Malignant phyllodes tumor of the breast in a young patient – case report

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ABSTRACT

Phyllodes tumor (PT) is an uncommon form of breast tumor. It occurs most commonly in women aged 35 to 65 years. The benign form represents about 85–90% of cases and only 10–15% of PTs are malignant. Clinically and radiologically, malignant phyllodes tumor (MPT) presents as regular, well-delimited, mobile nodules that are difficult to distinguish from fibroadenomas of the breast. The most important differential diagnoses of MPT include fibroadenoma, metaplastic carcinoma, and sarcoma. The prognosis of MPT exhibits a higher frequency of local recurrence and metastatic rate with larger tumors and inadequate surgical margins. The case presented here refers to a 24-year-old female patient, with a vast tumor in the right breast, with rapid and progressive growth, associated to local pain, and histological diagnosis of MPT. Surgery was the initial treatment, followed by adjuvant chemotherapy and radiotherapy. The purpose of this article was to report an atypical case of MPT of the breast in a very young woman as well as to make a brief literature review on this infrequent and dangerous disease.

KEYWORDS: phyllodes tumor; malignant phyllodes tumor; breast neoplasm; case reports.

INTRODUCTION

Phyllodes tumor (PT) of the breast is uncommon, representing 0.3–1.0% of all breast neoplasms and 2.5% of all fibroepithelial breast tumors. The estimated incidence is 2.1 cases per million women. It occurs most commonly in women aged 35 to 65 years. The benign form represents about 85–90% of cases. Only 10–15% of PTs are malignant (MPTs), and only 10–26% of MPTs are found with metastasis.

The presence of a painless unifocal mass with a history of fast growth, reaching a large size, and in advanced age may be clinical findings favorable to the diagnosis of the PT. Tumor size can vary between 1–45 cm, with an average size of 4–5 cm, although MPTs can reach larger dimensions. There are no specific clinical manifestations to distinguish benign from malignant subtypes.

The World Health Organization classifies these tumors as benign, borderline, or malignant according to a combination of histological features, including stromal cellularity, nuclear atypia, mitotic activity, stromal overgrowth, and tumor margin.

Clinically and radiologically, they present as regular, well-delimited, mobile nodules that are difficult to distinguish from fibroadenomas of the breast.

Surgery is the standard treatment. Generally, local excision is performed for benign and small tumors, while total mastectomy is considered for borderline, large, malignant, and recurrent tumors. Overall, segmental resection with adequate margins is the treatment of choice. The role of radiotherapy and chemotherapy remains controversial. Adjuvant radiotherapy has been shown to increase disease-free survival in MPTs treated with segmental resection. However, available data on increased overall survival in the literature are inconclusive.

This article aimed to report a case of MPT of the breast in a very young woman as well as to make a brief literature review on this infrequent and dangerous disease.

CASE REPORT

This is a 24-year-old female patient referred for evaluation of a nodule in the right breast, with rapid and progressive growth, for about two months, associated with local pain. Nulligest, without comorbidities or use of medication, she had a history of bilateral reduction mammoplasty eight years ago. Family history revealed...
two maternal great-aunts with breast cancer. On clinical examination, the patient presented a bulging and voluminous nodule in the upper lateral quadrant (ULQ) of the right breast, measuring 8.0 x 6.0 cm, with fibroelastic consistency and mobile; and non-palpable axillary lymph nodes. Ultrasound image evidenced a large oval, regular, and circumscribed mass, containing aneugenic areas inside, measuring approximately 7.0 x 6.0 x 5.0 cm in the ULQ. Breast magnetic resonance imaging showed a solid-cystic, oval, heterogeneous nodule with indistinct margins, early enhancement, and predominantly peripheral, in the ULQ/axillary extension of the right breast, measuring 7.0 x 5.0 x 4.0 cm, without plane of clear cleavage between the nodule and the pectoralis major muscle, in addition to right axillary adenopathy - Breast Imaging Reporting and Data System (BI-RADS 4®).

A core biopsy of the lesion was performed, with anatomopathological findings: pleomorphic neoplasm with a tubulosarcomatoid disposition, with the possibility of a MPT. Subsequently, the patient evolved with rapid lesion growth, significant local pain, and skin suffering in the region of the lesion (Figure 1). Chest and abdomen tomography showed no relevant changes. Surgical treatment was indicated and, after discussing the case, the patient opted for conservative surgery. Thus, a partial mastectomy was performed, with resection of the tumor with margins of the pectoralis major muscle fibers due to tumor infiltration, and of enlarged lymph nodes in the right axillary region, associated with the creation of a glandular and cutaneous flap for closure (Figures 2 and 3). Anatopathological and immunohistochemical results revealed high-grade pleomorphic/spindle cell malignancy, with myogenic differentiation, measuring 7.5 x 7.0 x 4.5 cm, free margins, and absence of metastasis in the five dissected lymph nodes, with a probable diagnosis of MPT.

