

Case Report

Multiple and giant juvenile fibroadenoma: a case report and literature review

Chen Chen¹, Dan Gao², Li-Bo Luo¹

¹Department of Breast and Thyroid Surgery, The First People's Hospital of Zunyi, Guizhou, China; ²Department of Ultrasound, The First People's Hospital of Zunyi, Guizhou, China

Received June 26, 2017; Accepted February 23, 2018; Epub May 15, 2018; Published May 30, 2018

Abstract: Clinically, juvenile multiple giant fibroadenomas are extremely rare. We describe a case of a 17-year-old girl who presented with 12 painless masses in her right breast. All the 12 tumors were surgically removed through a periareolar incision. The diagnosis of multiple and giant juvenile was confirmed both clinically and pathologically. Literatures were reviewed to verify the clinical features of breast fibroadenoma, including associated etiology, classification, recurrence rate and the risk of developing breast cancer.

Keywords: Breast fibroadenoma, juvenile fibroadenoma, giant fibroadenoma, multiple fibroadenomas, fibroadenomas.

Introduction

Fibroadenoma is the most common type of benign breast tumors that occurs in 25% of asymptomatic women. It can present at any age but are frequently diagnosed in young women in their 20s and 30s [1, 2], a time at which breast lobular structures are added to the ductal system. Incidence decreases after the age of 40 years. Breast fibroadenoma is usually single but can be multiple in about 15% cases [3]. Giant fibroadenoma generally refers to fibroadenoma that greater than 5 cm, and account for only 0.5~2% of all fibroadenomas [4, 5]. Fibroadenoma in adolescents that grow rapidly or to a large size is commonly classified as juvenile fibroadenoma. Histologically, juvenile fibroadenoma has more cellular stroma than a typical fibroadenoma [6]. Juvenile fibroadenoma is a rare clinical entity and forms less than 10% of the total fibroadenomas [7-9]. Clinically, juvenile multiple giant fibroadenomas are extremely rare. We present a rare case involving a 17-year-old girl with unilateral breast multiple giant fibroadenomas.

Case presentation

A 17-year-old Chinese girl presented with hypertrophy and rapid enlarging lumps in the right

breast for one year (**Figure 1**). The age of menarche was 12 years and without family history. History of pregnancy, trauma, chest radiation and oral contraceptives use was absent. On physical examination, superficial veins were prominent, and tens of painless masses were palpable in the right breast. The masses were tender, round or oval, smooth, well-circumscribed, mobile, and varied in size from 1~15 cm. There was no discharge from the nipple, and lymphadenopathy of the axillary, supraclavicular or subclavicular was absent.

Bilateral breast imaging was performed with ultrasonography (**Figure 2A**), mammography (**Figure 2B**) and MRI (see [Supplementary Files 1, 2](#)). The ultrasonic images revealed tens of hypo-echoic, well-circumscribed lesions in the right breast, with the largest one measuring over 10 cm. Consistent with previous reports, the diagnostic value of mammography in juvenile fibroadenomas is limited due to the high breast density as well as the extremely low risk of malignancy [8, 10, 11]. Multiple masses with typical benign features were identified through breast MRI, and no significant lesion was observed in the left breast. Routine hematological, biochemical and hormonal examinations were within normal limits.

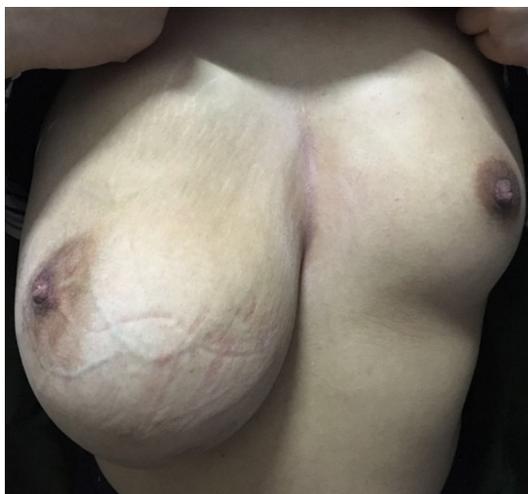


Figure 1. Preoperative photograph of a 17 years old patient with significant asymmetry breasts and multiple masses in the right breast.

Given the rapid tumor growth and significant breast size asymmetry, all the 12 tumors were surgically removed through a periareolar incision (**Figure 3A**). The largest excised mass measured 155*150*25 mm, while the smallest one measured 12*10*10 mm (**Figure 3B**). The final histopathological diagnosis of multiple and giant juvenile fibroadenomas was confirmed (**Figure 3C**).

