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CASE REPORT

Multidisciplinary management of phyllodes tumor: A case report and comprehensive approach from diagnosis to treatment

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ABSTRACT

Phyllodes tumors are rare fibroepithelial tumors, accounting for 2% to 3% of these neoplasms and less than 1% of all breast tumors. The standard treatment for localized disease is surgical intervention with wide margins, ideally more than 1 cm, which significantly improves local control and reduces recurrence rates. This case report describes the diagnostic and therapeutic challenges encountered in managing a 46-year-old patient with a malignant phyllodes tumor. We discuss the multidisciplinary approach required for optimal management, including surgical techniques, and the controversial roles of radiotherapy and chemotherapy. The report underscores the necessity of personalized treatment plans and highlights the importance of accurate diagnosis and tailored therapeutic strategies to improve outcomes in these rare and complex tumors.

Keywords: Phyllodes tumor; Surgery; Prognosis; Breast neoplasm; Fibroepithelial lesion.

Introduction

Phyllodes tumors (PT) are rare in breast tissue, ranging from benign, similar to fibroadenomas, to malignant forms capable of developing metastasis. Although initially called "cystosarcoma phyllodes" in the 19th century, these tumors are distinct from sarcomas both in origin and behavior [1,2]. They constitute less than 1% of all breast tumors and around 2-3% of fibroepithelial neoplasms of the breast, with a higher prevalence in women aged 35 to 45 years. Within the general population, an annual incidence of 2.1 cases per million people is recorded, being more frequent among Asian and Latina women[3,4]. Histologically, PTs are characterized by their biphasic structure, including epithelial and stromal components. According to classifications by the World Health Organization (WHO) since 1982, PTs are divided into benign, borderline, and malignant[3,5]. Given the low frequency of this pathology, there are few studies on its etiology and risk factors. Its pathogenesis is not yet fully understood, but a relationship between PTs and Li-Fraumeni syndrome has been identified [6,7].

Surgery with wide margins is the standard treatment, with adjuvant radiotherapy and chemotherapy as options in selected cases. Participation in clinical trials is key due to the limited treatment options. Multidisciplinary collaboration is essential for optimal management, given the complexity of these tumors and their variability[8-11].

We describe the case of a 46-year-old patient with a malignant right breast PT. This case is unique due to the unusual clinical presentation where the initial biopsy suggested a borderline tumor, but subsequent pathology revealed malignant characteristics, highlighting the heterogeneity within the same tumor. Additionally, the surgical management was complicated by initial positive surgical margins, necessitating reoperation to achieve clear margins.

This case provides new insights into the management of malignant PT by demonstrating the importance of continuous and thorough pathological evaluation. It also emphasizes the need for a multidisciplinary approach, integrating surgical, radiological, and pathological expertise to effectively tailor treatment plans. The findings from this case support the need for individualized treatment strategies and may inform future clinical guidelines for the management of phyllodes tumors. This case also underscores the importance of multidisciplinary collaboration in managing malignant phyllodes tumors.

Case

A 46-year-old female patient, a smoker, perimenopausal, with no significant family history, presented with a 1-year history of a nodule in the right breast that had rapidly grown in the past month. Physical examination revealed a roughly 10 cm fibro-elastic right breast lesion, mobile, painless, without skin alterations or changes in the areola-nipple complex. There were no axillary lymphadenopathies or lymph node involvement in other areas.

Given the clinical presentation, mammography and breast-axillary ultrasound were performed, revealing a well-defined, dense 11 cm diameter nodule in the right breast **(Figure 1).** Ultrasound showed a polilobulated nodule with homogeneous echostructure and increased vascularity. No adenopathies were noted in the right axillary region. BIRADS 4 C.

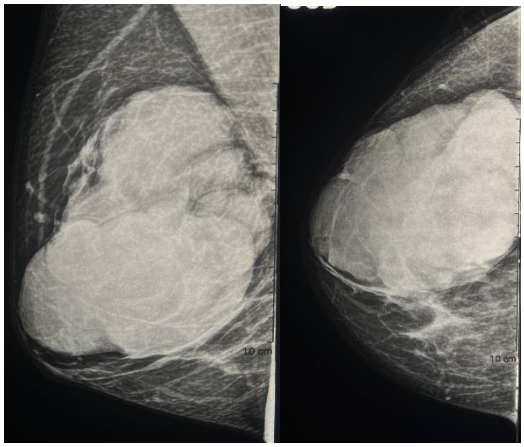

Figure 1 Mammography: polilobulated nodule in the right breast. BIRADS 4.

