

Phyllodes Breast Sarcomas: A Report on 5 Cases and Review of Literature

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Abstract

The objective of this study was to examine the clinical characteristics and management of five patients with phyllodes sarcoma of the breast. These patients were followed at the senology unit of the Philippe Maguilen Senghor health center in Dakar between 2012 and 2022. We conducted a retrospective study of five cases of phyllodes sarcoma managed at our unit. We collected clinical, histopathological, and therapeutic data from the patients' medical records. We also followed the patients' outcomes, including recurrence and survival, for up to 36 months after treatment. The mean age of the five patients at diagnosis was 28.8 years. Mastectomy was the primary treatment most of the patients. Two patients developed local recurrences within a very short time, between 4 and 20 months. The overall survival rate for the five patients was 40% at 24 months. Phyllodes sarcomas of the breast are rare tumors that require special attention due to their potential for progression. Early diagnosis and adequate surgical resection are crucial to reduce the risk of recurrence. This case report highlights the challenges of managing these tumors and emphasizes the importance of rigorous follow-up.

Keywords

Phyllodes Sarcoma, Breast, Oncology, Surgery

1. Introduction

Phyllodes tumours (PT) are a rare group of fibro-epithelial breast tumours [1]. The true incidence is unknown; breast sarcomas account for less than 1 per cent of breast tumours [2]. In 1981, the World Health Organisation classified phyllodes tumours of the breast into three categories based on the frequency of mitoses, the degree of peripheral infiltration, cellular atypia and the degree of cellularity [3].

There are therefore three categories: benign PT, borderline PT and malignant PT, or phyllodes sarcomas. This is most often a localised condition, with axillary involvement and metastasis being rare. Management is primarily surgical, and the prognosis depends largely on the surgery itself, in particular on the margin status. [4]. Indeed, several studies have already reported the prognostic benefits of leaving a margin of at least 1 cm, as this reduces the risk of local recurrence, which is very common with these tumours [5]. Apart from surgery, radiotherapy and chemotherapy have also been described as possible options in the management of phyllodes sarcomas, but their role in the management of these tumours remains controversial [4] [5].

Through five cases treated at our center, we aim to highlight the diagnostic aspects and therapeutic challenges associated with phyllodes sarcomas of the breast.

2. Observations

2.1. Observation 1

Ms. A.K., aged 31, with no significant medical history, presented with a large mass in her left breast that had been present for two years. On examination, a tumour measuring over 12 cm was found, accompanied by ipsilateral axillary lymphadenopathy. Cytology suggested benign epithelioid-connective tissue hyperplasia with reactive lymphadenitis, whilst the biopsy revealed a high-grade malignant phyllodes tumour. A mastectomy with clear surgical margins was performed. Twenty months later, a recurrence in the ipsilateral axillary lymph nodes occurred. Axillary lymph node dissection revealed two metastatic lymph nodes. Despite the absence of radiotherapy, the prognosis remained favourable after seven years of follow-up (Table 1 and Figure 1).

Table 1. Summary of the clinical, therapeutic and prognostic characteristics of phyllodes sarcoma cases.

Variables	Case 1	Case 2	Case 3	Case 4	Case 5
Age	31 yr	36 yr	24 yr	18 yr	35 yr
Parity	G5P5	G3P3	G3P4	G0P0	G5P5
Duration of the disease's progression	2 yr	6 yr	3 yr	Fast	Fast
Initial size	>12 cm	7 cm	Full breast	-	Full breast
Lymph node invasion	Yes	Yes	Yes	No	No
Histological grade	High grade	-	High grade	High grade	High grade
First treatment	Mastectomy	Chemotherapy	Mastectomy	Tumorectomy/ Mastectomy	Mastectomy
Margins	>1 cm	NA	>1 cm	<1 cm	>1 cm
Adjuvant treatment	-	Chemotherapy	-	Radiothérapie Chemotherapy	Chemotherapy

Continued

Recurrence	Yes (lymph nodes)	NA	No	Yes (parietal)	Yes (parietal)
Recurrence delay	20 month	NA	NA	4 month	4 month
Issue finale	Favorable 7 years of follow-up	Deceased (4 month)	Favorable 2 years of follow-up	Deceased (15 month)	Deceased (12 month)



Case 2: Starting stage/3rd month of chemotherapy



Case 3: Starting stage/After surgery



Case 5: Starting stage – ulcerative and necrotic areas of the breast

Figure 1. Clinical aspects of phyllodes tumours of the breast.

