Malignant Phyllodes Tumor of the Breast with Isolated Brain Metastasis: A Case Report of an Intriguing Aggressive Subtype

Abstract

Phyllodes tumors are rare breast tumor types and comprise 0.3%–1.0% of all breast tumors. They usually manifest in 35–55-year age group and are classified into benign, borderline, and malignant types based on the histopathological features. Certain cases of malignant tumors behave in an aggressive manner with an unpredictable and often dismal outcome. The present case report addresses such a scenario in a very young female who showed a rapid appearance of brain metastatic disease. We describe this case and present a brief literature review.

Keywords: *Aggressive, brain metastatic, breast tumor, phyllodes tumor*

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Introduction

Phyllodes tumor (PT) is a rare fibroepithelial neoplasm representing roughly 0.3%–0.9% of all breast cancer in women.[1] Historically known as cystosarcoma phyllodes owing to the leaf like projections, it appears histologically as a combination of hyper cellular stroma and cleft-like spaces lined by epithelium.[2] PT is classified as benign, borderline and malignant.[3] Majority of PT are benign/borderline with surgery as the mainstay of management. However, the malignant subtype, representing 10%–30% cases[1] have the potential to recur locally and/or metastasize.[3] The modes of tumor metastasis are primarily through blood and rarely through lymph nodes with the common metastatic sites being the lung, soft tissue, bone, and pleura.[4] Borderline and malignant PT metastasis rate is about 25%–31%, while the overall rate of all PT metastasis is 4%.[4] Central nervous system involvement by PT is very rare and usually occurs late in the course of the disease.[5] Literature review suggests that brain metastases almost always occur in the setting of multiorgan involvement rather than isolated.[5] The subtype of malignant PT that is prone for metastasis is still not clear and requires further understanding for better tumor control.

Case Report

An 18-year-old female, a proven case of malignant PT presented to our department after undergoing three surgeries for a right breast recurrent mass. She was referred for adjuvant radiotherapy (RT) for the recurrent nature of the lesion. At presentation, she was in a good general condition with an Eastern Cooperative Oncology Group performance score of one.

History of presenting illness

The patient had a 10-month history of a painless lump in her right breast, approximately, 3 cm × 3 cm in size, firm in consistency and progressive in nature. She had undergone a lumpectomy with a wide local excision (WLE) for it. Microscopy showed circumscribed breast mass with exaggerated stromal component. Stroma was hypercellular and comprised of bizarre spindle cells with angulated, pleomorphic hyper chromatic nuclei. Multinucleated giant cells were also noted and the mitotic activity was high [Figure 1]. Overall, the histopathological (HP) report was suggestive of a malignant PT with negative resection margins. She was initially put on follow-up, however, after one and half months, she had recurrence of the lump in the right breast, approximately 4 cm × 4 cm in size and associated with pain. A breast ultrasonography (USG) was performed and was suggestive of an ill-defined heterogeneous hypoechoic mass lesion measuring 4.1 cm × 3.2 cm × 3 cm diffusely involving whole quadrant of the right breast showing few cystic areas and significant interval vascularity with few septation

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and internal echoes. She further underwent a simple right mastectomy. HP revealed breast tissue with tumor composed of proliferating predominantly spindle cells and pleomorphic cells with nuclear atypia with increased mitosis and fair number of tumor giant cells [Figure 2]. Skin, areola, nipple, and posterior margins were free from malignancy. Final report was consistent with malignant PT. In view of the recurrent setting, she was advised adjuvant RT by the surgeon, but she defaulted for the same. After a 2 months' period, the patient again presented with a painful lump along the scar mark, measuring 2 cm × 2 cm in size which was excised again. The histology revealed soft tissue with tumor composed of mesenchymal element groups of spindle cells with slight nuclear variation [Figure 3]. It was consistent with recurrent PT and she was referred to our department for adjuvant RT.