Discussion

Clinically, cases of juvenile multiple giant fibroadenomas remain rare. We searched the PubMed database with term “breast fibroadenoma” in combination with the terms “giant”, “multiple” and “juvenile”. Less than 30 literatures were retrieved, among which were mostly case report papers, and cases involving more than ten lumps were extremely rare. We present another rare case involving a 17-year-old girl with unilateral breast multiple giant fibroadenomas of more than ten masses. We performed a relative minimal invasive surgery to remove all the lesions through one periareolar incision less than 5 cm. Reconstructive surgery was not performed due to the disagreement of the patient’s family. At 12 months after surgery, the patient showed no signs of relapse and was satisfied with cosmetic outcome. For the rarity of the disease, there exist no expert consensus or guideline to guide clinical practice. We therefore reviewed associated literatures to provide insights and experiences for better clinical management.

Etiology

The exact etiology of fibroadenoma is unknown. Since fibroadenoma can increase in size during pregnancy [12] or with estrogen therapy, and usually regress after menopause. It is widely accepted that estrogen play a key role in its growth and development [13-15]. As progesterone oppose the estrogen effects on the breast epithelial cells, the unbalanced ratio between estrogen and progesterone may be one contributing factor [16, 17].

Risk factors such as family history, the age of menarche [18], the age of menopause, oral contraceptives use [19-21], black population [22], prior history of benign breast disease and body mass index [23] may involve the development of fibroadenomas.

Some fibroadenomas are also related to rare diseases or syndromes such as Beckwith-Wiedemann syndrome [24-26], Maffucci syndrome [27], Cotard’s Syndrome [28], Carney’s syndrome [29] and Cowden syndrome [30].

Classification of fibroadenomas

There is no consensus regarding the classification of breast fibroadenomas. Based upon clinical or histologic characteristics, different subtypes were defined including giant fibroadenoma, juvenile fibroadenoma, complex fibroadenoma, intracanalicular or pericanalicular fibroadenoma.

1) Giant fibroadenoma generally refer to fibroadenoma that greater than 5 cm or 500 grams, or replaces at least 80% of the breast. 2) Fibroadenoma in adolescents between the ages of 10 and 18 years is common classified as juvenile fibroadenoma [31, 32]. Histologically, it has more cellular stroma than a typical fibroadenoma [6]. 3) Fibroadenomas with histologic characteristics including cysts (≥ 3 mm), sclerosing adenosis, epithelial calcifications, or papillary apocrine metaplasia are defined as complex fibroadenomas [33, 34]. 4) According to the arrangement of the stroma relative to the epithelial component, these neoplasms had once been classified into two types: intracanalicular and pericanalicular [35]. However, many fibroadenomas show a mixed pattern and this classification appears to have little clinical significance.