2.2. Observation 2

A 36-year-old female patient with a family history of breast cancer in a second-degree relative. She presented with a gradually enlarging mass in her right breast that had been developing for six years. Clinical examination revealed a large inflammatory breast tumour associated with axillary lymphadenopathy. An initial biopsy suggested a low-grade phyllodes tumour, whilst a second biopsy confirmed the diagnosis of phyllodes sarcoma. Given the locoregional spread, neo-adjuvant chemotherapy was initiated with doxorubicin combined with cisplatin. The response to treatment was poor, despite several lines of therapy, with rapid

local progression of the disease and the patient's death four months after diagnosis.

2.3. Observation 3

A 24-year-old female patient, with no significant medical history, presented with a mass in her right breast that had been present for three years. Clinical examination revealed a large breast tumour with an inflammatory appearance, comprising areas of induration and associated with axillary lymphadenopathy, against a background of generalised emaciation. Cytological examination suggested carcinoma, but the biopsy confirmed the diagnosis of phyllodes sarcoma. A mastectomy with clear surgical margins was performed. No adjuvant treatment was recommended for her. The prognosis was favorable, with no local recurrence or distant metastases after 24 months' follow-up.

2.4. Observation 4

An 18-year-old female patient, nulliparous and with no significant medical history, presented with a rapidly developing mass in her left breast. An initial lumpectomy was performed, followed by a mastectomy after a histopathological diagnosis of phyllodes sarcoma.

External beam radiotherapy following the mastectomy was subsequently recommended. Four months later, a parietal recurrence developed, presenting as a rapidly growing mass that required a parietal resection, the margins of which were invaded. The rapid progression of the disease made any further surgery impossible. Chemotherapy was initiated, the patient received eight cycles of doxorubicin plus cisplatin, administered every three weeks. Response was assessed clinically. Local disease progression was observed during chemotherapy, with an increase in the size of the ulcerated tumor mass. The patient died 15 months after diagnosis.

2.5. Observation 5

A 35-year-old patient, in her fifth pregnancy and fifth childbirth, with no significant medical history, who, one month after giving birth, presented with a rapidly growing mass in her right breast occupying the entire breast. Clinical examination revealed ulcerated and necrotic areas, with no palpable lymphadenopathy. A biopsy was consistent with phyllodes sarcoma of the breast. A radical mastectomy was performed. Pathological examination confirmed the diagnosis of phyllodes sarcoma, with clear surgical margins. No adjuvant treatment was recommended given the clear margins. A local ulcerative-budding recurrence developed four months later. Chemotherapy was recommended, and the patient received four cycles of doxorubicin in combination with cisplatin. Local progression of the disease led to a switch to paclitaxel (Taxol) in combination with bevacizumab (Avastin). The chemotherapy administered produced no response, and the patient died after 12 months of follow-up.

3. Discussion

Phyllodes sarcomas of the breast are very rare tumors, accounting for less than 1% of malignant breast tumors [2]. In our unit, they account for 0.6% of breast cancers.

Initially considered to be always benign, numerous definitions have been proposed over time (more than sixty to date). The first definition to classify phyllodes tumors as benign, malignant, or borderline was that of Norris and Taylor [6], and it is the one currently adopted by the World Health Organization (WHO) [3]. The pathophysiology of these tumours remains unclear. One hypothesis suggests that the stromal component plays a major role in tumour behaviour. Molecular alterations, particularly in the MED12 and TERT genes, are implicated in their development [7]. High-grade tumours exhibit increased genomic complexity, including alterations in TP53, RB1 or NF1 [8].

The analysis of these five cases of phyllodes sarcoma of the breast revealed several significant findings. The epidemiological profile of our patients is that of women with an average age of 28.8, who have had few or no previous pregnancies and no specific medical history. This average age is significantly lower than that reported in the literature, where the few published case series indicate a higher average age, around 45 years. Phyllodes sarcomas generally occur in older women, with a gap of at least 20 years between the age of onset and that of adenofibromas. This later age of onset should alert clinicians to any breast mass that appears during the perimenopausal period, even if it appears clinically benign. Regarding clinical characteristics, all cases presented with rapidly growing breast masses, often large, with most patients having tumors larger than 5 cm. These clinical characteristics are similar to those reported in the literature [9]. Radiologically, there are few specific signs, and the appearance may suggest a fibroadenoma. Mammography shows a rounded, polycyclic opacity with regular margins. On ultrasound, the lesion appears hypoechoic, oval and multilobed, sometimes with areas of cystic change; however, diagnosing malignancy is not always easy [9].

