Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Radiation Oncology

Malignant Phyllodes Sarcoma of the Breast in a 31-Year-Old Woman: A Case Report and Literature Review

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DOI: https://doi.org/10.36347/sjmcr.2026.v14i11.055 | **Received:** 17.09.2026 | **Accepted:** 13.11.2026 | **Published:** 16.11.2026

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Abstract | **Case Report**

Background: Phyllodes tumors are rare fibroepithelial breast neoplasms. Malignant phyllodes tumors may exceptionally show heterologous sarcomatous differentiation, including chondrosarcomatous differentiation. ***Case Presentation***: A 31-year-old woman with no relevant medical history presented with a two-year history of progressively enlarging left breast nodules and mastodynia. She underwent biopsy followed by left extended mastectomy, axillary dissection and flap reconstruction. Histology showed grade III malignant phyllodes sarcoma with a heterologous chondrosarcomatous component, stromal predominance, necrosis and 12 mitoses/10 high-power fields. Margins were negative, with the closest peripheral margin at 1 cm and the deep margin at 2 cm. All 24 lymph nodes were negative. S100 and desmin were negative in stromal cells, while Ki-67 showed moderate nuclear expression. CT staging did not identify a definite distant secondary lesion. Postoperative external-beam radiotherapy was planned. ***Discussion***: Heterologous differentiation in malignant phyllodes tumors is an exceptionally rare histopathological finding and is generally associated with aggressive tumor behavior. Several histopathological features have been identified as potential predictors of local recurrence, including stromal atypia and hypercellularity, stromal overgrowth, increased mitotic activity, tumor necrosis, and positive or close surgical margins. Achieving complete surgical excision with negative margins remains the cornerstone of treatment. However, the role of adjuvant radiotherapy remains controversial. Retrospective studies suggest that postoperative radiotherapy may improve local control in selected patients, particularly those with malignant histological features, large tumors, stromal overgrowth, or close/positive margins. Nevertheless, given the rarity of malignant phyllodes tumors and the absence of prospective randomized trials, there is currently insufficient evidence to demonstrate a clear overall survival benefit from adjuvant radiotherapy. ***Conclusion***: Heterologous chondrosarcomatous differentiation is exceptionally rare. Thorough pathology and multidisciplinary management are essential; adjuvant radiotherapy should be individualized according to local-recurrence risk and available evidence.

Keywords: Phyllodes tumor; malignant phyllodes sarcoma; chondrosarcoma; heterologous differentiation; breast; radiotherapy.

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1. INTRODUCTION

Phyllodes tumors are rare fibroepithelial neoplasms composed of epithelial and stromal components. They account for less than 1% of malignant breast tumors in classical series. [1] Their classification is mainly based on stromal characteristics, including cellularity, atypia, mitotic activity, stromal overgrowth, and tumor margins.

Phyllodes tumors are classified as benign, borderline, or malignant. Malignant forms may contain heterologous sarcomatous differentiation, including osteosarcomatous, chondrosarcomatous, liposarcomatous, angiosarcomatous, or rhabdomyosarcomatous differentiation [2, 3].

Chondrosarcomatous differentiation is exceptional. Several cases have been published, sometimes with a predominant chondrosarcomatous component and sometimes associated with other heterologous components [4, 5]. The rarity of this entity explains the absence of prospective trials and the persistence of therapeutic uncertainties.

We report a case of a grade III malignant phyllodes sarcoma of the left breast with heterologous

chondrosarcomatous differentiation in a 31-year-old woman, managed with surgery and subsequently referred for postoperative external-beam radiotherapy.

2. CLINICAL CASE

2.1. General Information and Medical History

A 31-year-old single woman, residing in the Lhaouz region and covered by AMO, was referred to the Radiation Oncology Department of CHU Mohammed VI, Marrakech, for complementary management of a left breast tumor. Her medical, surgical, and family history was unremarkable. Her menstrual cycles were regular, with no history of contraception; she was G0P0, and menarche occurred at 12 years of age.

