programs according to the type, scope, and hormone receptors of the cancer. Simple tumor resection is recommended for lobular carcinoma *in situ* within fibroadenoma [10,11]. However, simple mastectomy should be considered when the tumor is large, multifocal, or in the center of the breast. Compared with the same type of breast cancer, fibroepithelial intratumoral cancer is less biologically aggressive. This

may be related to the envelope of fibroepithelial tumors, restricting cancer growth [12], but further confirmation is needed. When a fibroadenoma suddenly enlarges or is found to be accompanied by calcification on radiography, a fine-needle needle biopsy should be performed to determine the nature of the mass.

### Author Contributions

Bin Zhou and Luoyan Wu, writing the manuscript. Liyuan Liu, Zhi Zhang and Minshi Ye, conducting the main experiments in this work. Ying Yang, Fangli Wei and Guijie Zhang, Data collection. Dongmei Ye, manuscript writing and critical review of manuscript. Li Qingwu: Conceiving and designing the study, providing financial support. All authors read and approved the final manuscript.

### Ethics Approval and Consent to Participate

All ethical approval and consent procedures were approved by the Nanchang First Hospital. We have obtained the patient's informed consent for publishing this article.

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