Phyllodes Tumor: Correlation of imaging and histopathologic features

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Learning objectives

To illustrate the imaging features of phyllodes tumor and correlate them with pathologic findings.

To discuss the difficulties of radiologic and histopathologic diagnosis of phyllodes tumor.

Background

Phyllodes tumor (formerly known as cystosarcoma phyllodes) is a rare tumor of the breast, that accounts for less than 1% of all solid breast lesions (1).

It is classified as a fibroepithelial tumor of breast (World Health Organization histologic classification-WHO), belonging to the same group as other pathologic entities such as fibroadenoma, periductal stromal sarcoma and mammary hamartoma.

It commonly occurs in women in the 4th decade of life, with an earlier onset in Asian countries (average 25-30 years) (2). Although only 5% of phyllodes tumor occur in girls under 20 years of age, it is the predominant breast neoplasm among adolescents. It has also been reported in men (2,3).

They are composed of proliferation of stromal and epithelial elements, developing from periductal stroma rather than intralobular stroma, resembling most of the time the harmless intracanicular fibroadenoma, although phyllodes tumor have a higher stromal cellularity (4). In addition, in contrast to fibroadenoma, phyllodes tumor can recur locally and has a metastatic potential. In other times, they resemble histologically pure stromal sarcomas. For these reasons they need to be distinguished and recognized.

Histologically they can be dived in benign (60%), borderline (20%) and malignant (20%), based on nature of tumor margins, growth of the connective tissue component, mitosis and stromal cellular atypia.

Phyllodes tumor usually appears as a rapidly enlarging, movable, painless lump. The mass may be 10 cm or more, being the average size about 5 cm. Tumors with diameters less than 1-2 cm are uncommon (5).

Haematogenous metastasis occur in 3-12% of cases (5), predominantly in lungs and bones (2).

Lymphatic involvement is uncommon.

The clinical course in unpredictable regardless of histological grade (1).
Current histologic classification and radiologic features have difficulty predicting clinical behaviour, including the development of local recurrences, distant metastasis, and overall survival.

Although recurrences are common in borderline and malignant phyllodes tumor, local recurrence and distant metastasis occur rarely with benign phyllodes tumor (6).

Recurrences tend to be the same grade, however in 25% of patients upgrading to the next category was observed (4).

Local recurrence rate depends on the width of excision margin, therefore a complete surgical excision with wide margins (1 cm) is necessary for all histologic types of tumors (1).

However many phyllodes tumors are misdiagnosed as fibroadenomas or benign breast tumors in both clinical and histological manifestations, being often treated with narrow margins at the initial intervention. Consequently adjuvant chemotherapy and/or radiotherapy in addition to surgery was proposed, although it has not yet been established for use in malignant and recurrent phyllodes tumor (6).

**Imaging findings OR Procedure details**

On mammography, phyllodes tumor usually manifests as a dense, round, oval or polylobulated non calcified mass with smooth borders.

Tumor size is variable, ranging from small tumors to large masses, occupying practically the entire breast.

The mammographic imaging findings overlap significantly between phyllodes tumor and benign lesions such as fibroadenoma.

Similarly, fibroadenoma is an oval or lobular equal density mass with smooth margins. By contrast, fibroadenoma can appear with peripheral calcifications ("popcorn calcifications") and with time it can be totally replaced looking like a "breast rock".

However, if a well circumscribed mass is larger than 6-8 cm in diameter is seen at mammography, or if a mass shows a rapid increase of size on serial mammograms it should arouse suspicion of a phyllodes tumor (5).

In adolescents giant juvenile fibroadenoma is difficult to distinguish from phyllodes tumor, since both have identical mammographic appearance and both may appear as a rapidly enlarging mass (5).
On ultrasound, the appearance of phyllodes tumor may be similar to that of fibroadenoma.

Like fibroadenoma it can be a smoothly marginated, well-defined, ovoid or lobulated hypoechoic homogenous mass.

However, phyllodes tumor often appears with an heterogeneous ecotexture, with irregular walls, fluid-filled spaces producing posterior acoustic enhancement and septations. These findings are characteristic of phyllodes tumor and rarely seen in fibroadenoma (3).

