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Malignant Phyllodes Tumor with Heterologous Osteosarcomatous Differentiation and Osteoclast-like Giant Cells: A Case Report of an Uncommon Neoplasm

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ABSTRACT

Background: Phyllodes tumor (PT), an uncommon fibroepithelial neoplasm accounts for less than 1% of all primary tumors of the breast. MPT with osseous differentiation often gets misdiagnosed on imaging as benign giant calcifications resulting in treatment delay. We describe a rare case of MPT with heterologous osteosarcomatous differentiation and osteoclast-like giant cells and review the literature to discuss clinical-radiological findings, differential diagnosis and treatment options.

Case Presentation: A 34-year-old female presented with a right breast lump. Mammography showed a high-density irregular mass with amorphous dense calcification, suggesting neoplastic etiology. Preoperative core needle biopsy raised the possibility of a phyllodes tumor versus a giant cell tumor. A wide local excision was performed to confirm the diagnosis, which revealed the presence of a biphasic tumor with an osteoid-like matrix and numerous osteoclastic giant cells. Immunohistochemistry was used to rule out metaplastic carcinoma or carcinosarcoma. The stromal cells were negative for panCK and P63 and positive for vimentin, CD10 and BCL-2. The osseous component was positive for Osteonectin and SATB2. Thus, a final diagnosis of malignant phyllodes tumor with heterologous osteosarcomatous differentiation and osteoclast-like giant cells was made.

Conclusion: MPT with osteosarcomatous differentiation is a rare and challenging entity associated with a poor clinical outcome. Accurate diagnosis requires a multidisciplinary approach involving breast surgeons, pathologists, and radiologists, along with careful histopathological examination. Wide local excision with close surveillance is crucial for the timely detection of tumour recurrence and metastasis.

INTRODUCTION

Phyllodes tumor (PT), an uncommon fibroepithelial neoplasm accounts for less than 1% of all primary tumors of the breast.[1] PT is classified as benign, borderline, or malignant based on several histopathological features like stromal cellularity, atypia, overgrowth, tumor border and mitotic index. Malignant phyllodes tumor, comprising 8-20% of PT cases, exhibits rapid growth and aggressive behavior resulting in local recurrence, and distant metastasis.

Presence of a heterologous sarcomatous component is sufficient to diagnose malignant phyllodes tumor, regardless of all the above parameters.[2] The stromal component may show transformation to liposarcoma, angiosarcoma,

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chondrosarcoma or rarely to osteosarcoma. MPT with osseous differentiation often gets misdiagnosed on imaging as benign giant calcifications resulting in treatment delay.[3] Timely management and better prognosis of patients is dependent on a strong clinical and radiological suspicion coupled with correct histopathological diagnosis.

This study describes a patient diagnosed with malignant phyllodes tumor with heterologous osteosarcomatous differentiation and osteoclast-like giant cells. Only a handful of MPT exhibiting osteosarcoma components have been reported in the literature, making this case report valuable.

CASE PRESENTATION

A 34-year-old female presented with a painless lump in her right breast that had been rapidly increasing in size over the preceding few months. On physical examination, a large mobile mass with hard consistency was palpated in the lower outer quadrant of right mammary tissue. Mammography revealed a partly circumscribed high-density irregular mass measuring 55x43x29mm with amorphous dense calcification in the retroareolar region, suggestive of neoplastic aetiology (Figure Ia-Ib).