2.2. History of the Disease

The history dated back approximately two years, marked by self-palpation of progressively enlarging nodules in the left breast, associated with mastodynia and no other reported associated symptoms. The disease evolved in a context of deterioration of the general condition. An initial consultation was performed in the Gynecology Department of CHU Mohammed VI.

2.3. Surgery

Following biopsy, the patient underwent left extended mastectomy with left axillary lymph-node dissection, followed by flap reconstruction as a second-stage procedure.

2.4. Histopathology

The left extended mastectomy specimen associated with axillary lymph-node dissection was consistent with a grade III phyllodes sarcoma. The heterologous component was chondrosarcomatous. Histological examination showed stromal predominance, 12 mitoses/10 high-power fields, and foci of necrosis.

There was no vascular embolism or perineural invasion. The internal, external, superior, and inferior margins were clear; the closest peripheral margin was 1 cm. The deep margin was clear at 2 cm. Axillary lymph-node dissection was negative: 0 involved nodes out of 24.

2.5. Immunohistochemistry

Marker	Result	Key finding
S100	No expression	Negative in stromal cells
Desmin	No expression	Negative in stromal cells
Ki-67 (MIB-1)	Moderate nuclear expression	Quantitative value not specified

2.6. Imaging and Staging Work-Up

Thoraco-abdomino-pelvic CT showed no pleuropericardial effusion or mediastinal/hilar lymphadenopathy. No suspicious pulmonary nodule or mass was described. The abdominopelvic assessment showed no secondary visceral lesion or peritoneal lymphadenopathy. Bone abnormalities were described in the iliac wings and femoral necks, without radiological evidence of secondary involvement.

The CT conclusion described a large, locally infiltrative left breast mass extending toward the chest wall, without intrathoracic extension or adjacent bone lysis, associated with ipsilateral axillary lymphadenopathy, with no other detectable lesion suggestive of secondary disease.

2.7. Clinical Examination in Radiation Oncology

The patient was conscious, with a performance status of 0 according to the medical record. The left breast scar was clean and the flap was in place. The right breast was unremarkable. Examination of the lymph-node areas revealed no reported clinical abnormality, and the remainder of the physical examination was unremarkable.

2.8. Staging and Treatment

The case was considered a malignant phyllodes sarcoma of the left breast, classified as pT4N0M0, stage IIIB, in a patient with a performance status 0. Postoperative external-beam radiotherapy was planned.

Radiotherapy Adjuvant

Postoperative radiotherapy was planned using a CT-based treatment planning system. The clinical target volume included the left chest wall and the surgical bed. The organs at risk, including the heart and both lungs, were delineated to optimize treatment planning and minimize unnecessary irradiation of normal tissues.

The patient received external beam radiotherapy to the left chest wall with a total dose of 50 Gy delivered in 25 fractions of 2 Gy, at five fractions per week. The treatment was completed over five weeks, with no additional boost to the tumor bed.

3. LITERATURE REVIEW AND DISCUSSION

3.1. Rarity and Criteria for Malignancy

Phyllodes tumors are rare, and malignant forms constitute a minority. Malignancy is mainly determined by stromal characteristics. Heterologous sarcomatous differentiation is an exceptional presentation [1, 2]. The literature emphasizes the importance of extensive histological sampling when the stromal component is highly developed, in order to identify any heterologous components [2-5].

3.2. Chondrosarcomatous Differentiation

Cases of malignant phyllodes tumors with chondrosarcomatous differentiation have been described for several decades. Garcia *et al*., reported a case with stromal overgrowth and predominant chondrosarcomatous differentiation, highlighting the diagnostic difficulty when the sarcomatous component becomes predominant [5]. Vera-Sempere and García-Martínez described a 37-year-old woman in whom the chondrosarcomatous component represented more than 80% of the tumor volume [4]. Warrier *et al.,* reported two cases of phyllodes tumors with heterologous differentiation, one of which contained both chondrosarcomatous and osteosarcomatous components [1]. More recent cases have also confirmed the extreme rarity of chondrosarcoma/osteosarcoma associations [6, 7].