Multiple and giant juvenile FA

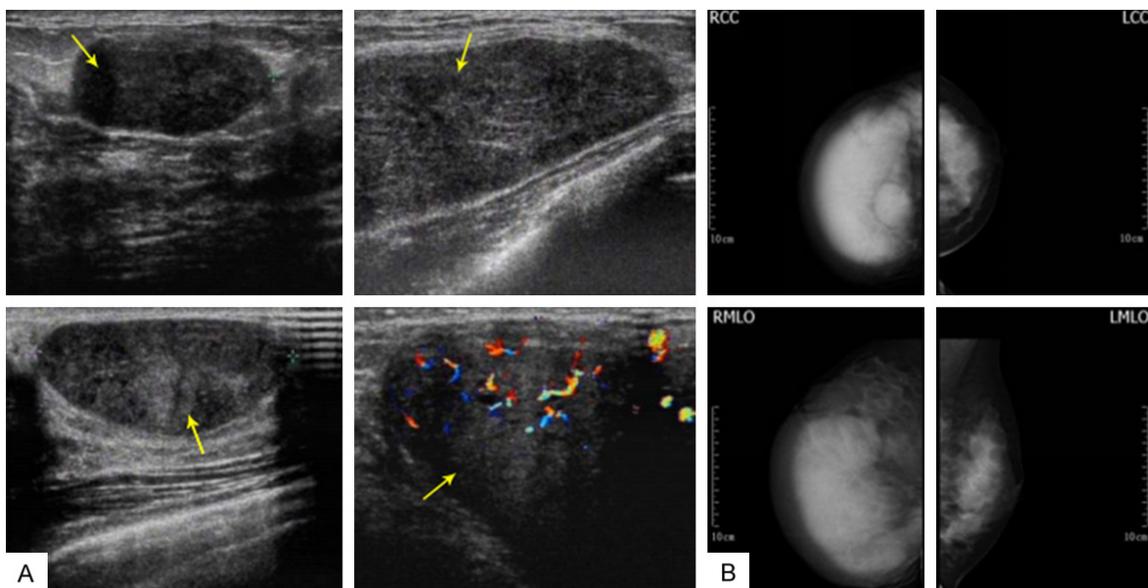


Figure 2. Preoperative breast imaging of (A) ultrasonography and (B) mammography. The hypo-echoic, well-circumscribed lesions were indicated with arrows.

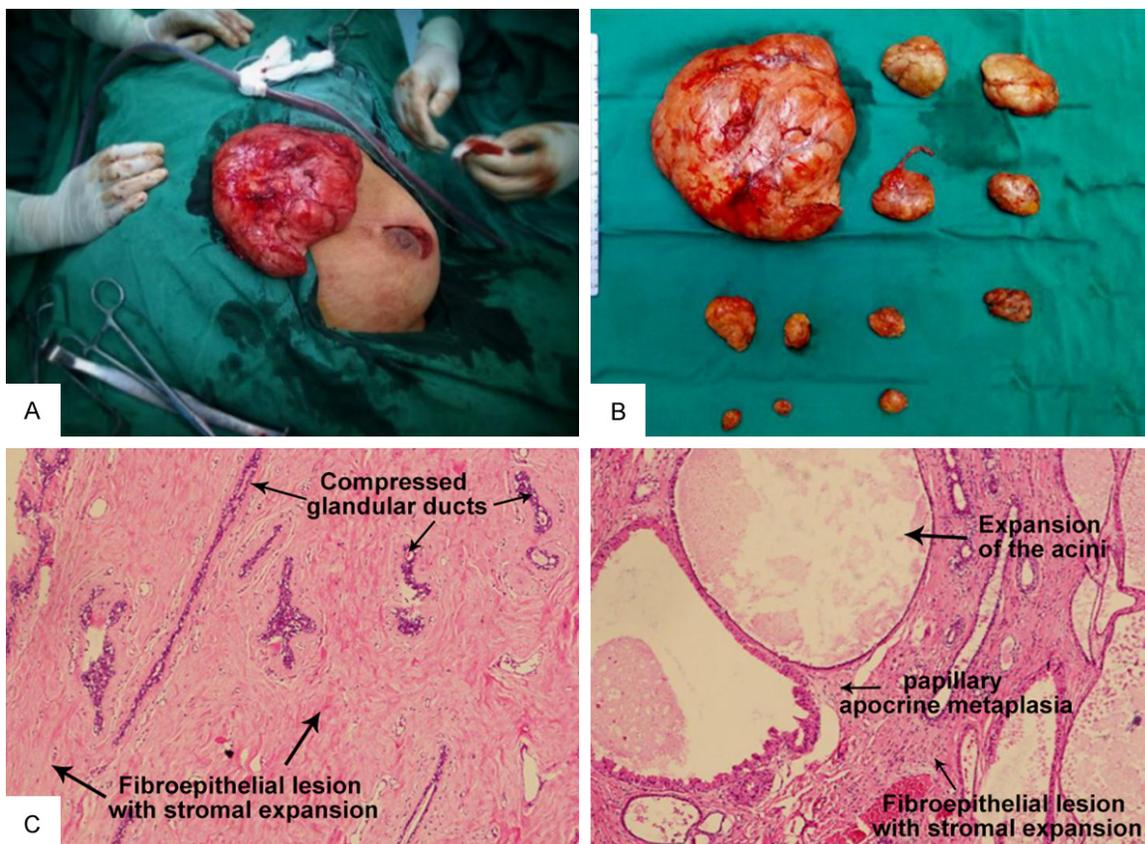


Figure 3. A. The 12 fibroadenomas were surgically removed through one periareolar incision. B. The largest tumor measured 155*150*25 mm. C. The diagnosis of fibroadenomas was confirmed histopathologically.

