Bilateral Multiple Phyllodes Tumors of the Breast, "Giant" on one Side: Report of a Case

Chi-Wen Tu, Ching-Chung Chiang, Chen-Hsien Su

The phyllodes tumor is a rare fibroepithelial breast neoplasm, which mostly presents as a rapidly growing but clinically benign breast lump. The size of such a tumor is variable, ranging from 1 to 41 cm. We report a 38-year-old female patient with synchronous bilateral multifocal phyllodes tumors, with a giant left breast tumor so large (28 × 23.5 × 18 cm) as to cause obvious asymmetry of breasts. The patient was successfully treated with bilated mastectomy and the patient remained free of disease during a two-year follow-up. The literature on the clinicopathological features and management of this rare tumor is also reviewed.

Key words: giant phyllodes tumor, synchronous, breast

The phyllodes tumor is a rare fibroepithelial lesion that accounts for less than 1% of all breast neoplasms.[1] The original term cystosarcoma phyllodes was coined by Johannes Muller in 1838 to describe the gross appearance of such a "cystic, fleshy, and leaf-like tumor of the breast." [2] However, only occasionally does it has cystic components, and it is not a true sarcoma in terms of either cellular origin or biologic behavior. Thus, cystosarcoma phyllodes is now felt to be a misnomer.[3] Since the appearance of the original description, more than 60 synonyms have been proposed; however, the World Health Organization currently regards phyllodes tumor as the most appropriate name.[4] Most phyllodes tumors present as rapidly growing but clinically benign breast lumps. The size of these tumors is variable, ranging from 1 to 41 cm (average 7 cm).[5] Herein, we report the case of a 38-year-old female patient with a giant phyllodes tumor producing marked distortion of the breast contour.

Case Report

A 38-year-old woman presented with a palpable left breast mass that had first been noticed six months previously. The mass had grown rapidly during this period of time, eventually resulting in obvious asymmetry of both breasts, leading to her subsequent attendance at our clinics because of embarrassment with physical appearance. On physical examination, one painless giant tumor (25 × 20 cm) was found in the left breast (Fig 1). The mass was movable and firm in consistency. Superficially, dilated veins and blue discoloration were visible. The contour of the left nipple-areolar complex was distorted. Besides, two other well-demarcated movable masses (approximately 3 × 4 cm and 5 × 5 cm) were palpable in the upper inner quadrant and lower inner quadrant of the right breast, respectively (Fig 1). No obvious lymphadenopathy was detectable in the axillary region on either side. On ultrasound examination, the left breast mass showed a smooth contour with homogeneous low ehcogenicity. The right breast lumps had a well-demarcated margin with homogeneous echogenicity (Fig 2). Mammography of the left breast could not be performed because of its huge size. On post-contrast computed tomography (CT), the left breast was polylobulated with tumor enhancement (Fig 3). Subsequently, two isolated lobulated and enhanced tumors were detected in the right breast. The patient underwent left total mastectomy because of the significant asymmetry caused by the neoplasm in the left

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breast, with intra-operative frozen section confirming the diagnosis of phyllodes tumor. Further flap reconstruction was unnecessary, and primary closure of the skin flap and simultaneous simple mastectomy for the two lumps in the right breast were performed.

Histopathological examination revealed a giant left breast tumor (grossly 28 × 23.5 × 18 cm) of gray-white meaty consistency, and firm multinodular fibrogelatinous tissues with pushing borders. Microscopically, the tumor consisted of intralobular connective tissues enclosing epithelial lined cystic space, and the appearance was consistent with phyllodes tumor. The stromal cellular atypia was mild and the mitosis rate less than 5 per 10 high power fields. There was no stromal overgrowth and, based on the criteria proposed by Azzopardi[6] and Salvadori et al, the histological type was benign. The other two masses excised from the right breast (5 × 4 × 3 and 6.5 × 5.5 × 3.0 cm) were both subsequently diagnosed as benign phyllodes tumors based on the microscopic findings.

The postoperative course was uneventful, without any skin margin necrosis of the left breast wound. The patient remained free of disease during a two-year follow-up.

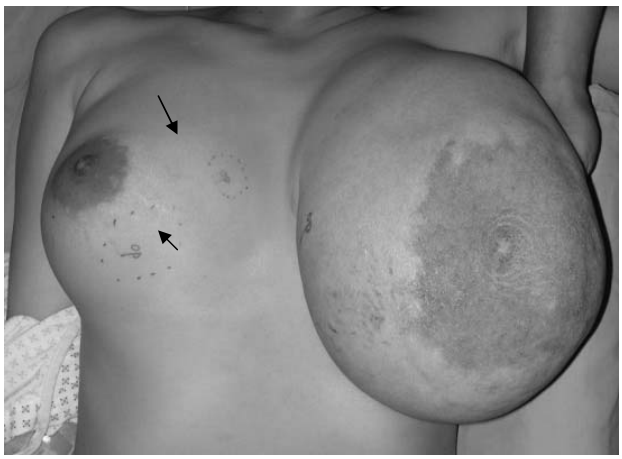

Fig 1. Gross appearance and obvious asymmetry of breasts. Arrows indicate the location of two right breast tumors.

