

SHORT REPORT

OPEN ACCESS

Full open access to this and thousands of other papers at <http://www.la-press.com>.

Unusual Presentation of Multiple Fibroadenomas in Bilateral Breasts and Axillary Accessory Breast

Rong-rong Zhang¹, Scott Bevan², Ping Sun¹, Jim Z Lu³ and Yan Peng²

¹Department of Pathology, No. 2 People's Hospital, Wuxi, Jiangsu Province, China. ²Department of Pathology, University of Texas Southwestern Medical Center, Dallas, TX, USA. ³GoPath Diagnostic Laboratories, Changzhou, Jiangsu Province, China. Corresponding author email: yan.peng@utsouthwestern.edu

Abstract: We report an extremely rare case with a total of 50 fibroadenomas simultaneously presented in bilateral breasts and left axillary accessory breast, up to 8 cm in size, in a 20 year-old Chinese woman. The histopathologic and immunophenotypic features of the fibroadenomas are described and possible underlying pathogenesis is discussed. To our knowledge, this is the first case with such a large number of bilateral multiple breast fibroadenomas in a young female reported in the literature.

Keywords: multiple fibroadenoma, bilateral breasts, axillary accessory breast

Breast Cancer: Basic and Clinical Research 2012;6:95–99

doi: [10.4137/BCBCR.S9512](https://doi.org/10.4137/BCBCR.S9512)

This article is available from <http://www.la-press.com>.

© the author(s), publisher and licensee Libertas Academica Ltd.

This is an open access article. Unrestricted non-commercial use is permitted provided the original work is properly cited.

The patient was a first year college student and had never taken any oral contraceptives or other medications. Based on her knowledge, she had not been exposed to any chemicals or harmful materials. She underwent an excisional biopsy for a fibroadenoma of the left breast 5 years ago. Two years later, she was present with numerous mass lesions in bilateral breasts and the left axilla. Physical examination revealed two grossly enlarged breasts with symmetrical nipples and no retraction or hemorrhage. The overlying skin demonstrated no peau d'orange appearance. Within the breasts, there were many palpable masses throughout all quadrants, ranging from less than 1.0 to 6.0 cm in size. The masses were well circumscribed and mobile, and had a firm, rubbery texture. The left axillary mass measured approximately 8.0 cm and compressed the superficial blood vessels of the overlying skin (Fig. 1). Ultrasonography showed solid masses in bilateral breasts that had a distinct, clear envelope like appearance and relatively uniform echoes. Color flow imaging showed short strip-shaped color flow signals that were visible in the breast masses (Fig. 2). Routine laboratory testing showed the levels of sexual hormones were within the normal ranges. The patient did not have any mass lesions elsewhere outside of her breasts and left axilla. There was no family history of breast lesions including fibroadenoma. The patient underwent excisions of bilateral breasts and left axillary masses followed by bilateral mammoplasty.

Gross Findings

The masses were round or elliptical and had intact thin fibrous capsules on their surfaces. The cut sections of the masses showed grayish-white, with rubbery texture and a slightly lobular, bulging architecture. There were 29 masses identified in the left breast ranging from $1.0 \times 1.0 \times 0.5$ cm to $5.5 \times 4.0 \times 4.0$ cm in size, 20 masses in the right breast ranging from $1.0 \times 1.0 \times 1.0$ cm to $6.0 \times 5.0 \times 4.0$ cm, and a single left axillary mass measuring $8.0 \times 6.5 \times 5.0$ cm (Fig. 3).

Microscopic Examination

The masses were composed of a biphasic growth pattern with epithelial and stromal proliferation. The loose fibrous stroma compressed surrounding benign ducts with an intracanalicular growth pattern. The ductal epithelium was composed of two layers of cells, an inner cuboidal or columnar epithelium and an outer myoepithelial layer in which some of the cells showed clear cytoplasm. The ducts showed focal hyperplastic changes. No epithelial and stromal cell atypia or malignancy was identified. Histomorphological features of the masses were diagnostic of fibroadenoma (Fig. 4). Immunohistochemical stains for estrogen receptor (ER) and progesterone receptor (PR) were diffusely positive in the tumor cells.

