

CASE REPORT

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A rare case of a large breast phyllodes tumor

Manuel Alexandre Viana Ferreira, Mariana Leite, Sandra Ferreira,
Alberto Midões, Ana Gonçalves

ABSTRACT

Introduction: Phyllodes tumor is a rare form of breast cancer, and the malignant form, the rarest presentation. Although the Phyllodes tumors rarely metastasizes, they can grow faster than any other breast tumor. Diagnosis and treatment are crucial, and surgery is the first line of action. Large tumors represent a surgical challenge because the excision with free margins is essential to prevent local recurrence and metastatic spread. In this presentation, we report a rare case of a giant Phyllodes tumor weighing 7.15 kg on a 66-year-old woman and a review of the literature highlighting some issues surrounding the management of phyllodes tumors. **Case Report:** A 66-year-old women, without known relevant precedents, was admitted to breast pathology consult due a large, ulcerated and infected tumor. An incisional biopsy revealed borderline Phyllodes tumor. No distant metastasis were identified. After infection control, a left mastectomy was performed, with primary closure of the defect by mobilizing the skin flaps. The postoperative period was uneventful.

Pathological examination revealed a 30x28x18 cm, 7150 gr malignant Phyllodes tumor with free margins. After one year follow-up there is no evidence of local or distant recurrence. The patient refused plastic reconstructive surgery. **Conclusion:** Phyllodes tumor is a rare breast tumor, with the malignant phenotype being the rarest of them all. Surgical therapy is the gold standard for the treatment of phyllodes tumors. Phyllodes tumors should be removed with, at least, 1 cm free margins, especially if they're malignant tumors. The role of adjuvant therapy is still controversial.

Keywords: Breast cancer, Fibroepithelial neoplasm, Phyllodes tumor

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Manuel Alexandre Viana Ferreira¹, Mariana Leite¹, Sandra Ferreira², Alberto Midões³, Ana Gonçalves⁴

Affiliations: ¹MD, Resident of General Surgery in the General Surgery Department of Hospital de Santa Lúzia, Viana do Castelo, Portugal; ²MD, Breast Surgeon, Department of Breast Surgery, in the Hospital de Santa Lúzia, Viana do Castelo, Portugal; ³MD, Director of the General Surgery Service in the Hospital de Santa Lúzia, Viana do Castelo, Portugal; ⁴MD, Director of the Department of Breast Surgery in the Hospital de Santa Lúzia, Viana do Castelo, Portugal.

Corresponding Author: Manuel Alexandre Viana Ferreira, Rua António De Mariz, nº22, 4715-279 Braga, Portugal; Email: manuel.alexandre.ferreira@gmail.com

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INTRODUCTION

Fibroepithelial breast tumors, including fibroadenoma and phyllodes tumor (PT), are biphasic neoplasms characterized by proliferation of both epithelial and stromal components [1]. PT is a rare fibroepithelial neoplasm making up 0.3 to 0.5% of all breast tumors and approximately 2.5% of fibroepithelial tumors of the breast [1].

The clinical behaviour and prognosis of PTs are quite different from those of fibroadenoma. Patients with PT are usually 10 to 20 years older than patients with fibroadenoma, with an average age of 44 years. With a

median size of 4cm, the PTs are often larger in size than fibroadenomas and occur most commonly isolated and unilaterally [2]. 20% of these tumors grow larger than 10cm and there are few articles reporting PTs with a diameter larger than 30 cm. This giant PT may present focus of haemorrhagic and necrotic areas [3, 4].

The World Health Organization (WHO) subclassified the PTs histologically, as benign, borderline, or malignant according to its features such as tumor margins, stromal overgrowth, tumor necrosis, cellular atypia, nuclear pleomorphism and mitotic rate [5]. Cellular atypia, mitosis, stromal overgrowth and surgical margins ("AMOS criteria") are independent predictive factors of clinical behaviour and recurrence of PTs [6]. The majority of PTs are considered benign (35% to 64%), while malignant comprise about 25% of cases [7].

Accurate preoperative pathological diagnosis allows correct surgical planning and avoids reoperation. At one extreme, malignant PTs, if inadequately treated, have a propensity for rapid growth and metastatic spread [5]. In contrast, benign PTs on clinical, radiological, and cytological examination are often indistinguishable from fibroadenomas and can be cured by local surgery [5]. With the nonoperative management of fibroadenomas widely adopted, the importance of PTs today lies in the need to differentiate them from other benign breast lesions [5].

In this article, we report a rare case of a giant PT weighing 7.2 Kg weight on 66-year-old women and highlight some issues surrounding the diagnosis and management throughout this unusual case.

CASE REPORT

A 66-year-old woman, without known relevant precedents, was admitted to our breast pathology department with a giant local invasive breast tumor.

The patient stated she had noticed a small lump in her left breast six years earlier but ignored it. Due to her fear of surgery, she allowed the mass to grow year after year without consulting a doctor. At the time she admitted, the lump had become so large that the patient couldn't walk properly, having to carry her breast like a small baby. The patient decided to seek medical attention only after the tumor became necrotic and infected.