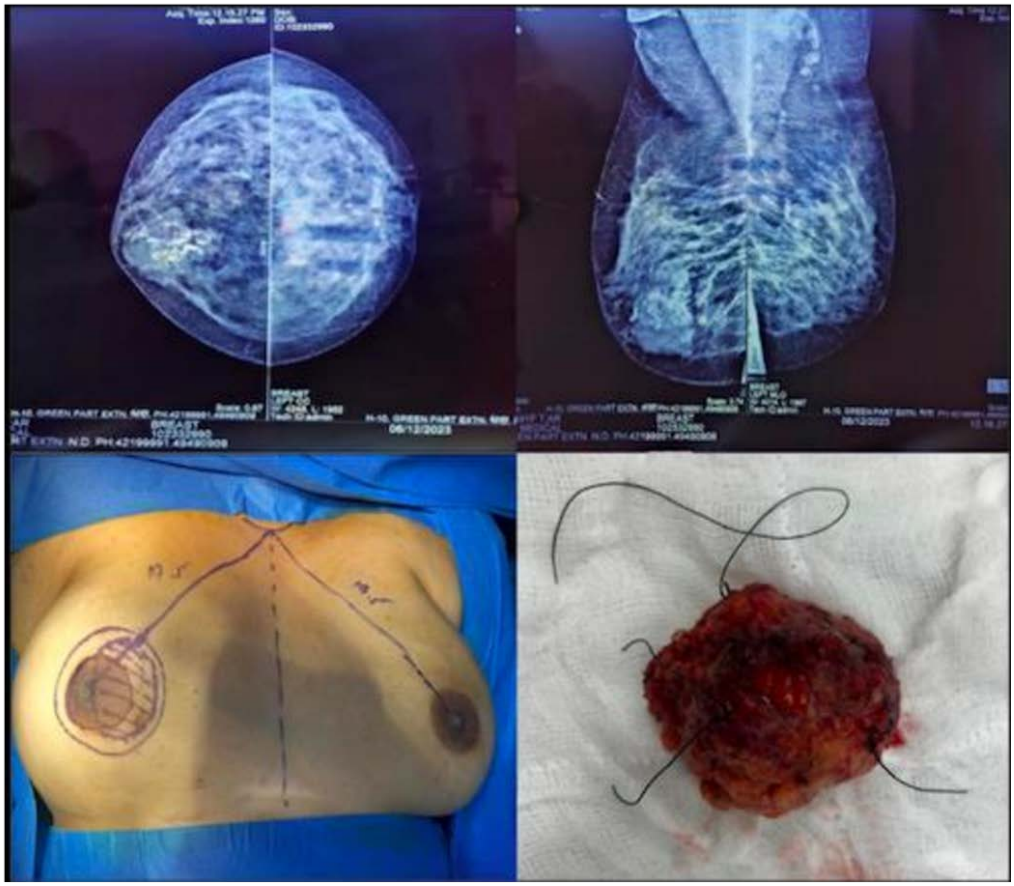

Figure 1. 1a-1b: Mammography (a-craniocaudal view, b-mediolateral oblique view) revealed a partly circumscribed high density irregular mass measuring 55x43x29mm in the retroareolar region of the breast. Amorphous dense calcifications can be seen within the mass. 1c: Pre-operative image of the right breast. 1d: Gross image of the wide local excision specimen measuring 6x6x5.5cms in size.

A core needle biopsy was performed and histopathological examination showed stromal hypercellularity and an abundance of osteoclast-like giant cells raising the possibility of phyllodes tumor versus giant cell tumor of the breast. For confirmation of diagnosis, the patient underwent a wide local excision with clear margins.

On gross inspection, the specimen measured 6x6x5.5cms in size (Figure Ic-Id). The cut section revealed a hard grey-white tumor measuring 5.5x4.5x3cms with large areas of calcification. Microscopy showed the presence of a focally infiltrative stromal tumor exhibiting large areas of eosinophilic, lace-like osteoid matrix with osteoblastic rimming and abundant osteoclastic giant cells. The tumor showed moderate stromal cellularity and cellular atypia with a mitotic rate of >10/10hpf (Figure IIa-IIe). Extensive sampling revealed epithelial components with a leaf-like pattern resembling phyllodes tumor, thereby excluding the possibility of primary osteosarcoma.