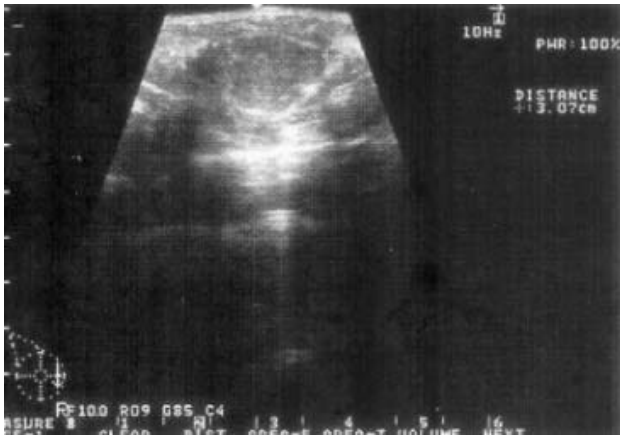

Fig 2. The right breast lump had a well-demarcated margin with homoheneous echogenicity on ultrasound examination.

Discussion

Phyllodes tumors are uncommon fibroepithelial breast tumors with a diverse range of biological behavior. At one extreme, malignant phyllodes tumors have a propensity for rapid growth and metastatic spread if not adequately treated. By contrast, however, benign phyllodes tumors are similar to benign fibroadenomas on clinical, radiological and cytological examination and can be successfully treated using local surgery. Thus, the clinical presentation of phyllodes tumor varies widely with a broad range of pathological behavior, and they should be regarded as a spectrum of fibroepithelial neoplasms rather than a single disease entity.

In the English literature, phyllodes tumors are reported over a wide age range (9~93 years),[7] with the median age of 45 years. Pyllodes tumor are rare in adolescence, however, and are more common in the Asian population;[8] most present as smooth, multinodular and

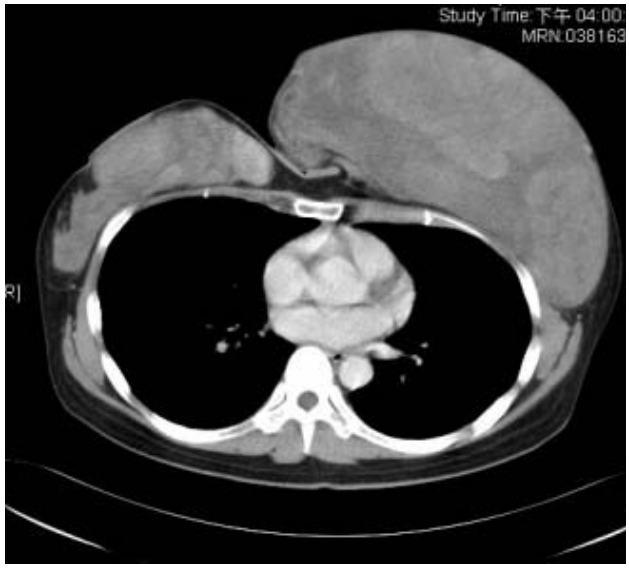

Fig 3. The left breast is polylobulated on post-contrast CT.

rapidly growing breast lumps. The size of phyllodes tumors also varies greatly, with a maximum diameter of up to 20 cm typical reported. Given today's earlier breast screening and generally improved detection of breast lesions, most tumors are smaller compared to a decade ago. In the present case, the extreme size resulted from the delay in seeking surgical intervention. Phyllodes tumors are found more commonly in the upper outer quadrant, with an equal propensity for occurrence in either breast.[9] Synchronous bilateral multifocal phyllodes tumors are rare, however, and only seen in a limited number of case reports.[10]