Mammography and ultrasonography are limited in differentiating phyllodes tumor from benign lesions and cannot predict its histologic grade (5,3).

Whether MR can differentiate fibroadenoma and phyllodes tumor remains unclear. Wurdinger et al., reported that phyllodes tumor and fibroadenoma cannot be precisely differentiated on breast MR (7).

There is limited information on the possible correlation between MR features and histologic grades.

Yabuchi et al., conducted a retrospective study that evaluated MR imaging findings of 30 phyllodes tumors (19 benign; 6 borderline; 5 malignant) and compared them with histologic grade.

They reported that: Tumor signal intensity lower or equal to normal breast tissue signal intensity on T2 weighted images and low apparent diffusion coefficient (ADC), correlated significantly with histologic grade of phyllodes tumor, corresponding histologically to the unfavourable stromal hypercellularity. Cystic change with irregular wall correlated significantly with histologic grade of phyllodes tumor and high signal intensity on T1 weighted images was more frequent in the malignant and intermediate group, suggesting malignancy but did not correlate significantly with histologic grade. These characteristics corresponded histologically to necrosis and haemorrhagic infarction, respectively. Tumor size, cystic changes with smooth wall and time-signal intensity curve pattern did not correlate significantly with histologic grade of phyllodes tumor (8).

**Pathological findings**

Grossly, the most typical feature of phyllodes tumour is the clefts within a tan or grey whorled, elastic stroma.

Microscopically, these leaf-like structures are lined by a bilayer of epithelium and myoepithelium embedded within a cellular stroma.

The degree of stromal hypercellularity, cytological atypia, mitotic activity, stromal overgrowth and type of border (infiltrative vs. pushing) defines the histological
classification malignant, borderline and benign phyllodes tumours. Stromal hypercellularity and cytological atypia are mild in benign phyllodes tumours and increase in borderline and malignant phyllodes tumours.

An infiltrative border is typical of malignant phyllodes tumors. A pushing border occurs most frequently in benign phyllodes tumors. Borderline phyllodes tumors can have both.

Stromal overgrowth is defined by the absence of epithelial elements in a low-power field (x40) and is a characteristic of malignant phyllodes tumours. Mitotic activity is quantified per 10hpf (high-power fields, x400). Benign phyllodes tumours have less than 5 mitosis per 10 hpf, borderline tumors have between 5 and 9 mitosis per 10 hpf and malignant borderline tumors have more than 10 mitosis per 10hpf (10).

CASE 1

Malignant phyllodes tumor in a 68-year-old woman with a palpable lump in the upper outer quadrant of the left breast. The patient was submitted to left mastectomy. One year later died of recurrence and metastatic involvement to thoracic wall and lungs (figs. 1,2).

CASE 2

Borderline phyllodes tumor in a 62 year-old woman. For more than 10 years the patient had been followed for a left breast nodule, that months before coming to our Institute had rapidly enlarged. Meanwhile the patient had been treated by homeopathy without result (figs 3,4,5).

CASE 3

Relapsed borderline phyllodes tumor in a 25-year-old woman, who was submitted to tumorectomy 2 years before (figs 6,7,8,9).

CASE 4

Malignant phyllodes tumor in a 73-year old woman. The patient was being followed for a small nodule in the right upper external quadrant. Two years later mammograms show a dense, polylobulated, non calcified mass with smooth borders (figs 10,11,12,13,14).

CASE 5
Benign phyllodes tumor in a 50-year-old woman, which was previously misdiagnosed as fibroadenoma with fine needle biopsy. Surgical biopsy revealed a benign phyllodes tumor without free margins. The patient was reoperated (figs 15,16,17).

CASE 6

39 year old patient with surgical histologic diagnosis of borderline phyllodes tumor with focal areas of malignancy. Previously she had been submitted to fine needle biopsy which diagnosed benign/borderline phyllodes tumor (figs 18,19,20,21).