Discussion

Breast fibroadenoma, a benign biphasic tumor, occurs most frequently in women of child-bearing age, espe-



Figure 1. Enlarged bilateral breasts with symmetrical nipples, and normal skin appearance, and a large left axillary mass.

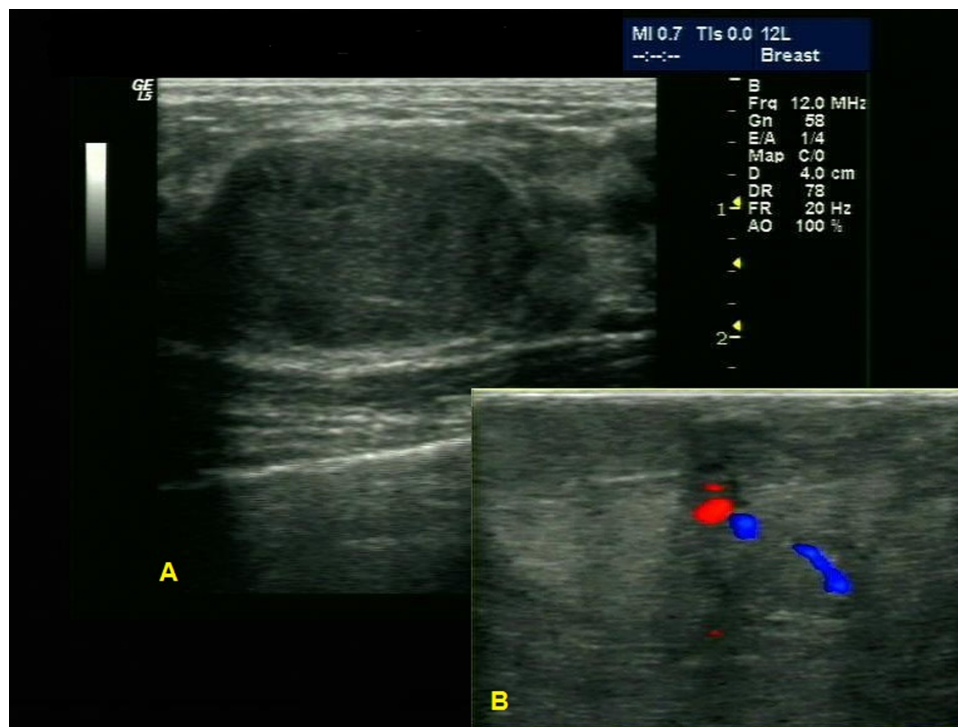


Figure 2. (A) Ultrasonography shows solid masses in the left breast with a sharp demarcation from the background breast tissue and relatively uniform echoes. (B) Color Flow Imaging shows that short strip-shaped color flow signals are visible in the breast masses.

cially those under 30 years. Fibroadenoma is usually a slowly growing lesion with size up to 3 cm.¹ Most fibroadenomas are present as a single mass, however, the presence of multiple fibroadenomas can be seen in 15% to 20% of the patients.¹ Majority of fibroadenomas do not recur after being completely excised, but in adolescent patients, one or multiple new fibroadenomas can occur in areas adjacent to the prior surgical excision site of the same breast or even in the contralateral breast. It has been reported that the average number of masses in cases of multiple fibroadenomas was 3 to 4 in a single breast.^{2,3} The occurrence of more than five fibroadenomas in an individual patient is much less common. Unlike women with a single fibroadenoma, most of the patients with multiple fibroadenomas have a strong family history of these tumors.²

The etiology of multiple breast fibroadenomas has not yet been clearly established. A possible connection between multiple fibroadenomas and oral contraceptives was proposed but has not been well documented on the literature yet.⁴ In addition, other possibilities of the pathogenesis may be related to imbalance of in vivo estrogen level, hypersensitivity of local breast tissue to estrogen, dietary factors,

or inherited predisposition. Another possible explanation was that the physiologic level of estrogen in such patients did not increase, but instead, the number of estrogen receptor increased.² The increased sensitivity to estrogen may subsequently lead to mammary gland hyperplasia and even the development of carcinoma. A previous study of a large cohort of women with fibroadenoma revealed that the overall prevalence of atypical epithelial hyperplasia within fibroadenomas was 0.81% and only around 7% of women with atypia developed invasive carcinoma on follow-up.⁵ An additional large case series of women with fibroadenoma showed carcinoma in situ (ductal and/or lobular) was found in 2% of these patients.⁶ Therefore, patients with fibroadenoma may have a slightly increased risk of developing breast cancer.