Finally, patient recovered well in the postoperative period, with preserved right upper limb mobility, and, after evaluation of clinical oncology, adjuvant chemotherapy with six cycles of doxorubicin and ifosfamide was indicated. Adjuvant radiotherapy was performed with a hypofractionated protocol of 15 sessions, and a concomitant boost in the surgical area (total dose of 40 Gy in the breast and 48 Gy in the operative site). Germline genetic panel was not performed. Before the chemotherapy treatment, the medical team discussed with the patient and a fertility preservation technique was performed, through ovulation induction with gonadotropins and oocyte collection for cryopreservation.
DISCUSSION

PT is a rare form of breast tumor. It was first described by Johannes Muller in 1838 and constitutes 0.3–1.0% of all breast tumors. MPTs are extremely rare and can imitate benign tumors such as fibroadenomas on clinical examination. The median age for presentation of MPT is 50 years old. Regarding histopathological aspects, PTs are defined as a group of circumscribed biphasic tumors, similar to fibroadenomas, composed of periductal stroma and ductal epithelium, with a double-layered foliar growth pattern with hypercellular stroma, characterized by pleomorphism and stromal overgrowth, infiltrative borders, and usual mitoses. Clinically, the most common finding is the breast lump — mobile and painless. Dilated veins can be seen overlying large PTs. Axillary metastases are uncommon, and most palpable axillary lymph nodes are reactive, not metastatic.

Diagnosis should preferably be made by histopathological study, obtained by core needle biopsy or excisional biopsy. Fine needle aspiration (FNA) does not provide the information necessary for a differential diagnosis. Due to the similarity of cytological features for benign PT and cellular fibroadenoma, these two biphasic fibroepithelial lesions cannot be properly differentiated on FNA. A PT with a bland stromal component can mimic a fibroadenoma; whereas a PT with a stroma that appears overtly sarcomatous can be challenging to differentiate from a sarcoma. MPT is defined by the combination of marked nuclear pleomorphism of stromal cells, stromal overgrowth, infiltrative borders, and usual mitoses. Clinically, the most common finding is the breast lump — mobile and painless. Dilated veins can be seen overlying large PTs. Axillary metastases are uncommon, and most palpable axillary lymph nodes are reactive, not metastatic.

Although PT is primarily treated by surgical excision, literature data demonstrate that all PTs can recur regardless of their histology, with lower incidences of recurrence evidenced in benign tumors and higher rates observed in borderline and malignant ones. Local recurrence (LR) rates vary by 15–40% among different types of PT. The risk factors most commonly associated with LR comprehend not only positive margins but also the existence of necrosis, stromal overgrowth, and a larger tumor size. No difference was found in terms of LR among patients undergoing mastectomy or breast-conserving surgery. Our patient underwent partial mastectomy and margins were free on anatomicopathological analysis. A large retrospective and multicenter study on MPT management demonstrated that a 3 mm margin threshold was appropriate, with no impact of larger margins on overall survival. Hence, they recommended re-excision to achieve wider margins in cases with 0–1–2 mm margins. The National Comprehensive Cancer Network (NCCN) guideline recommends wide excision with clean margins ≥1 cm for MTP. Axillary lymph node dissection showed no added benefit on the recurrence or disease-free survival in MPT. Most lymphadenopathy in MPT is usually either reactive to tumor necrosis or to infected ulcerated skin lesions, with less than 1% of pathological involvement.

The role of adjuvant radiotherapy in MTP is still controversial. Several studies have shown that radiation therapy is associated with reduced LR but did not have any impact on overall survival. The use of adjuvant chemotherapy is more questionable and its effect on PTs is doubtful. Adjuvant cytotoxic chemotherapy lacks evidence of benefits both for reducing LRs and for improving overall or disease-free survival. Owing to the low frequency of distant metastasis, only a small number of retrospectively analyzed cases have been reported and a treatment strategy for MPT has not been established. Nevertheless, it can be considered for large tumors, when adjacent structures such as the chest wall are involved, or unresectable distant metastasis. In these cases, chemotherapy regimens of soft tissue sarcomas are generally employed. NCCN guideline recommends anthracycline plus ifosfamide as the first line of treatment. Although pathologically, they express estrogen receptors in 58% and progesterone receptors in 75% of cases; endocrine therapy has not proven to be beneficial in the treatment of PTs.

The prognosis of MPT exhibits a higher frequency of LR (12–65%) and metastatic rate (up to 27%) with larger tumors and inadequate surgical margins. The most common spots for metastasis are the lungs, pleura, and bone. The 5-year survival is around 65%. Kapiris et al. reported a 5-year survival rate of 54% and a 10-year survival rate of 23%, with a significant association of results according to tumor size and surgical margins.

Germline genetic panel is not routinely ordered for patients with PT. The NCCN practice guidelines do not include PT as criteria for genetic counseling or as testing criteria for any of the known heritable cancer syndromes. Recently, in a multi-center contemporary cohort of 550 PTs, Rosenberger et al. found that roughly 10% of PT patients tested for germline cancer predisposition genes carried a deleterious mutation, similar to that seen among women with breast adenocarcinoma.

CONCLUSIONS

MPTs are rare entities. These tumors should be correctly recognized and effectively treated at first diagnosis since they have an elevated risk of recurrence. The PT diagnostic hypothesis should be raised in tumors with benign characteristics, rapid growth, and large dimensions. Accurate pathological classification of PTs is relevant to foresee the risk of recurrence and survival rate. Benign and borderline PTs have less aggressive disease behavior.
than MPT. Excision with adequate margins is the recommended therapy. There is no stated consensus concerning the optimal type of surgery and indications for radiotherapy and chemotherapy in these cases. The establishment of adequate and standardized therapeutic strategies for MPTs is needed to reduce the risk of local and distant tumor recurrence.

**AUTHORS’ CONTRIBUTION**

CFH: Conceptualization, Investigation, Methodology, Supervision, Validation, Visualization, Writing – review & editing. ACOP: Investigation, Validation, Writing – review & editing. JPSS: Formal analysis, Investigation, Writing – original draft. ITR: Formal analysis, Investigation, Writing – original draft.

**REFERENCES**