CASE 7

Borderline phyllodes tumor in a 62-year-old women who had been followed for several years for multiple fibroadenomas. In 2003, she had been submitted to surgical removal of a malignant phyllodes tumor and in 2006 to a surgical removal of a fibroadenoma. Eight years later, the patient comes to our Institute with a rapidly enlarging painless left breast lump (figs 22,23,24,25).

CASE 8

Benign phyllodes tumor in a 36-year-old woman (figs 26,27,28).

CASE 9

Benign phyllodes tumor in a 55-year-old woman, which was previously diagnosed by fine-needle biopsy as a fibroadenoma (figs 29,30,31).

CASE 10

Benign phyllodes tumor in a 60 year-old -woman.

Screening mammograms showed multiple small rounded nodules interpreted as fibroadenomas. Two years later, again in screening mammograms, one of these nodules enlarges. Microbiopsy reveals a benign phyllodes tumor (figs 32,33,34,35,36).
Fig. 1: CASE 1. Malignant phyllodes tumor. Craniocaudal mammogram shows a large, well-defined, lobulated, homogeneously dense mass. US images show a lobulated mass with heterogeneous ecotexture, with cystic changes and with irregular walls producing acoustic enhancement and septations.
Fig. 2: CASE 1. Malignant phyllodes tumor, high-power view. Stromal overgrowth with no evidence of epithelial elements. Stromal hypercellularity with brisk mitotic activity and moderate nuclear atypia (H&E, 400x).
Fig. 3: CASE 2. Borderline phyllodes tumor. MR shows marked breast asymmetry caused by an enormous mass that occupies all left breast, slightly lateraled to the left. The mass is polylobulated, with approximately 13x11 cm, strongly heterogeneous, with cystic non enhancing areas and with an high signal intensity on T2 weighted images that corresponds to solid areas with rapid and increasing enhancement (50% of the mass). The mass doesn't invade the pectoralis major muscle. There are neither internal mammary nor axillary adenopathies.
Fig. 4: CASE 2. Borderline phyllodes tumor. 20cmx17cmx10cm mastectomy specimen which contains a 15cmx11cmx10cm white multinodular tumor, with central necrotic areas and extension to the epidermis with ulceration.
Fig. 5: CASE 2. Borderline phyllodes tumor, moderate-power view. Ducts embbeded in a moderately cellular stroma, without cytologic atypia (H&E, 100x).
**Fig. 6:** CASE 3. Borderline phyllodes tumor. US image show in the left periareolar region, at the surgical bed architectural disorganization and a solid, hypoechoic, lobulated, well-defined nodule with heterogeneous ecotexture, measuring 27x15x22mm.
Fig. 7: CASE 3. Borderline phyllodes tumor. 7x6x5cm tumorectomy specimen with a 3cm, multinodular, tan tumor.
**Fig. 8:** CASE 3. Borderline phyllodes tumor, low-power view. The tumor has on its vast majority a pushing margin, although some areas of infiltrative borders can be documented (H&E, 40x).
**Fig. 9:** CASE 3. Borderline phyllodes tumor, high-power view. The tumor has moderate stromal hypercellularity with moderate nuclear atypia (H&E, 200x).

**Fig. 10:** CASE 4. Malignant phyllodes tumor. The patient was being followed for a small nodule in the right upper external quadrant. Two years later mammograms show a dense, polylobulated, non calcified mass with smooth borders.
Fig. 11: CASE 4. Malignant phyllodes tumor. US images show a well defined, polybulated, hypoechoic mass with heterogeneous echotexture, fine septations and fine fluid-filled clefts producing posterior acoustic enhancement. Colour Doppler demonstrates flow signal at the periphery of the mass.

Fig. 12: CASE 4. Malignant phyllodes tumor. 8x6x4cm tumorectomy specimen with a well-circumscribed, white, nodular 7cm tumor.
**Fig. 13:** CASE 4. Malignant phyllodes tumor, low-power view (40x). The tumor has ill-defined, pushing margins.
**Fig. 14:** CASE 4. Malignant phyllodes tumor, high-power view. Stromal overgrowth with no evidence of epithelial elements. Stromal hypercellularity with brisk mitotic activity and moderate nuclear atypia (H&E, 400x).
**Fig. 15:** CASE 5. Benign phyllodes tumor. CC mammogram shows in the right internal periareolar region a focal, well-circumscribed, dense nodule with polylobulated appearance.