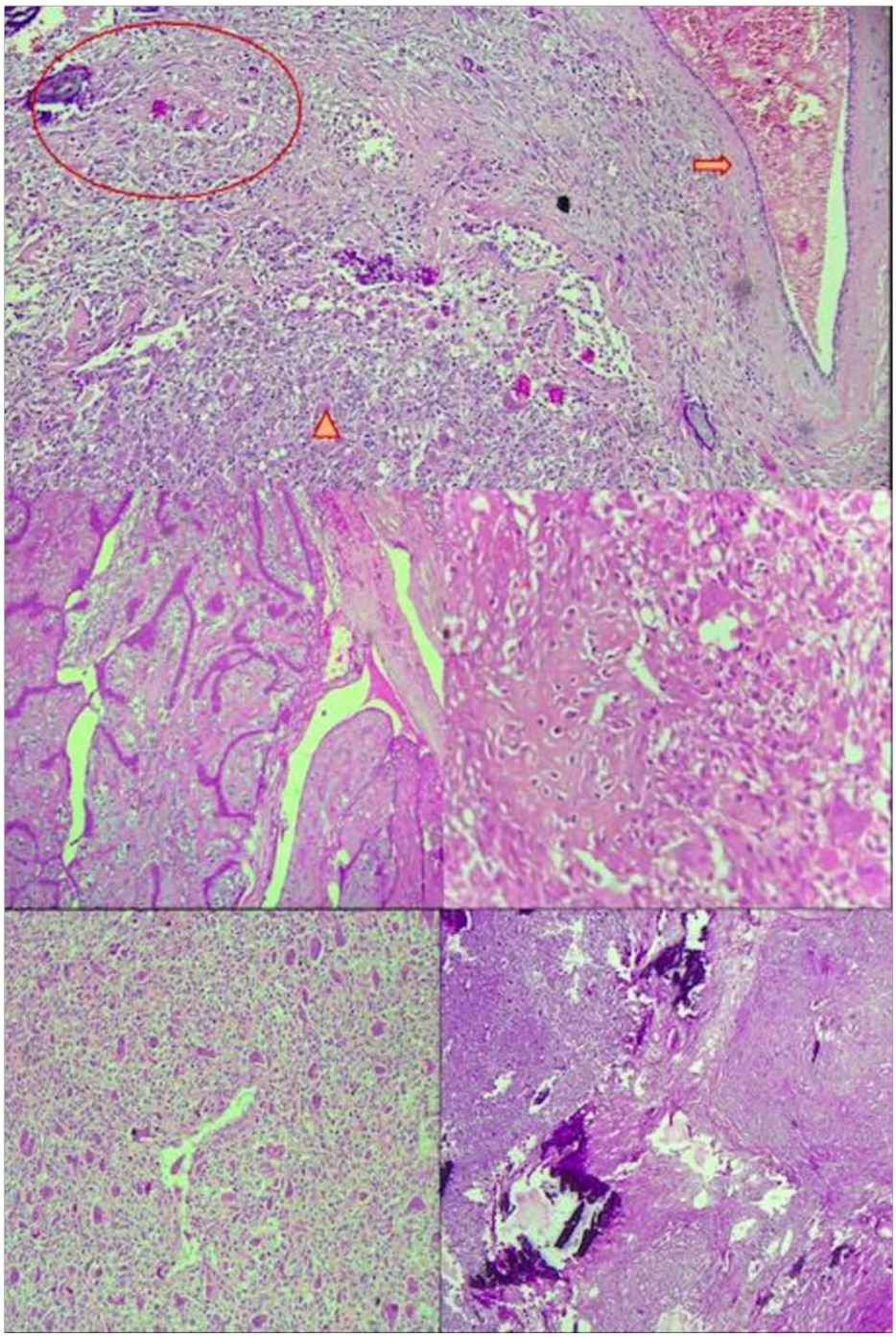

Figure 2. Hematoxylin and eosin staining of the resected specimen. IIa- Stromal tumor exhibiting focal epithelial pattern (arrow) with eosinophilic, lace like osteoid matrix showing osteoblastic rimming, calcifications (circle) and abundant osteoclast-like giant cells (arrowhead) (100x). IIb- Epithelial leaf-like proliferation reminiscent of phyllodes tumor (100x). IIc- Lace like osteoid matrix (400x) IId- Stromal cells with numerous osteoclastic giant cells (100x). IIe- giant calcifications (100x).

A panel of immunohistochemistry markers was ordered to rule out metaplastic carcinoma or carcinosarcoma. On IHC, stromal cells were positive for vimentin, CD10 and focally for BCL-2. The osseous component was positive for osteonectin and SATB2 (Figure IIIa-IIId). The tumor cells were negative for panCK and P63 (Figure IIIe-f).

Thus, a final diagnosis of malignant phyllodes tumor with heterologous osteosarcomatous differentiation and osteoclast-like giant cells was made. All the resected margins were free of tumor. The patient did not undergo axillary lymph node dissection. The tumor was staged as pT2NxM0 as per the AJCC 8th edition and the WHO recommendations.[2,4]

