Cancer Association of South Africa (CANSA)

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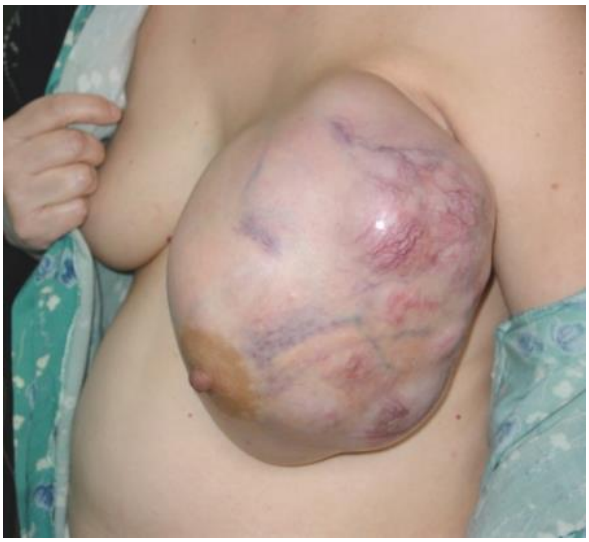
Fact Sheet
on
Phyllodes Tumours

Introduction

Phyllodes tumours also known as cystosarcoma phyllodes, cystosarcoma phylloides, serocystic disease of Brodie and phylloides tumour, are typically large, fast-growing masses that form from the periductal stromal cells of the breast. It accounts for less than 1% of all breast neoplasms.



[Picture Credit: Phyllodes Tumour]

Phyllodes tumours are a fibro-epithelial tumour composed of an epithelial and a cellular stromal component. They may be considered benign, borderline, or also malignant, depending on histologic features including stromal cellularity, infiltration at the tumour's edge, and mitotic activity (having to do with the presence of dividing or proliferating cells). Cancer tissue generally has more mitotic activity than normal tissues. All forms of phyllodes tumours are regarded as having malignant potential. They are also known. Phyllodes tumours rarely spread outside the breast.

Phyllodes Tumour

Although most phyllodes tumours are benign (not cancerous), some are malignant (cancerous) and some are borderline (in between non-cancerous and cancerous with a tendency to probably become cancerous). All three kinds of phyllodes tumours tend to grow quickly, and they require surgery to reduce the risk of a phyllodes tumour coming back in the breast (local recurrence).

Phyllodes tumours can occur at any age, but they tend to develop when a woman is in her 40s. Benign phyllodes tumours are usually diagnosed at a younger age than malignant phyllodes tumours. Phyllodes tumours are extremely rare in men.

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The three main types of phyllodes tumour:

- Non-cancerous (benign) tumours – these make up about 50–60% of phyllodes tumours.
- Borderline tumours – these are not yet malignant (cancerous) but are more likely to turn malignant.
- Cancerous (malignant) tumours – these make up about 20–25% of all phyllodes tumours.

Hamdy, O., Saleh, G.A., Raafat, S., Shebl, A.M. & Denewer, A. 2019.
Introduction: Phyllodes tumors are rare breast tumors. The best treatment is wide local excision with 1 cm safety margin unless metastatic. The three pathological types (benign, borderline and malignant were reported in men.
Case presentation: A 73year-old male with huge left breast swelling extending from the clavicle to the left hypochondriac region. Core needle biopsy suggested malignant phyllodes tumor. Postcontrast CT revealed a huge mass seen at the left anterolateral chest wall measuring about (22 x 25 x 26 cm). Simple mastectomy was performed en bloc with the tumor. The microscopic examination led to the diagnosis of high grade malignant phyllodes. IHC showed diffuse positive vimentin, CD10 and negative CK in the neoplastic cells. The patient lost follow up for three months.Then he was presented with fungating local recurrence with bilateral metastatic pulmonary. The patient underwent palliative excision. After the second surgery, he was prepared for palliative chemoradiotherapy but the patient died one month later at home.
Discussion and conclusions: Very few cases of phyllodes tumor were reported in men. Pathologically, phyllodes tumors are subdivided into three types: benign, borderline and malignant according to mitotic frequency, nature of margins, stromal growth, cellularity and atypia. Malignant phyllodes tumors tend to spread via hematological route mainly to the lung, then to the bone. Phyllodes tumors even benign type tend to recur even after complete excision with higher tendency for malignant cases. Wide local excision is the standard of care for phyllodes tumors with or without adjuvant radiotherapy in malignant lesions- with no proved value for chemotherapy or hormonal therapy.