The pathogenesis of formation of the numerous breast fibroadenomas in this patient is unknown. Presumably constant stimulation of estrogen to the breasts and/or increased sensitivity of breast tissue to estrogen during adolescence may cause the fibroadenomas to increase dramatically in size, up to 8 cm, and in quantity to a number of 50, which has not been reported on the literature.

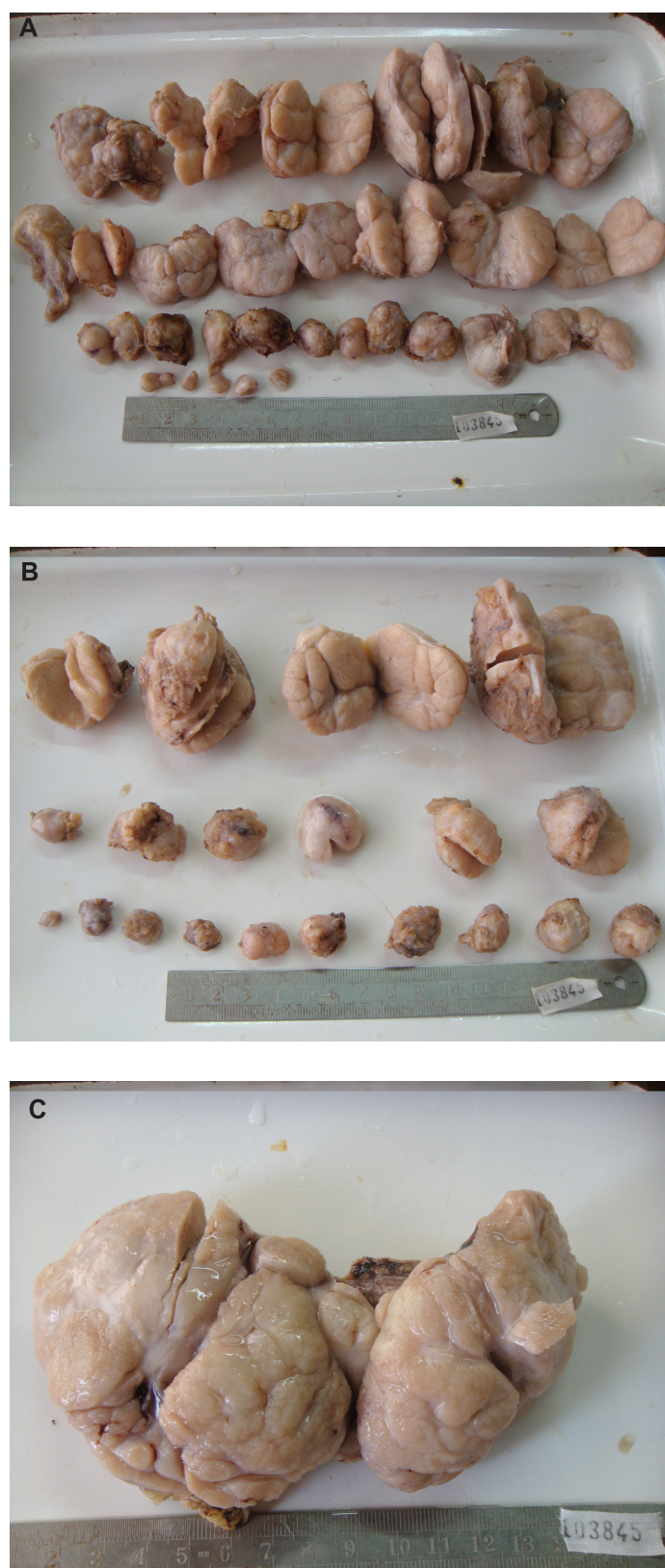


Figure 3. The fibroadenomas have a grayish-white and lobulated cut-surface and hard texture on gross examination. (A) Left breast masses with a total number of 29. (B) Right breast masses with a total number of 20. (C) Single large left axillary mass.