**Fig. 16:** CASE 5. Benign phyllodes tumor. US shows smooth-bordered macrolobulated hypoechoic, slightly heterogeneous nodule, with small anechoic foci.
**Fig. 17:** CASE 5. Benign phyllodes tumor. The tumor shows an intracanalicular growth pattern with slightly increased stromal cellularity (H&E, 40x).

**Fig. 18:** CASE 6. Borderline phyllodes tumor with focal areas of malignancy. US images show a well defined strongly heterogeneous mass, with solid components, internal cystic changes and septa with irregular walls. Color Doppler demonstrates vascularization at the periphery of the mass.

**Fig. 19:** CASE 6. Borderline phyllodes tumor with focal areas of malignancy, low-power view. The tumor is heterogeneous with areas of high and low cellularity (H&E, 40x).
**Fig. 20:** CASE 6. Borderline phyllodes tumor, high-power view. The tumor has areas of stroma with higher cellularity (H&E, 100x).
**Fig. 21:** CASE 6. Borderline phyllodes tumor, high-power view. The tumor has paucicellular areas of stroma (H&E, 100x).
Fig. 22: CASE 7. Borderline phyllodes tumor. CC and MLO mammograms show in the inner upper quadrant a smoothly marginated, dense, well-defined, lobulated nodule.
**Fig. 23:** CASE 7. Borderline phyllodes tumor. US image shows a sharply circumscribed lobulated hypoechoic nodule with anechoic linear clefts.
**Fig. 24**: CASE 7. Borderline phyllodes tumor. The tumor shows an intracanalicular growth pattern with increased cellularity (H&E, 40x).
**Fig. 25:** CASE 7. Borderline phyllodes tumor. This high-power view demonstrates increased stromal cellularity with nuclear pleomorphism (H&E, 400x).
**Fig. 26:** CASE 8. Benign phyllodes tumor. The tumor is obscured by a dense breast tissue.

**Fig. 27:** CASE 8. Benign phyllodes tumor. US images show an oval, echoic nodule with a small hypoechoic focus. This lesion was misdiagnosed as a fibroadenoma by fine needle biopsy.
Fig. 28: CASE 8. Benign phyllodes tumor, low-power view. The intracanicular growth pattern and moderately cellular stroma can be observed (H&E, 40x).

Fig. 29: CASE 9. Benign phyllodes tumor in a 55-year-old woman, which was previously diagnosed by fine-needle biopsy as a fibroadenoma.
Fig. 30: CASE 9. Benign phyllodes tumour, low-power view. The tumor has a pushing margin (H&E, 40x).
Fig. 31: CASE 9. Benign phyllodes tumor, medium-power view: The tumor shows a leaf-like growth pattern with slightly increased stromal cellularity (H&E, 100x).

Fig. 32: CASE 10. Benign phyllodes tumor. Screening mammograms showed multiple small rounded nodules interpreted as fibroadenomas. Two years later, again in screening mammograms, one of these nodules enlarges.
Fig. 33: CASE 10. Benign phyllodes tumor. Microbiopsy reveals a benign phyllodes tumor.

Fig. 34: CASE 10. Benign phyllodes tumor. 45x30x20mm tumorectomy specimen, which contains a 16x13x11mm white nodule.
**Fig. 35:** CASE 10. Benign phyllodes tumor, medium-power. The intracanicular growth pattern and moderately cellular stroma can be observed (H&E, 100x).
Fig. 36: CASE 10. Benign phyllodes tumor with a pushing margin into normal breast tissue (H&E, 40x).
Conclusion

Mammography and ultrasonography are limited in differentiating phyllodes tumor from benign lesions and cannot predict its histologic grade.

There is limited information on the possible correlation between MR features and histologic grades.

There are sometimes difficulties on the pathologic assessment of malignancy based on histologic characteristics.

Current histologic classification does not always correlate with clinical outcome.

References


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