Upon medical examination, the patient presented a giant mass with 30cm maximum diameter almost replacing her left breast, with infected ulcerated areas. The skin over the remaining mass was stretched and revealed dilated veins (Figure 1). After infection control, an incisional biopsy was performed and proceeded with staging studies such as blood tests, computed tomography (CT) and bone scintigraphy. The biopsy revealed a borderline PT and the tomography exam showed a giant left mammary tumor with 28cm long axis, suggesting signs of skin invasion probably reaching the pectoral muscles (Figure 2). Distant metastasis were not identified.

A left mastectomy was performed. Due the high vascularity, a vessel sealing technology (Ligasure by medtronic®) was used to easily control the blood loss. The breast was removed with 1cm margin from the palpable mass, with the need to remove the fascia and a superficial layer of the pectoral muscle (Figure 3). Lymphadenectomy was not performed. Primary closure of the defect was done and a suction drain placed after mobilizing the skin flaps. The postoperative period was uneventful. The patient received no further treatment.

The final histology revealed a 30x28x18 cm, 7150 gr malignant PT with free margins between 1-2,5 cm. The lesion was markedly cellular with virtually non-existent epithelial component, presenting only some peripheral glandular structures and discreet myoepithelial atypia, compressed by a giant stromal component covered by a single epithelial layer with a leaf-like pattern. The cell showed varying degrees of atypia, with smaller cells with regular nuclei and other areas (most of the lesion) with atypical cells, pleomorphic hyperchromatic nuclei and very numerous mitoses counting foci with >30 mitoses/single field (Figure 4). The lesion was surrounded by fibrous tissue with no signs of muscular layer invasion. After 1 year follow up there is no evidence of local or distant recurrence.

DISCUSSION

This case highlights the behavior and the potential of these tumors to grow aggressively and places an emphasis on the importance of an appropriate diagnosis and resection.

Clinically PT is traditionally a well delineated and circumscribed tumor such as fibroadenoma, albeit usually larger. The cut surface shows sliced spaces with interspersed of stromal overgrowth and the dilated ducts [1]. Large tumors may rarely show haemorrhagic and necrotic areas, and malignant PT may have sarcoma-like



Figure 1: Patient with a large tumor in the left breast prior to surgery.

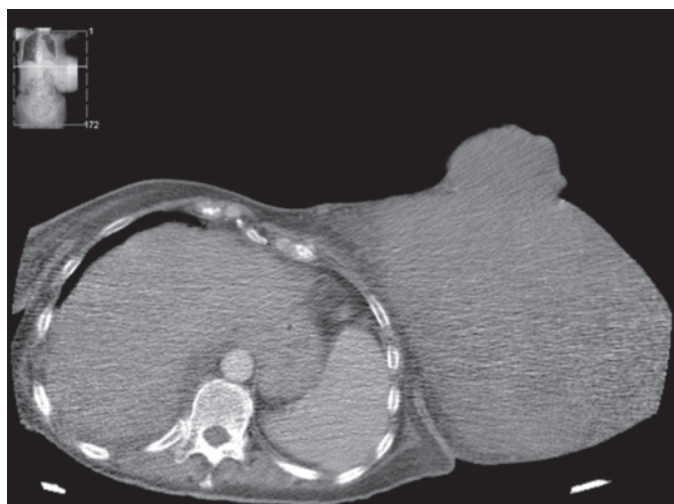


Figure 2: Preoperative CT scan.



Figure 3: Resected Phyllodes tumor, weighing 7.2 Kg and measuring 30x28x18 cm. The tumor presented five ulcerated areas with dimensions between 2 and 12 cm.

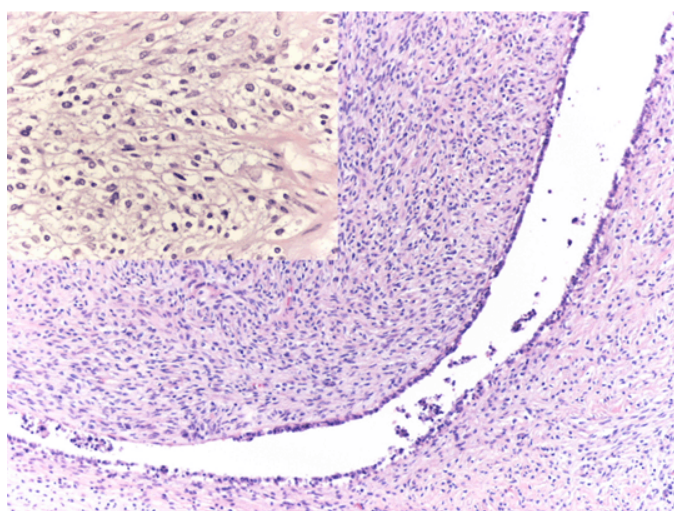


Figure 4: Hematoxylin and eosin staining of the breast tissue revealing an epithelial component with a leaf-like pattern. In the superior right corner, a magnification of the same area where its possible to see two mitosis (10X, inset 40X).

cut surface. Microscopically, PT present hypercellular stroma with the stromal elements being more numerous than the epithelial ones and with leaf like protrusions into the cystic spaces [1].