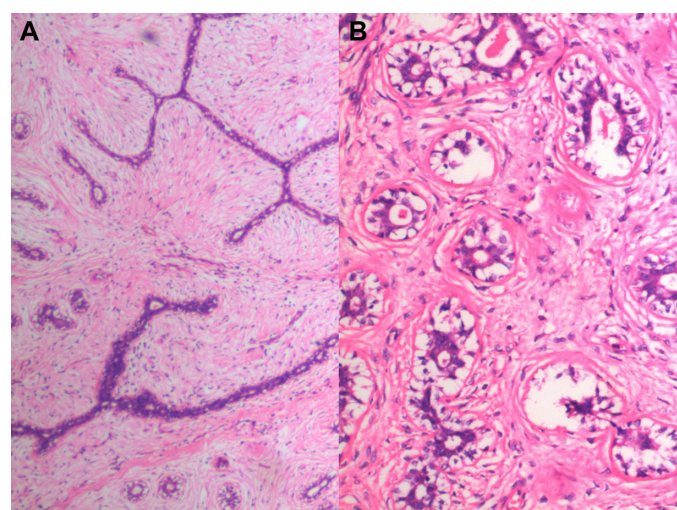


Figure 4. Representative histologic sections from the fibroadenomas. (A) Biphasic growth proliferation composed of benign breast ducts and stroma (HEx40). (B) Higher magnification view showing the benign ducts with 2 layers: inner luminal epithelium and outer layer of myoepithelial cells with clear cytoplasm (HEx200).

Some authors defined fibroadenomas larger than 5 cm as giant fibroadenomas.¹ However, this definition is not universally accepted. The postoperative recurrence of fibroadenomas in this patient perhaps was due to the constant presence of the predisposing factors and should not be considered a relapse. Based on microscopic evaluation of this case, there was no evidence of atypical epithelial hyperplasia, carcinoma in situ, or invasive carcinoma in these fibroadenomas.

There is paucity on the literature on multiple fibroadenomas in bilateral breasts and axillary accessory breast. We report this case with an extremely unusual presentation of multiple fibroadenomas in hoping to expand the literature and to provide insight to aetiology of multiple fibroadenoma formation, its natural history, and advice on management.

Author Contributions

Conceived and designed the experiments: YP, RZ, PS, JZL. Analysed the data: YP, RZ. Wrote the first draft of the manuscript: YP, RZ. Contributed to the writing of the manuscript: YP, RZ, SB. Agree with manuscript results and conclusions: all authors. Jointly developed the structure and arguments for the paper: all authors. Made critical revisions and approved final version: YP. All authors reviewed and approved of the final manuscript.



Disclosures and Ethics

As a requirement of publication author(s) have provided to the publisher signed confirmation of compliance with legal and ethical obligations including but not limited to the following: authorship and contributorship, conflicts of interest, privacy and confidentiality and (where applicable) protection of human and animal research subjects. The authors have read and confirmed their agreement with the ICMJE authorship and conflict of interest criteria. The authors have also confirmed that this article is unique and not under consideration or published in any other publication, and that they have permission from rights holders to reproduce any copyrighted material. Any disclosures are made in this section. The external blind peer reviewers report no conflicts of interest.

References

1. Bellocq JP, Magro G. Fibroepithelial tumors. In: Tavassoli F, Devilee P, editors. *World Health Organization Classification of Tumours: Pathology and Genetics: Tumours of the breast and female genital organs*. Lyon: IARC Press; 2003:99–100.
2. Wiegenstein L, Tank R, Gould VE. Multiple breast fibroadenomas in women on oral contraceptives. *N Engl J Med*. 1971;284:676.
3. Amshel CE, Sibley E. Multiple unilateral fibroadenomas. *Breast J*. 2001;7(3):189–91.
4. Williamson ME, Lyons K, Hughes LE. Multiple fibroadenomas of the breast: a problem of uncertain incidence and management. *Ann R Coll Surg Engl*. 1993;75(3):161–3.
5. Carter BA, Page DL, Schuyler P, Parl FF, et al. No elevation in long-term breast carcinoma risk for women with fibroadenomas that contain atypical hyperplasia. *Cancer*. 2001;92:30–6.
6. Kuijper A, Mommers EC, Van der Wall E, Van Diest PJ. Histopathology of fibroadenoma of the breast. *Am J Clin Pathol*. 2001;115:736–42.