Upon diagnosis, the case was discussed in a multidisciplinary breast oncology panel, involving specialists in radiology, pathology, surgery, and medical oncology. The initial core biopsy revealed a fibroepithelial proliferation with stromal overgrowth featuring mild to moderate atypia of the stromal cells. It showed a mitotic count of up to 7 mitoses in 10 high-power fields, accompanied by scant epithelial elements without atypia. Diagnostic conclusion: Histopathological features consistent with a borderline phyllodes tumor.

Further regional assessment was completed using breast and axillary magnetic resonance imaging (MRI), which revealed a well-defined, mass-like enhancement with polilobulated contours occupying the right breast, measuring 11 cm x 8 cm in diameter. The mass contained cystic and solid areas. No axillary lymphadenopathies were identified. BIRADS 4 **(Figure 2).**

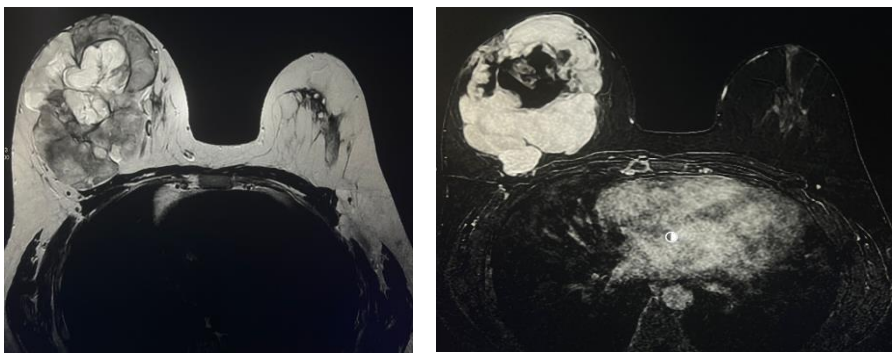

Figure 2: MRI showing a well-defined, mass-like enhancement with polilobulated contours in the right breast, measuring 11 cm x 8 cm in diameter.

The diagnostic evaluation was completed with distant staging using computed tomography (CT) of the chest, abdomen, and pelvis, which ruled out metastatic disease.

With the diagnosis of localized borderline phyllodes tumor and given that the breast-to-tumor ratio did not allow for conservative surgery with a good aesthetic outcome, a total right mastectomy was performed.

Pathology confirmed the diagnosis, describing macroscopically a tumor measuring 153 x 140 x 70 mm, weighing 1002 grams, and exhibiting myxoid and fleshy areas. The entirety of the specimen extensively contacted the margins **(Figure 3)**.

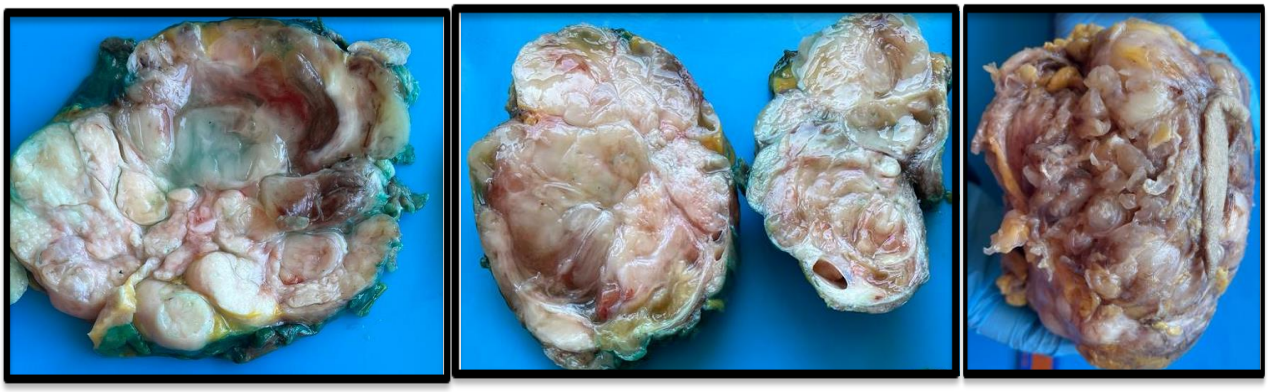

Figure 3: Specimen of the right breast tumor.