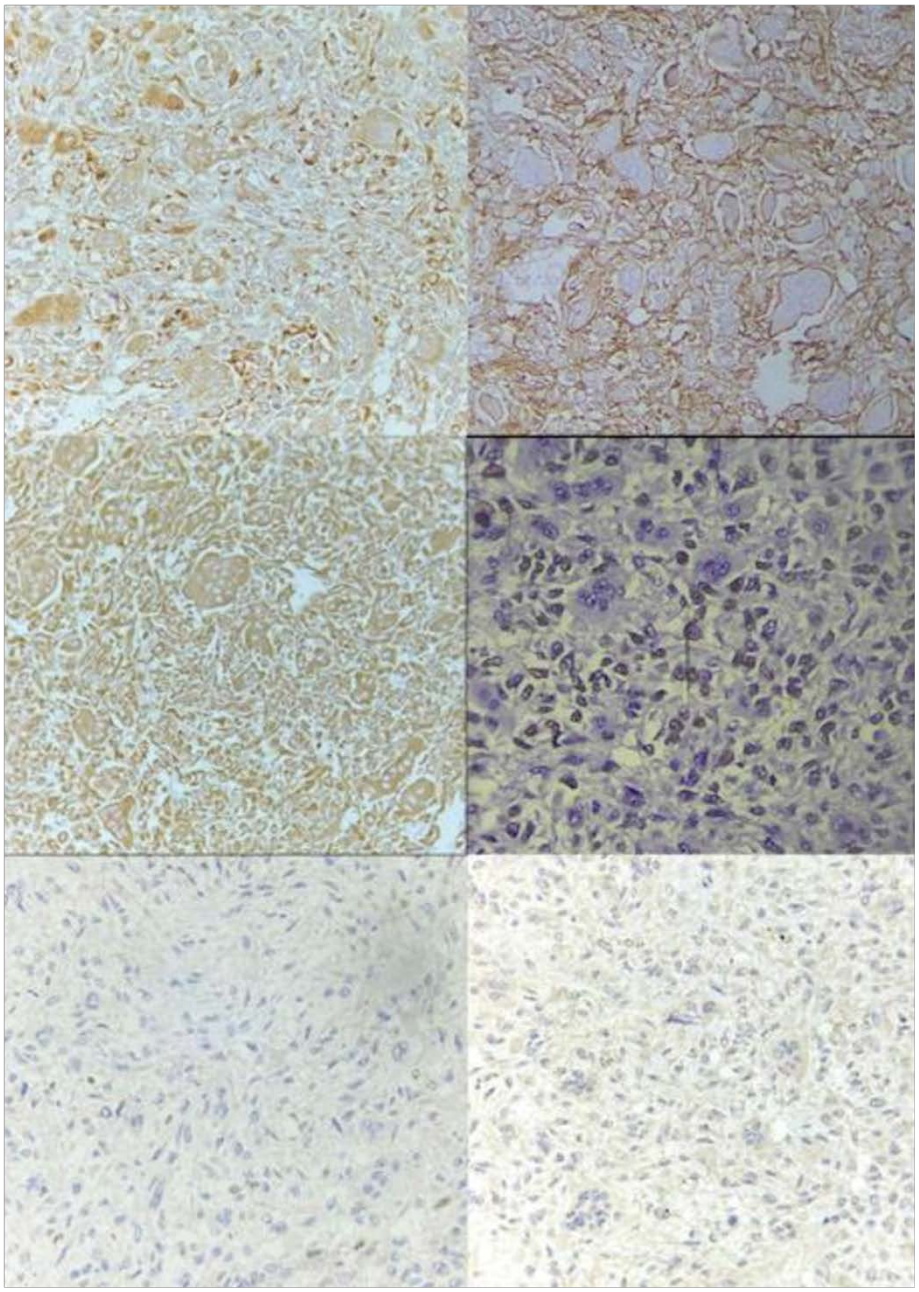

Figure 3. Immunohistochemistry: Positive markers (400x). a-Vimentin diffuse cytoplasmic positivity, b-CD10 membranous positivity, c-Osteonectin diffuse cytoplasmic positivity, d-SATB2 focal nuclear positivity. Negative markers (100x): e-panCK, f-p63

DISCUSSION

Malignant phyllodes tumor is a rare entity that poses several diagnostic and therapeutic challenges. It usually presents as a unilateral mass with an average size of 4-5 cm. Larger tumors (> 10 cm) may distort the mammary architecture and cause skin ulceration due to pressure effects and ischemia. [2] PT is primarily seen in older women (40-50 years), but our patient was aged 34 which was similar to a case reported by Jha N *et al.*[5] Osteosarcomatous transformation of MPTs is extremely uncommon, accounting for 1.3% of breast phyllodes tumors. The proportion of osseous component is variable and may replace the entire tumor tissue.[6]

The imaging profile of phyllodes tumor is variable and prediction of tumor grade on radiology alone is unreliable. MPT tends to display an irregular shape on radiology as opposed to good circumscription in the benign category. Calcifications are not a common finding associated with PT. According to a study by Lee JS *et al.*, coarse and amorphous calcifications suggest a benign process, whereas the presence of linear and branched calcifications is indicative of malignant lesions.[7] The mammography findings of our patient showed a partly circumscribed mass and coarse calcifications. A rapidly increasing mass coupled with suspicious radiology substantiated the need for a confirmatory biopsy.