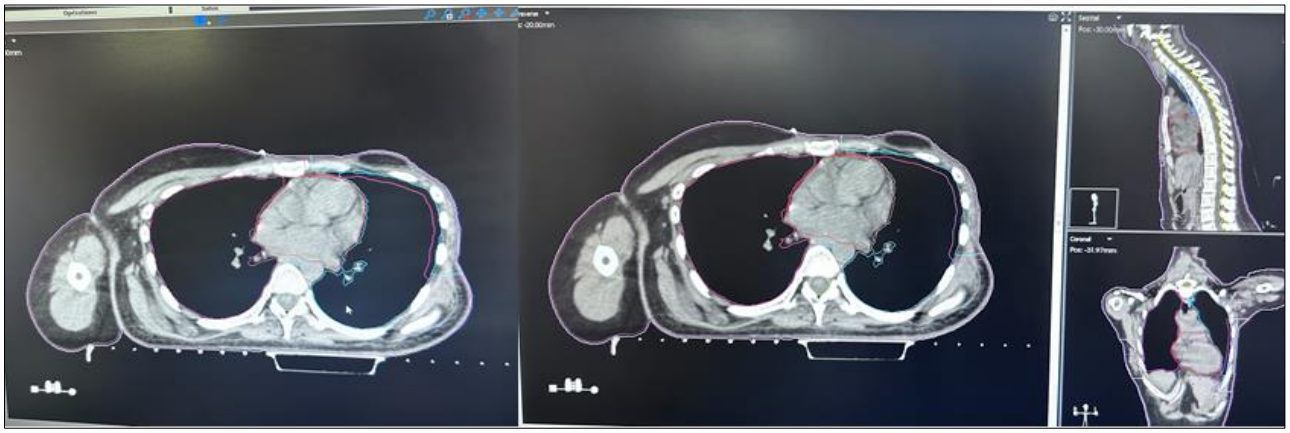


Figure 1: T-based radiotherapy treatment planning on an Elekta linear accelerator, showing delineation of the left chest wall target volume and the organs at risk, including the heart and lungs

Tableau 1: Published cases of malignant phyllodes tumors with chondrosarcomatous differentiation

Reference	Patient	Type of differentiation / Main characteristics	Significance of the case
Garcia *et al*., 1999 [5]	Case of malignant phyllodes tumor	Predominant chondrosarcomatous differentiation; stromal overgrowth with a large chondrosarcomatous component	Highlights diagnostic difficulty when the sarcomatous component becomes predominant
Vera-Sempere & García-Martínez, 2003 [4]	37-year-old woman	Chondrosarcomatous differentiation; chondrosarcomatous component >80% of tumor volume	Illustrates major chondrosarcomatous differentiation
Warrier *et al*., 2015 [1]	2 patients	Heterologous differentiation including chondrosarcomatous differentiation; one case associated with osteosarcomatous differentiation	Confirms the rarity and diversity of heterologous differentiation
Patil Okaly *et al*., 2015 [6]	40-year-old woman	Osteosarcomatous + chondrosarcomatous differentiation; malignant phyllodes tumor with multiple heterologous differentiation	Rare example of chondrosarcoma–osteosarcoma association
Ko, 2023 [7]	52-year-old woman	Osteosarcomatous + chondrosarcomatous differentiation; malignant phyllodes tumor with dual heterologous differentiation	Confirms the exceptional nature of this association
Our current case	31-year-old woman	Chondrosarcomatous differentiation; grade III, 59 cm in size, stromal predominance, 12 mitoses/10 HPF, necrosis, clear margins, 0/24 lymph nodes	Our case is rare, characterized by chondrosarcomatous differentiation and a large tumor size.