Histological examination is the gold standard diagnostic tool for phyllodes tumors, as it can determine their dual conjunctive and epithelial components and establish the prognosis. Immunohistochemistry can help in cases of diagnostic uncertainty. However, this dual tissue component sometimes makes diagnosis complex, particularly in countries where specimens are stored for long periods in formaldehyde, which can degrade them and complicate interpretation. This highlights the need for mandatory increases in staffing levels for this discipline, which is essential to all medical specialities. The management of phyllodes tumors of the breast is primarily surgical, as confirmed by several studies [1] [4] [5]. In fact, it is generally recommended to perform a total mastectomy with clear margins of at least 1 cm, as axillary lymph node dissection is not routinely carried out [10] [11]. However, there are still differences of opinion regarding the type of surgery—whether it should be conservative or radical [1]. Indeed, Fou's 2006 study, which examined 384 phyllodes tumors, including 27 cases of malignant forms, found no

significant difference in disease-free survival between radical and conservative treatment [11], the prognosis depends mainly on the initial tumor size, the extent of invasion of the surrounding tissues, mitotic activity and tumor necrosis [1] [2]. This study concluded that it was possible to carry out conservative treatment for small masses whilst maintaining a 1 cm margin [4] [11] [12]. Radical surgery was recommended for four of the five patients treated at our center. In the remaining patient, surgery was not feasible because of advanced disease. Apart from surgery, other therapeutic approaches have been described in the literature [1] [2] [13] [14]. This is the case with chemotherapy, which is generally indicated for metastatic phyllodes sarcomas or in cases where primary surgery is not possible [13]. The efficacy of this neoadjuvant chemotherapy remains controversial, with only a few case series reported in the literature and no consensus on the most appropriate treatment regimen [13] [15]. This is confirmed by Zelek's study, one of the largest cohort studies involving 90 patients between 1954 and 1991, which found no benefit in neoadjuvant chemotherapy, as phyllodes tumors are largely unresponsive to chemotherapy, with response rates of 20 to 40 per cent [16]. The same study reported that surgery was never an option following chemotherapy in cases of locally advanced tumors [16]. In our series, one patient underwent neoadjuvant chemotherapy, while two others received chemotherapy to treat local recurrence. However, none of these patients demonstrated improvement in their local disease following chemotherapy. A prospective study involving 28 patients found no improvement in recurrence-free survival with adjuvant treatment with doxorubicin and dacarbazine compared with no chemotherapy. Similar results were observed in a retrospective cohort from the French Sarcoma Group comprising 212 patients, of whom 23 (11 per cent) received adjuvant chemotherapy; this was not associated with improved local control or overall survival in the multivariate analysis [17].

Another treatment option described for phyllodes sarcomas is radiotherapy, which is generally used as an adjuvant treatment following surgery. The expected benefit of this radiotherapy is improved local control. However, this requires adequate initial surgery with clear margins [14].

The prognosis for malignant phyllodes tumours of the breast is variable. It depends both on the characteristics of the tumour—its size and histological criteria for malignancy—and on the quality of the surgical resection. A large tumour size and tight resection margins have also been associated with local recurrence [18]. In our series, two patients presented with local recurrence despite radical surgery with resection margins exceeding 1 cm. One patient developed histologically confirmed lymph node recurrence, which is an unusual pattern of spread in malignant phyllodes tumors [17].

This review highlights the challenges associated with the management of malignant phyllodes tumours and emphasises the importance of histopathological examination by experts, as well as multidisciplinary discussion. Surgery remains the mainstay of treatment, the aim being to achieve clear margins of 1 cm wher-

ever possible. The role of neoadjuvant chemotherapy remains uncertain and may be considered in certain patients with inoperable disease, following discussion within a multidisciplinary team specialising in sarcomas.

4. Conclusion

Malignant phyllodes tumours of the breast are rare and present therapeutic challenges. In our series of five cases, the course of the disease was characterised by early local recurrences and bad response to chemotherapy. These observations highlight the importance of early management and close follow-up. The development of genomic research in Africa could improve our understanding of these tumours and enable us to explore any specific characteristics within African populations.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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