Mammographically, phylloees tumors are well defined with a smooth and occasionally lobulated border. A radiolucent “halo” may be seen around the lesion, due to compression of the surrounding breast stroma.[11] Coarse micorcalcification has been reported within both fibroadenoma and phyllodes tumors, but malignant clustering microcalcification is rare.[11] No mammographic indicators have been identified that allow one to distinguish fibroadenomas from benign or malignant phyllodes tumors.[11] On ultrasound examination, phyllodes tumors often show smooth contours with low level homogeneous internal echoes and the absence of posterior ascoustic enhancement.[12] As with mammography, no reliable ultrasonic indicators have been identified that differentiate between benign and malignant lesions.[13] Although magnetic resonance imaging (MRI) may provide more accurate definition of the true extent of disease in the breast prior to surgery, few data support the routine use of MRI in imaging phyllodes tumors.[14] MRI may be most helpful when mastectomy is being considered to achieve adequate margins. As both phyllodes tumors and fibroadenomas belong to a spectrum of fibroepithelial lesions, accurate cytological diagnosis of phyllodes tumors by fine-needle biopsy aspiration (FNA) and core biopsy can be difficult and most cytologic features fail to distinguish fibroadenoma and phyllodes tumors.[15] The huge left breast mass in this case challenged us to make an accurate pre-operative diagnosis by imaging studies or biopsy, and the intra-operative frozen section served to differentiated between phyllodes tumors and fibroadenoma or rarely coexisting carcinoma within the sarcoma component.

Microscopically, phyllodes tumors are characterized by epithelial lined cystic spaces into which a hypercellular stroma projects. The presence of both epithelial and stromal elements are necessary to confirm the diagnosis. The stromal elements are a key component for differentiation of phyllodes tumor from fibroadenoma, and distinguishing between benign and malignant phyllodes variants. Numerous studies have attempted to determine the histological features useful for predicting clinical behavior. The criteria proposed by Azzopardi[6] and Salvadori et al, for classification of histological type are widely accepted by most pathologists. The four classification features are based on margin, stromal cellularity, cellular atypia and the number of mitoses per 10 high power fields, with the resultant differentiation delineating benign, borderline or malignant types. In our patient, the bilateral multifocal tumors all met the classification criteria for benign phyllodes tumor.

The core principle of local therapy for phyllodes tumors, whether benign or malignant, is wide excision (with a margin of at least 1 cm of normal breast tissue) particular for borderline and malignant variants.[16] Aa malignant phyllodes tumors spread hematogeneously and the proportion of lymph node metastasis is approximately 10%, routine axillary lymph node dissection is not recommended.[5] Radical surgery offered no survival advantage[17] and more conservative surgical approaches have been adopted. Total mastectomy was unavoidably in our patient because of the near-complete neoplastic involvement of the left breast.

The role of adjuvant breast radiotherapy is unclear as it has not been the subject of large randomized controlled trials.[17] In a study of eight patients from the MD Anderson Cancer Center who received adjuvant RT for positive or close surgical margins, tumor size > 10 cm or recurrent disease, there were no local or distant failures at a median follow-up of 3 years.[18] Some authors have suggested that postoperative RT be considered for patients with histologically malignant phyllodes tumors.[19] There is no consensus on this issue as yet, however, and adjuvant chemotherapy may be considered for large and malignant phyllodes tumors, although its use remains controversial.

The prognosis for phyllodes tumors is favorable, with reported 5-year disease-free survival rates of 96%, 74% and 66% after surgery for benign, borderline and malignant phyllodes tumors, respectively.[5] Based on pooled cancer registry data, Vorherr et al, estimated an overall 5-year survival rate of 80% for malignanat phyllodes tumors.[20] Most series have been reported low local recurrence rates with tumor less than 2 cm in diameter.[21] However, no correlation between tumor size and the risk of local recurrence has been demonstrated.[21] The size of the tumor in relation to the breast appears important as this usually determines the extent of surgery and the resulting specimen resection margins. Surgical margins are the best predictor of local recurrence from phyllodes tumors; wide margin (> 1 cm) are associated with the lowest risk of recurrence.[16]

In summary, we report a case of synchronous bilateral multifoci phyllodes tumors in a middle-aged

female patient, with the larger tumor in the left breast resulting in obvious asymmetry of both breasts. A diagnosis of a phyllodes tumor should be considered in all women who present with a rapidly growing but clinically benign breast lump, especially in those over the age of 35 years.

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巨大的雙側乳房多發性葉狀肉瘤：病例報告

涂啟文　江慶鐘　蘇振賢

葉狀肉瘤是罕見的乳房纖維上皮腫瘤，它的發生率佔乳房腫瘤不到百分之一。大部分的葉狀肉瘤是以生長快速但臨床良性表徵的無痛性腫塊來作為臨床表現。葉狀肉瘤的大小差異很大，文獻上從1公分至40公分都有被報導。本文報告一位38歲的女性病患，雙側乳房同時出現多發性的葉狀肉瘤，其中左側的葉狀肉瘤相當巨大，因而造成雙側乳房外觀明顯的不對稱及左側乳房結構的破壞。本案例接受左側全乳房切除及右側乳房腫塊切除手術後，於門診追蹤2年內並未發現腫瘤復發或轉移。本文同時回顧文獻上有關乳房葉狀肉瘤的臨床病理特徵及治療方式。

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