In addition to be classified as benign breast diseases, fibroadenomas can also be considered

as aberrations of breast development [16, 36]. Dent once reported that some fibroadenomas

Multiple and giant juvenile FA

might disappear spontaneously in women younger than the age of 20 [37, 38]. Nevertheless, giant or multiple fibroadenomas should be considered as diseases rather than the aberration of normal lobule development [16]. Although several non-surgical managements are available for some specific patients [39], surgical interventions should be considered for the following indications [39-41]: mass > 5 cm; a rapidly enlarging mass; mass that causes the patient pain, discomfort, or deformity; adolescent patients or their families who were extremely anxious.

A differential diagnosis from phyllodes tumor

The distinction between phyllodes tumor and fibroadenomas is important due to overlapping features and different management. The key in the treatment of phyllodes tumors, including benign, borderline, and malignant subtypes, is surgical excision with tumor-free margins of 1 cm or greater and in some cases may require radiation therapy [42, 43]. For Lumpectomy aimed to remove fibroadenomas, such tumor-free margins have not been emphasized.

The distinction of the two was mainly made in pathological level. However, the use of core needle biopsy to make the definite diagnosis preoperatively is challenging due to overlapping histological features. A repeated core needle biopsy is also not helpful if the first biopsy is not definitive [44]. No individual feature is completely specific for fibroadenoma or phyllodes tumor, and the more features that are present, the more likely is the distinction be made. The following features favor the diagnosis of phyllodes tumors [6]: increased stromal cellularity, stromal overgrowth, stromal mitoses, stromal atypia, stromal fragmentation and stromal heterogeneity. As the risk of malignancy is negligible for women under 20 years [16], to avoid over-treatment, the WHO recommends a diagnosis of fibroadenoma rather than benign phyllodes tumor when there is histological ambiguity [45].

The differential diagnosis of fibroadenomas should also include a circumscribed fibrocystic mass, lipoma, hamartoma, unilateral breast hypertrophy, and various carcinomas [4, 10].

Recurrence

As the scarcity of follow-up data, the recurrence rate of multiple, giant or juvenile fibroadeno-

mas remains inconclusive. For single giant fibroadenoma, the chance of recurrence was described as common fibroadenomas [8]. A higher incidence of local recurrence was noticed in patients with multiple fibroadenomas, especially in the non-white population [46, 47]. The recurrence of fibroadenomas mainly appears before the age of thirty, and then declined with the increasing age [48]. To avoid unnecessary mastectomy, it is worth noted that de novo tumors should be distinguished from the true recurrences [49].

Risk of developing breast cancer

Benign breast diseases are usually subdivided into nonproliferative lesions, proliferative disease without atypia (PDWA), and atypical hyperplasias (AH) [50]. Fibroadenomas are now considered proliferative breast lesions [51]. Women with simple fibroadenomas have about 1.5~3.2 times the risk of developing breast cancer compared with women in the general population [20, 33, 52]. Controversy surrounds breast cancer risk in patients with complex fibroadenoma [33]. Dupont concluded that the relative risk increased to 3.10 among complex fibroadenoma patients, and remained elevated for decades. However, it was reported by Aziza Nassar that complex fibroadenoma does not confer the increased risk of breast cancer beyond that of other established histologic features such as PDWA and AH. Given the lack of literature report, the subsequent breast cancer risk of multiple or juvenile fibroadenomas is not known; however, they seem rare events from clinical experience [53].

Notably, malignant lesions can arise within multiple fibroadenomas simultaneously [54-56]. Thus, core needle biopsy or surgical intervention may be considered if there is doubt about the diagnosis, especially in elderly patients.

Conclusion

Fibroadenomas are the most common type of benign breast tumors. The exact etiology of fibroadenoma is unknown, but estrogen may be one of the leading contributing factors. Giant or multiple fibroadenomas should be considered as diseases rather than the aberration of normal lobule development. The distinction between phyllodes tumor and fibroadenomas is important due to overlapping features and different management. The local recurrence inci-

Multiple and giant juvenile FA

dence seems to be higher than common fibroadenomas. And the subsequent breast cancer risk of fibroadenoma is slightly higher than the general population, but still rare events from clinical experience. Surgical excision is recommended for patients with a significant psychological burden, physical discomfort or unclear diagnosis. Priority should be put on cosmesis as well as retention of function when juvenile fibroadenomas were involved.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Li-Bo Luo, Department of Breast and Thyroid Surgery, The First People's Hospital of Zunyi, Huichuan District, Zunyi, Guizhou, China. Tel: +86-18984958640; E-mail: 767219705@qq.com

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Multiple and giant juvenile FA

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