Incidence of Malignant Phyllodes Tumour in South Africa

The outdated National Cancer Registry (2017) known for under reporting, does not reflect the incidence of Phyllodes Tumour. However, according to the National Cancer Registry (2017) the following cases of histologically diagnosed breast cancer cases in South Africa among women was as follows. Histologically diagnosed means that a tissue sample (biopsy) was forwarded to an approved laboratory where a specially trained pathologist confirmed the diagnosis of cancer:

According to the outdated National Cancer Registry (2017), known for under reporting, the following number of breast cancer cases in women was histologically diagnosed during 2017:

Group 2017	Actual Number of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	9 642	1 : 25	23,11%
Asian females	515	1 : 17	39,52%
Black females	4 077	1 : 45	25,53%
Coloured females	1 365	1 : 19	29,81%
White females	3 667	1 : 10	21,48%

Frequency of Histologically Diagnosed Cases of Breast Cancer

According to the National Cancer Registry (2017), the frequency of histologically diagnosed cases of breast cancer in women in South Africa is as follow:

Group 2017	0 to 19 Years	20 to 29 Years	30 to 39 Years	40 to 49 Years	50 to 59 Years	60 to 69 Years	70 to 79 Years	80 + Years
All females	5	144	942	2 109	2 229	2 142	1 339	624
Asian females	0	4	43	112	129	124	81	22
Black females	5	95	595	1 091	1 088	737	419	187
Coloured females	0	17	102	311	323	348	175	89
White females	0	28	202	598	826	933	814	325

Signs and Symptoms of Phyllodes Tumour

These tumours will usually present as a smooth lump felt beneath the skin. The breast may become red or warm to the touch. These tumours can grow very fast, so it is important to have them evaluated as soon as possible. Symptoms can also mimic those of other types of breast cancer.

Differential Diagnosis of Phyllodes Tumour

The differential diagnosis of Phyllodes Tumour include:

Juvenile Fibroadenoma	Low Grade Phyllodes Tumour
No leaf-like architecture	Prominent leaf-like architecture
No condensation around ducts	Stromal condensation around ducts
Does not infiltrate	May infiltrate surrounding breast

The histologic border between these two is not always sharp

Juvenile Fibroadenoma	High Grade Phyllodes Tumour
No stromal atypia	Atypical stroma
Stromal mitotic rate < 3/10 hpf	Elevated stromal mitotic rate
No stromal overgrowth	Stromal overgrowth
Does not infiltrate	May infiltrate surrounding breast

Stromal overgrowth defined as at least one low power field (40x total magnification) composed entirely of stroma

Fibroadenoma	Low Grade Phyllodes Tumour
Lacks significant stromal hypercellularity	Hypercellular stroma is prominent
No stromal overgrowth	May have stromal overgrowth
No leaf-like architecture	Prominent leaf-like architecture
No condensation around ducts	Stromal condensation around ducts
Does not infiltrate	May infiltrate surrounding breast

The histologic border between these two is not always sharp

Metaplastic Carcinoma	Phyllodes Tumour
Spindled component may be positive for high molecular weight keratin or p63	Stromal component negative for high molecular weight keratin and p63
Epithelial component is malignant	Epithelial component is benign
Squamous differentiation may be present	No squamous differentiation

Pure Sarcoma of the Breast

- Very rare
- The presence of an epithelial component defines phyllodes tumour

Fibromatosis

- Bland spindle cells
- Stellate configuration
- Absence of intrinsic epithelial component
    - May entrap normal breast lobules

Myofibroblastoma

- Resembles solitary fibrous tumour
- Lacks intrinsic epithelial component

Zhang, Y. & Kleer, C.G. 2016.
CONTEXT: Phyllodes tumor (PT) of the breast is a rare fibroepithelial neoplasm with risks of local recurrence and uncommon metastases. The classification proposed by the World Health Organization for PTs into benign, borderline, and malignant is based on a combination of several histologic features. The differential diagnosis between PT and fibroadenoma and the histologic grading of PT remain challenging. In addition, the molecular pathogenesis of PT is largely unknown.
OBJECTIVE: To provide an updated overview of pathologic features, diagnostic terminology, and molecular alterations of PT.
DATA SOURCES: Current English literature related to PT of the breast.
CONCLUSIONS: Phyllodes tumor shows a wide spectrum of morphology. There are no clearly distinct boundaries between PT and fibroadenoma. Strict histologic assessment of a combination of histologic features with classification can help to achieve the correct diagnosis and provide useful clinical information. The genomic landscapes of PT generated from genomic sequencing provide insights into the molecular pathogenesis of PT and help to improve diagnostic accuracy and identify potential drug targets in malignant PT.

Diagnosis of Phyllodes Tumour
Phyllodes Tumour is diagnosed as follows:

Like other less common types of breast tumours, phyllodes tumours can be difficult to diagnose because doctors do not encounter them all that often. A phyllodes tumour also can look like a more common type of benign breast growth called a fibroadenoma. A fibroadenoma is a solid, growing lump of normal breast cells that is the most common kind of breast mass, especially in younger women.