3.3. Histopathological Profile of Our Case

Our patient presents several unfavorable histological factors: grade III, stromal predominance, 12 mitoses/10 HPF, necrosis, and heterologous chondrosarcomatous differentiation. Conversely, the margins were reported as clear, with no vascular emboli or perineural invasion, and lymph-node dissection was negative in all 24 nodes.

This combination illustrates the value of a comprehensive histopathological analysis allowing local-risk factors to be distinguished from factors associated with nodal extension.

3.4. Tumor Size

The giant nature of our tumor is a remarkable feature of this case. Giant phyllodes tumors, usually defined by a size greater than 10 cm, are rare and present

particular diagnostic, surgical, and therapeutic challenges. Their large size may be associated with locally advanced presentation and an increased risk of recurrence.

In a 2024 report by Laohawiriyakamol *et al*., the authors described a 24-year-old woman with a giant malignant phyllodes tumor measuring 59 × 53 × 26 cm and weighing 14.5 kg. The tumor showed tumor necrosis accounting for approximately 20% of the tumor volume and a high mitotic activity of 12 mitoses per 10 high-power fields (HPF). The authors noted that phyllodes tumors may usually measure up to 45 cm, whereas this case represented an exceptionally large form.

3.5. Surgery and Margins

Surgery is the main local treatment. Retrospective data emphasize the importance of the surgical margin status in the risk of recurrence. A real-world evidence meta-analysis identified margin status, stromal atypia and hypercellularity, stromal overgrowth, mitotic activity, and necrosis among factors associated with recurrence [8]. Other series suggest that a clear margin of at least 1 cm may be sought, although the exact optimal width remains debated [9, 10].

In our case, the closest peripheral margin was 1 cm and the deep margin was 2 cm.

3.6. Axillary Lymph-Node Dissection

Lymph-node metastases are uncommon in phyllodes tumors, and systematic axillary surgery is generally not recommended in the absence of documented nodal involvement [9-11]. Nevertheless, our patient underwent axillary lymph-node dissection, which was negative in all 24 nodes. This should be presented as a characteristic of the management of this particular patient rather than as a general indication.

3.7. Adjuvant Radiotherapy

The primary objective of adjuvant radiotherapy is to reduce the risk of local recurrence. Available data show a benefit mainly in terms of local control, without a clearly demonstrated overall survival benefit. It is particularly considered in large, high-grade malignant phyllodes tumors, tumors with close or positive margins, or after breast-conserving surgery.

The dose commonly used is 50 Gy in 25 fractions of 2 Gy to the chest wall after mastectomy or to the breast after breast-conserving surgery. A boost to the tumor bed may be added, particularly after breast-conserving surgery, to reach approximately 60–66 Gy to the tumor bed. Recent recommendations report an overall postoperative dose in the range of approximately 50–66 Gy depending on risk and the surgical context.

In our case, given the giant size of the tumor, grade III histology, stromal predominance, high mitotic activity, necrosis, and chondrosarcomatous differentiation, adjuvant radiotherapy to the chest wall was selected after mastectomy.

Table 2: Main literature data regarding adjuvant radiotherapy for phyllodes tumors

Study	Population	Radiotherapy	Main results
Zeng *et al*., 2015 – Meta-analysis	8 studies; borderline and malignant tumors	45–70 Gy according to the series; breast-conserving surgery or mastectomy	Reduced local recurrence risk, particularly after breast-conserving surgery; no clearly demonstrated overall survival benefit
Chao *et al.,* 2019 – Meta-analysis	17 studies, 696 patients	Breast-conserving surgery or mastectomy; variable protocols	Local recurrence: 8% with RT versus 12% without RT; substantial heterogeneity between studies, particularly related to margin status
Belkacemi *et al*.,	159 patients; borderline and malignant tumors	109 breast-conserving surgeries / 50 mastectomies; median dose 50 Gy (37–60 Gy)	Benefit in local control mainly observed after breast-conserving surgery
Pei *et al*., 2021	Borderline and malignant phyllodes tumors	50 Gy/25 fractions after mastectomy; 50 Gy/25 fractions + 10 Gy/5 fractions boost after breast-conserving surgery or mastectomy	RT mainly aims to improve local control
Association of Breast Surgery, 2025	Recommendations concerning phyllodes tumors	Breast-conserving surgery or mastectomy; 50–66 Gy	RT should be considered particularly in large (>5 cm), multifocal malignant tumors or tumors with high-risk factors