Under microscopy, the specimen showed biphasic cellular proliferation composed of spindle cells, with areas of high cellularity made up of atypical cells with eosinophilic cytoplasm, increased nuclear-cytoplasmic ratio, and cigar-shaped nuclei with fine chromatin. These nuclei surround and compress an epithelial proliferation formed by a double cell layer without atypical elements. A count of 15 mitoses was observed in 10 high-power fields.

Immunohistochemical study:
- AML positive for neoplastic cells
- AME positive for neoplastic cells
- Desmin negative for neoplastic cells
- CD34 positive for blood vessels and negative in areas of differentiation loss
- Ki67 at 80%
- S100 negative for neoplastic cells

Given the pathological report of positive margins, a surgical expansion of the margins was performed, resulting in a specimen without neoplastic remnants, associated with granulation tissue related to the previous surgical resection.

The case was discussed in a multidisciplinary breast oncology panel, and it was decided not to proceed with adjuvant chemotherapy or radiotherapy. Following the surgery, the patient remains under clinical and imaging surveillance, and breast reconstruction surgery will be planned.

Discussion

The diagnosis and management of PT pose unique challenges due to their low incidence. This type of neoplasm exhibits a predisposition primarily affecting women aged between 35 and 55 years, as evidenced in the current clinical case[3,4].

Although concomitance with fibroadenoma can be found in 20% of cases, or a previous history of fibroadenosis in 12.5%, no predisposing factors for phyllodes tumor have been identified, except for Li-Fraumeni syndrome [6,7]. The presented clinical case shows the disease manifesting de novo, without indicators suggesting its development in association with genetic risk.

Clinically, the patient presented with a rapidly growing breast nodule, in the absence of skin alterations or lymphadenopathy. It is important to note that secondary lymph node involvement is rare, representing less than 1% of cases, which is consistent with the findings in this clinical case [3,8].

The diagnosis of the breast lesion is based on breast and axillary ultrasound, mammography, with histopathological confirmation through biopsy. From an imaging standpoint, there are no pathognomonic features; the most common presentations are smooth and polilobulated masses on mammography, similar to breast ultrasound where lesions typically appear as solid, hypoechoic, and well-circumscribed, characteristics that match the lesion observed in the patient. Given that it was classified as BIRADS 4C, which indicates a high suspicion of malignancy, histopathological confirmation via biopsy is pursued. It is noteworthy that core needle biopsy is preferred for histopathological diagnosis, as fine needle aspiration biopsy carries a significant risk of false negatives, reaching up to 40% [11,12].

From a histological perspective, PT are categorized as benign, borderline, or malignant based on stromal atypia, mitotic activity, tumor margins, and the presence of excessive stromal growth. Benign PTs exhibit mild to moderate stromal atypia and low mitotic activity (less than 4 mitoses per 10 high-power fields), with clear, circumscribed margins and no excessive stromal growth. Borderline PTs have a higher degree of cellularity and stromal atypia, a mitotic rate of 4 to 9 mitoses per 10 high-power fields, microscopic infiltrative edges, and do not show excessive stromal growth. Meanwhile, malignant PT exhibit high atypia, more than 10 mitoses per 10 high-power fields, infiltrative margins, and stromal growth,

indicating aggressiveness. The excessive stromal growth suggests metastatic potential, including the possible transformation into various types of sarcomas, though conversion to sarcoma is very rare, with only about 30 cases reported since 1979. Liposarcoma is the most commonly observed type, and isolated cases of rhabdomyosarcoma and leiomyosarcoma have been documented. This classification directly influences the treatment and prognosis of the disease% [13-16].