Due to the overlapping clinical and histological features between fibroadenomas and small PTs, many studies have shown the need for biomarkers for more accurate preoperative evaluation such as Ki-67, a nuclear protein expressed only in cycling cells, and p53, a tumor suppressor, essential for cell cycle control, DNA damage repair, and apoptosis [8, 9].

Ki-67 has been significantly correlated with a disease-free status and overall survival rates and is usually increased in both borderline and malignant PTs [1]. The proliferative activity of the PTs by Ki-67 index is now one of the WHO criteria for PT grading. A p53 increase in PT is positively associated with an increased Ki-67 index. No p53 nuclear staining is observed in benign tumors or fibroadenomas. Immunohistochemistry for p53 may be helpful for grading PTs but not for the differentiation of fibroadenomas from benign tumors [1].

Other biomarkers had been studied such as B-catenin, a protein expressed in nuclear of stromal cells that is increased from normal breast tissue to benign PTs to borderline PTs, and then decreased in malignant PTs. E-Cadherin is an adhesion molecule forming complexes with catenin's at epithelial cell to cell adherens junctions. It is only positive in the epithelial cells, not in stromal cells, and so is significantly correlated with an increased average time of recurrence. IMP3 is a novel biomarker for triple-negative invasive mammary carcinoma. Its expression is associated with a more aggressive phenotype and decreased overall survival and is also implied in malignant PTs [1].

Surgical therapy is the gold standard for the treatment of PTs but the kind of surgery has been a source of study and debate over the years. Studies have shown no differences between breast conserving surgery versus mastectomy as far as metastasis-free survival, despite the higher incidence of local recurrence that comes with breast conserving surgery [5].

According to National Comprehensive Cancer Network (NCCN) Guidelines for the Management of PT, PTs should be removed with, at least, 1cm free margins, especially if they're malignant tumors. For benign PTs, a "watch and wait" policy may be safe. With such an approach, local recurrence in five years is 4% and survival rate 96%. If the decision is to perform a local excision, one should check the margins [5].

Large tumors (usually larger than 10cm) imply a challenge for the surgeon. Since a local excision requires free margins, it's often impossible to perform a safety procedure on these patients and a mastectomy should be considered. If chest wall invasion occurs, an extended incision of the pectoral muscle should be performed, followed by reconstruction of the chest. There is no contraindication to immediate reconstruction after mastectomy in cases of giant PT [5].

The role of adjuvant therapy is controversial. The benefits of radiotherapy (RT) and chemotherapy (QT) in soft tissues sarcomas suggest that there may be room to use these therapies in PTs. Chaney *et al.* [10] found adjuvant RT to be beneficial in patients with adverse features such as positive surgical margins, hypercellular stroma, high nuclear pleomorphism, high mitotic rate, presence of necrosis, and increased vascularity. Richard J. *et al* [11] demonstrated that margin-negative resection combined with adjuvant RT is an effective therapy for local control of borderline and malignant PTs. MD Anderson Cancer Center recommended RT only for tumors with positive surgical margins. QT, including anthracyclines, ifosfamide, cisplatin and etoposide or hormonal therapy such as tamoxifen has shown no benefits [5].

Local recurrence rate of PTs is 10% to 18% with negative and positive resection margins, respectively, and is also associated with inadequate excisions, mitotic activity and stromal cellular atypia and necrosis rather than with tumor size. In multivariable analysis, the surgical margins are found to be the only independent predictive factor for local recurrence [1].

Tumor grade is a controversial subject. For many years it wasn't considered important for higher local recurrence, but recent studies showed that recurrence occurred in 8% to 10% of benign, 14% to 20% of borderline, and 29% to 50% of malignant PTs [6, 12]. Additionally, malignant PTs have the potential of systemic spread and 9% to 27% of this malignant PTs can also metastasize to distant organs through the lymphovascular way [12, 13]. The most common sites are the lungs (66%), bone tissue (28%) and central nervous system (9%). Benign PT may also transform into a higher grade and recur as borderline or malignant PT [13].

Since PTs are locally recurrent tumors, it is recommended to follow up with the patient regularly at a 6-month interval for the first two years because chances of recurrence are maximum in the first two years. Patients should be examined and if any abnormality is detected they should be subject to any one of these procedures: an ultrasonography, a mammogram, a magnetic resonance imaging (MRI), or a tissue biopsy [1].

In our case, the patient presented a very large malignant tumor (30x28x18 cm weighing 7.2 Kg) with ulcerated areas.

CONCLUSION

Phyllodes tumor is a rare breast tumor, with the malignant phenotype being the rarest of them all. Only 20% achieve a size bigger than 10cm and usually don't present with ulcerated areas, which turns this report noteworthy. This case gives insight into the natural history of PT and shows the potential consequences when it's left untreated.

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Author Contributions

Manuel Alexandre Viana Ferreira – Substantial contributions to conception and design, Acquisition of

data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Mariana Leite – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Sandra Ferreira – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Alberto Midões – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Ana Gonçalves – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor of Submission

The corresponding author is the guarantor of submission.

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None.

Consent Statement

Written informed consent was obtained from the patient for publication of this case report.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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