Course

At presentation, the patient was largely asymptomatic and in a fit general condition. Local examination had revealed healed scar of prior surgical intervention. Her baseline hematological, chest X ray, and abdominal USG findings were well within normal limits. She was planned to receive external beam RT to the chest wall region using cobalt-60 gamma rays to a total dose of 5000 centigray/25 fractions. The patient was undergoing treatment uneventfully but after 10 fractions she had sudden onset of headache, vomiting, and weakness of right upper and lower limbs. Her neurological examination revealed grade 1 power in right upper and lower limbs with absent deep tendon reflexes. She underwent an urgent computerized tomography scan that revealed multiple multiloculated thick hypodense lesions in the left frontoparietal region with gross surrounding edema and compression of ipsilateral ventricle causing midline shift, suggestive of brain metastases [Figure 4]. Interestingly, her X ray chest, USG whole abdomen and whole body bone scan did not reveal any abnormality. The patient was hospitalized and managed with supportive therapy aimed at reducing intracranial tension that comprised of steroid administration and further planned to receive whole brain RT and adjuvant chemotherapy (CT) for her metastatic disease. However, she succumbed to the disease due to neurological complications.

Discussion

The lesions in breast PT are often unilateral, single, nodular, painless masses with an insidious onset and slow progression. The usual presenting history is that of painless masses growing rapidly. Tumor volume varies widely and sizes <1 cm up to 40 cm have been reported.[6] The World Health Organization has established the diagnostic criteria for benign, borderline, and malignant PT based on the tumor cell atypia, excessive growth, mitosis, and tumor boundary.[7] However, not all malignant tumors recur or metastasize while some borderline tumors do. Various studies have reported the local recurrence (LR) rate at around 20% regardless of histological classification.[8] Potential factors associated with an increased LR are tumor size, positive surgical margins, stromal overgrowth, high mitotic count, and necrosis[9-11]

The biggest challenge that is faced by the treating oncologist is to predict which patient would develop LR, metastatic disease or both. Primary treatment for PT tumor is surgical with a WLE being the treatment of choice.

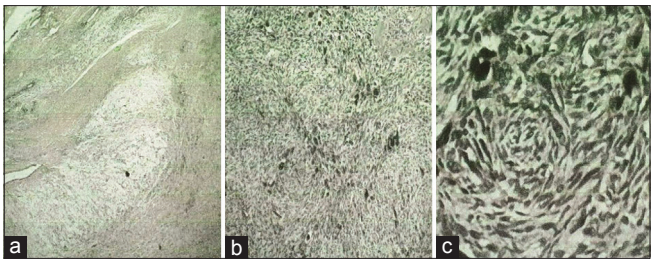

Figure 1: First surgery histopathology showing (a) slide scanner view (b) H and E ×10 and (c) H and E ×40 showing hypercellular stroma composed of spindle cells and hyper chromatic nuclei

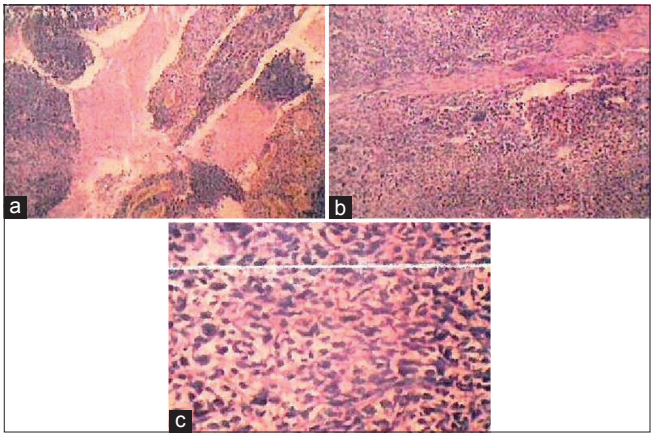

Figure 2: Second surgery after one and half months histopathology showing (a) Slide scanner view (b) H and E ×10 and (c) H and E ×40 showing breast tissue with spindle cells and pleomorphic cells tumor giant cells

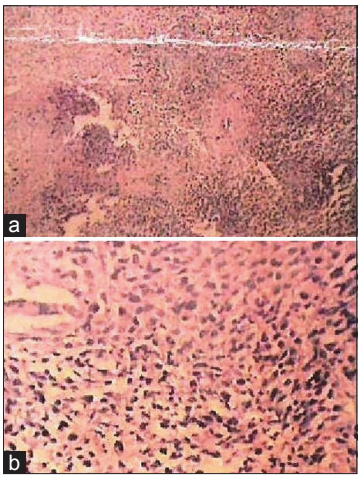

Figure 3: Third surgery, 2 months after the second histopathology showing (a) H and E ×10 and (b) H and E ×40 showing soft tissue composed of mesenchymal spindle cells