In this case, the histopathological presentation revealed a borderline PT. However, the mastectomy specimen showed evidence of a malignant PT. This progression highlights the heterogeneity and progressive transformation of these tumors. The discrepancy between the findings underscores the gradual malignization across different areas of the tumor, evidenced by aggressive histological features and a high rate of cellular proliferation. This case emphasizes the need for thorough analysis and careful management, illustrating how different sections of the same tumor can vary in degrees of malignancy.

This case emphasizes the need for thorough analysis and careful management, illustrating how different sections of the same tumor can vary in degrees of malignancy. This underscores the importance of comprehensive and accurate evaluation for appropriate treatment.

Given that the primary pathway for disease dissemination is hematogenous, with a higher incidence in the lungs and an elevated risk in cases of malignant histology and to a lesser extent in borderline cases, a complete staging using chest CT is recommended. This procedure helps define subsequent treatment[1,16]. In the clinical case presented, the disease is localized in the breast region. To complement the locoregional evaluation, an MRI is performed, in which a well-defined, polilobulated lesion with cystic and solid areas inside is observed. No axillary lymphadenopathies are detected. This lesion is classified as BIRADS 4, consistent with previous imaging studies.

With a diagnosis of localized borderline PT, surgical treatment has been chosen as the preferred approach, as previously mentioned. Although evidence suggests that mastectomy does not provide a significant survival benefit compared to conservative surgery, the decision to perform a mastectomy is based on factors such as the size of the tumor and the ratio of the tumor to the breast tissue. In this particular case, the breast-tumor ratio determined that mastectomy was the treatment of choice for this patient. This decision underscores the importance of individualized treatment planning based on specific clinical and anatomical circumstances. The primary goal of surgery is to achieve negative margins, preferably 1 cm or more, as suboptimal or positive margins have been shown to significantly increase the risk of local recurrence, by approximately 21%. In the case of malignant or borderline tumors with positive margins following surgery, margin expansion is recommended, as was carried out in this clinical case. An alternative to surgery is adjuvant radiotherapy, both aimed at reducing the risk of local recurrence [17-20].

The patient in question did not undergo sentinel lymph node biopsy or systematic lymphadenectomy, as there was no formal indication for these procedures. This is due to the low risk of lymph node involvement, supported by the absence of clinical and imaging evidence of lymph node compromise [17-19].

There is limited evidence regarding the effectiveness of adjuvant chemotherapy. Some studies suggest potential benefits in tumors with a high risk of recurrence, especially those with lesions larger than 10 cm or in cases of recurrent disease. However, the evidence is not conclusive in terms of a significant increase in local control, reduction of recurrence risk, or improvements in survival. Therefore, the decision was made to offer the patient post-surgery follow-up instead of adjuvant chemotherapy[18,19].

The use of adjuvant radiotherapy remains a subject of debate. Two meta-analyses concluded that adjuvant radiotherapy in these patients reduces the risk of local recurrence in malignant and borderline tumors, although no benefit is observed in overall survival and disease-free survival[18,21].

It's important to note that, in this context, adjuvant hormone therapy does not play a significant role due to the limited presence of beta estrogen receptors in the stromal component of the pathology in question[22].

There are no specific follow-up guidelines for these patients; however, it is recommended to conduct clinical and imaging controls using ultrasound and mammography every six months during the first two years, and annually thereafter. This approach aims to detect any recurrence early, as there is a significantly higher incidence in the first two years following diagnosis, with reports indicating local recurrence rates of 30% and distant recurrence rates of 5% to 20% [4,9].

Conclusions

PT is a rare oncological entity with an unknown etiology, predominantly affecting women in their fourth decade. It typically presents as a unilateral, rapidly growing mass that can reach considerable sizes at the time of diagnosis. Differentiating it from fibroadenoma using fine needle biopsy is challenging, highlighting the importance of core needle biopsy for accurate diagnosis.

Given its rarity, the management of PT emphasizes the need for a multidisciplinary approach that integrates specialists in medical and radiation oncology, surgery, imaging, and pathology to optimize both diagnosis and treatment. This teamwork is essential to address the complexity of the disease, personalize therapeutic management, and improve clinical outcomes in this specific population.

The management of these tumors involves surgery with widely negative margins and, in specific situations, radiotherapy, given the significant likelihood of recurrence.

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