Diagnosing phyllodes tumours usually involves a combination of steps:

- A physical (clinical) examination of the breasts. The doctor may be able to feel the lump in the breast, or a patient may feel it herself during a breast self-examination
- A mammogram to obtain X-ray images of the breast and locate the tumour. On a mammogram, a phyllodes tumour appears as a large round or oval mass with well-defined edges. Sometimes the tumour might look like it has rounded lobes inside it. Calcifications can show up as well. Calcifications are tiny flecks of calcium - like grains of salt - in the soft tissue of the breast. The doctor likely will need to do additional testing to confirm that the lump is a phyllodes tumour
- Ultrasound to obtain sound-wave images of the breast. The images form as the sound waves are 'echoed back' by the tissue. On ultrasound, phyllodes tumours look like well-defined masses with some cysts inside of them
- MRI to obtain additional images of the tumour and help in planning surgery
- Biopsy to take samples of the tumour for examination under a microscope. Although imaging tests are useful, biopsy is the only way to tell if the growth is a phyllodes tumour. The doctor can perform one of two procedures:
    - core needle biopsy, which uses a special hollow needle to take samples of the tumour through the skin
    - excisional biopsy, which removes the entire tumour

Some experts believe it is better to use excisional biopsy if a phyllodes tumour is suspected. Examining the whole tumour is often necessary to make the right diagnosis. The smaller tissue samples taken during core needle biopsy may not be enough to confirm that a lump is a phyllodes tumour. A pathologist then examines the tumour tissue under a microscope to make the diagnosis. He or she also classifies the phyllodes tumour as benign, borderline, or malignant. In a benign tumour:

- the edges are well-defined
- the cells are not dividing rapidly
- the stromal cells (connective tissue cells) still look somewhat like normal cells
- there is not an 'overgrowth' of stromal cells - there are epithelial cells (the types of cells that line the ducts and lobules) as well

In a malignant tumour:

- the edges are not well-defined
- the cells are dividing rapidly
- the stromal cells have an abnormal appearance
- there is an overgrowth of stromal cells, sometimes with no epithelial cells present at all

Joshua, J.X., Chan, W.C., Chau, H.H.L., Wu,, C. & Tse, G.M. 2019.
"A 54-year-old woman presented with a left breast mass, discovered 4 years ago but was static until 2 months before presentation, when it showed a rapid increase in size and became painful. Mammography showed a large lobulated mass with internal cystic components (BI-RADS 4B). A biopsy was performed, followed by modified radical mastectomy. The histologic diagnosis was malignant phyllodes tumor (PT). The patient developed local recurrence 4 months later while on adjuvant radiotherapy and she had a salvage resection. Two months later, she developed massive

left pleural effusion. Pleural fluid cytology showed single discohesive markedly atypical cells with hyperchromatic and enlarged nuclei, irregular nuclear membrane, and distinct macronucleoli. Multinucleated forms were also seen. The mononuclear and multinucleated tumor cells cytomorphologically resembled that of the recurrent tumor, indicative of recurrence. Positron emission tomography/computed tomography confirmed recurrence at the left pleura. The patient opted for palliative care and succumbed 1 month later. The current case demonstrated a rare clinical presentation of recurrent malignant PT as massive unilateral malignant pleural effusion. Correlation with previous histologic and cytologic specimens may be useful as similar cytologic features could be identified in subsequent recurrent tumors."

Treatment of Benign Phyllodes Tumour

Phyllodes tumours are always treated with surgery. This may be a wide local excision. or a mastectomy, depending on the size. The specialist will discuss with the patient the type of surgery she needs.

The aim of the surgery is to remove all of the tumour and an area of healthy tissue around it, known as clear margin (border). This is because it is important to have a clear margin of healthy tissue when the lump is removed to reduce the risk of it coming back. If a clear margin was not achieved by the initial surgery further surgery is usually recommended.

Treatment of Malignant (Cancerous) Phyllodes Tumour

Malignant phyllodes tumours are treated by removing them along with a wider margin of normal tissue, or by mastectomy (removing the entire breast) if needed. Malignant phyllodes tumours are different from the more common types of breast cancer. They do not respond to hormone therapy and are less likely than most breast cancers to respond to radiation therapy or the chemotherapy drugs normally used for breast cancer. Phyllodes tumours that have spread to distant areas are often treated more like sarcomas (soft-tissue cancers) than breast cancers.

Lohmeyer, J.A., Huster, N., Lühr, C., Lindner, C., Wittig, K.S. & Keck, M.K. 2020.

"Phyllodes tumours (PTs) of the breast are classified as benign, borderline and malignant based on the constellation of defined histological parameters. Surgical excision is the primary therapy, but the need to maintain certain safety margins is still controversially discussed for all three categories.This paper aims to provide a critical opinion on the existing recommendation on safety margins for resection.In our breast centre, all patients with phyllodes tumours were identified retrospectively on the basis of the histopathological documentation from 1999 to 2018. The cases were evaluated, in particular, with a view to recurrences and the occurrence of multicentricity.A total of 66 patients were diagnosed with a PT. In 38 cases, the tumours were benign, in 15 borderline and in 13 malignant. Local recurrences were observed in one benign PT, 7 borderline and 5 malignant PTs. Two PTs that were initially classified as borderline tumours progressed to malignant PTs. Multicentricity occurred in about 20 % of borderline and malignant PTs but only in 5 % of benign PTs.The resection margins for phyllodes tumours should be chosen depending on dignity and recurrence. The key question to be challenged is whether or not there is a need to maintain a certain safety margin in benign PTs. In case of recurrence of borderline or malignant PTs, a mastectomy should be considered early."

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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