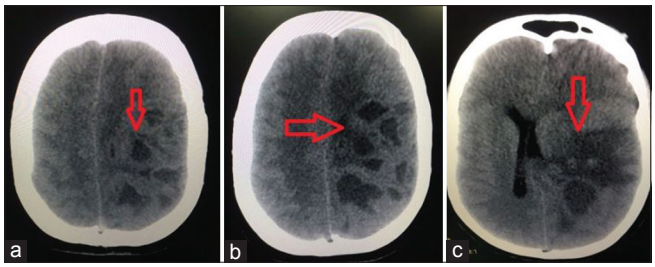

Figure 4: Multiple metastases in the left frontoparietal region (a and b) with gross surrounding edema and compression of ipsilateral ventricle causing midline shift (c)

If margins of 1 cm cannot be attained then a simple mastectomy is the next best option. Margins of 1 cm are equivalent to mastectomy results in terms of overall survival.[12] In general, borderline tumors metastasize but the incidence has been reported to be as low as 4%[13] On the other hand, malignant PT is prone to metastases and the incidence has been reported to be between 9 and 32%.[3] The presentation of brain metastases in PT is usually late and is often associated with poor response to treatment. Literature reveals a mean survival of merely around a month, in contrast to a 2-year survival at other sites.[5,14] In the present case, the presenting age (18 years) was much less than that reported in literature (35–55 years)[3] and the patient developed isolated brain metastases while being on local RT.

The concept of adjuvant treatment in PT is still not very clear. In a study by Morales-Vásquez *et al*.,[15] the use of postoperative adjuvant doxorubicin and dacarbazine treatment versus no treatment did not confer any statistically significant survival. However, on the lines of soft tissue sarcoma and as evidenced by limited data, it appears to be a reasonable option to offer adjuvant CT to patients with large (>5 cm), high-risk or recurrent PT.[3] Turalba *et al*.[16] have reported some efficacy with doxorubicin and ifosfamide-based CT in metastatic PT but level 1 evidence is still not available. Narayan *et al*.[17] reported a case of malignant PT with chondro and osteosarcomatous differentiation who developed lung metastasis within 2 months of surgery. After three cycles of palliative CT including ifosfamide, adriamycin, and cisplatin, her lung metastasis cleared completely.

Hormonal therapy is also not effective in PT despite the presence of positive hormone receptors. The possible understanding is the fact that hormone receptors are a component of the epithelial aspect of the tumor whereas the metastatic behavior is owing to the stromal aspect of the tumor.[18] Although our patient was planned to receive adjuvant CT in light of the aggressive metastatic chain of events, she did not survive to that point.

The definite role of adjuvant RT for the various subtypes of PT is also not clearly defined. Few studies have stressed the significance of adjuvant RT in patients undergoing local resection of tumor size >2 cm and mastectomy of tumor size >10 cm.[19] Pandey *et al*.[11] reported a significant 5 years disease free survival and Belkacémi *et al*.[20] reported an improved 10-year local control rates with adjuvant RT in borderline and malignant PT groups, but it did not affect overall survival. In a recent meta-analysis, Zeng *et al*.[21] assessed the efficacy of adjuvant RT for borderline and malignant PT in the context of either a breast conservation surgery (BCS) or total mastectomy. Their results demonstrated a benefit of adding RT following BCS in patients with borderline and malignant PT in terms of decreased LR. However, the combined hazard ratio for LR in the total mastectomy group did not demonstrate that adjuvant RT was superior to no RT. No significant differences were observed in overall survival or disease-free survival between the two groups. The analysis further suggested that adjuvant RT for borderline and malignant PT decreased the LR rate in patients undergoing BCS but does not exert an effect on overall or disease-free survival.

Conclusion

There are different reports regarding the HP features, and surgical procedures of breast PT that are closely linked with the recurrence, appropriate surgical management, and adjuvant RT for the high-risk cases seems to be a reasonable approach. However, there is an aggressive subtype, yet undefined that fares poorly despite the management in accordance with the current norms. Our patient presented in a very young age and rapidly progressed to brain metastasis ultimately succumbing to it. Our report and similar such reports in literature mandate a thorough research in identifying the aggressive variants of breast PT and formulating appropriate management for the same.

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Conflicts of interest

There are no conflicts of interest.

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