3.8. Chemotherapy

The role of chemotherapy in malignant phyllodes tumors remains limited and controversial. Available data are mainly retrospective and do not demonstrate a clear benefit of adjuvant chemotherapy after complete excision.

The regimens used are generally extrapolated from those used for soft-tissue sarcomas, particularly

doxorubicin-based combinations with or without ifosfamide [13]. Chemotherapy may be more strongly considered in recurrent or metastatic disease, particularly when the disease is not amenable to local treatment. Doxorubicin, alone or combined with ifosfamide, is among the most frequently reported regimens.

However, because of the rarity of the disease and the absence of randomized studies, no standard regimen has currently been established. In our case, no neoadjuvant or adjuvant chemotherapy was administered. Despite the histologically aggressive features of the tumor (grade III, extensive stromal component, 12 mitoses/10 HPF, necrosis, and chondrosarcomatous differentiation), complete excision was achieved with clear margins and 0/24 involved lymph nodes. The therapeutic strategy therefore consisted of surgery followed by consideration of adjuvant radiotherapy.

3.9. Prognosis and Follow-Up

The risk of local recurrence is higher in malignant forms and increases with several unfavorable histological characteristics. A meta-analysis including more than 9,000 cases confirmed a higher recurrence rate in malignant phyllodes tumors [8]. Malignant forms may also give rise to hematogenous metastases, particularly pulmonary metastases. Follow-up should therefore be prolonged and adapted to the individual risk. In our case, the initial staging work-up did not identify any definite secondary lesion.

3.10. Value of this Case Report

This case combines young age, exceptional tumor size, prolonged disease evolution, high-grade histology, high mitotic activity, necrosis, and chondrosarcomatous differentiation, with clear margins and no nodal involvement. The literature on phyllodes tumors with heterologous differentiation is based mainly on isolated cases and small series [17].

Table 3: Comparative table of selected published cases

Reference	Patient	Heterologous component	Reported treatment / Main message
Garcia *et al*., 1999 [5]	Case of malignant phyllodes tumor	Predominant chondrosarcoma	Excision; importance of exhaustive sampling
Vera-Sempere, 2003 [4]	37 years	Chondrosarcoma >80%	Excision; major chondrosarcomatous overgrowth
Warrier *et al*., 2015 [1]	50 and 53 years	Chondrosarcoma/osteosarcoma ± liposarcoma	Surgery; rarity and prognostic uncertainty
Patil Okaly *et al*., 2015 [6]	40 years	Osteosarcoma + chondrosarcoma	Wide excision; multiple heterologous differentiation
Atram *et al*., 2022 [2]	11 cases	Several heterologous sarcomas	Retrospective series; need for subtyping
Ko, 2023 [7]	52 years	Osteosarcoma + chondrosarcoma	Mastectomy; rare case with imaging data
Our current case	31 years	Chondrosarcoma	Mastectomy + axillary dissection; external-beam RT selected; grade III, 0/24 lymph nodes, clear margins

4. CONCLUSION

Malignant phyllodes sarcoma with heterologous chondrosarcomatous differentiation is an exceptional entity [1, 2]. Our case concerns a young patient with a grade III tumor characterized by stromal predominance, high mitotic activity, necrosis, and chondrosarcomatous differentiation, but with histologically clear excision margins and negative lymph-node dissection. Complete surgery and expert pathological assessment are central to management. Adjuvant radiotherapy may be considered in malignant forms at high risk of local recurrence, but the available evidence remains mainly retrospective [11, 12]. Multidisciplinary decision-making and prolonged follow-up are recommended.

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