Table 1. Brief summary of clinicopathological characteristics of cases diagnosed as MPT with osteosarcoma differentiation in the last three years

Author, year	Age	Laterality	Radiology	Surgery	Size (largest dimension)	Heterologous element	Mitotic rate	Necrosis	Lymph node status	pTNM stage	Recurrence/Metastasis
Present study	34 yrs	Right	partly circumscribed high density irregular mass with amorphous dense calcification	WLE	5.5cms	Osteosarcomatous transformation with osteoclast-like giant cells	>10/10hpf	absent	negative	pT2Nx	absent
Li W et. Al. 2024 [14]	59	Left	Hypoechoic irregular mass in the left upper quadrant, of size 23x25x19mm	Mastectomy and SLN biopsy	3.0cms	Osteosarcoma and chondrosarcoma differentiation	10/10 hpf	absent	negative	pT1N0M0	absent
Ko SY et. al. 2023 [15]	52 yrs	Right	Heterogenous solid and cystic mass with coarse and amorphous calcifications (BIRADS 6)	MRM with axillary LN dissection	7cms	Osteosarcoma and chondrosarcoma components	>10/10 hpf	absent	Suspicious on imaging, Negative on histology	NA	absent
Jha N et. al. 2023 [5]	32 yrs	Left	Large irregular hypoechoic with partially circumscribed margins (BIRADS IVb)	Total mastectomy	10 cm	Osteosarcoma originating from MPT	NA	absent	Clinically palpable, Negative on histology	pT4N0	absent
Hall RR et. al. 2023 [11]	63 yrs	Left	Calcified lobulated mass with calcifications	Lumpectomy, Revised Mastectomy post recurrence	Initial size: 1.5cms Recurrence: 5.5cms	Osteosarcomatous differentiation	5/10hpf	absent	Negative on radiology	pT1Nx	Local recurrence 18 months post lumpectomy
Liu R et. al. 2023 [6]	57 yrs	Right lung	Soft tissue density mass in the upper lobe on CT	Right superior lobectomy	5.0cms	Metastatic MPT with osteosarcoma component in a known case of breast MPT with pleomorphic liposarcomatous component	>10/10hpf	present	Hilar nodes free of tumor	NA	Present, right lung
Jin Y et. al. 2021 [3]	59 yrs	Left	Hyperdense nodule with irregular borders (BIRADS IV)	WLE	5.5 cms	Osteosarcoma with osteoblast component	NA	absent	Negative on radiology	NA	absent

Correct diagnosis with preoperative tissue biopsy prevents secondary surgical interventions. However, owing to the biphasic nature and marked heterogeneity of MPT, sensitivity of core needle biopsies is low. Research has reported the use of larger needle diameters and taking at least three samples from the lesion to improve accuracy.[8] In our patient, biopsy raised the differential diagnosis of phyllodes tumor versus giant cell tumor (GCT) due to the presence of numerous interspersed osteoclast-like giant cells. Due to the heterogeneous nature of phyllodes tumor, surgical excision with clear margins was planned for confirmation of diagnosis. Primary GCT arising from the soft tissues of breast is extremely rare. Presence of an epithelial component, stromal hypercellularity, cellular pleomorphism and osteoid matrix ruled out the diagnosis of this rare entity in our case.[9]

Several parameters are used to categorise phyllodes tumor as benign, borderline and malignant. Despite moderate stromal cellularity and atypia, our case was diagnosed as malignant due to the presence of the ostesarcomatous component, which is according to the criteria mentioned in WHO.[2] Furthermore, MPT may predominantly comprise sarcomatous components on histopathology, making

its diagnosis extremely challenging. In such cases, a thorough sampling of different areas of the tumor is warranted to identify epithelial structures indicative of phyllodes tumor. Our case showed a preponderance of osteoid matrix with rimmed osteoblasts and numerous osteoclastic giant cells raising the possibility of primary extraosseous osteosarcoma. Numerous samples were taken to visualise ductal and leaf-like structures and arrive at a correct diagnosis. Metaplastic carcinoma, an important differential consideration of MPT, was excluded using pan CK and P63 immunohistochemistry markers in our patient.

MPT with osteosarcomatous transformation has been linked with poor clinical outcomes and a biological behavior similar to its soft tissue sarcoma counterpart. These tumors hold a great propensity for local recurrence and distant metastasis.[10] The mesenchymal stem cell niche is considered responsible for metastatic spread via hematogenous route. Distant metastasis has been reported in nearly all internal organs, but the lung is the most common site.[10] A comprehensive review conducted by Hall RR. *et al.* on phyllodes tumor with osteosarcomatous transformation reported metastatic spread in 52% with majority exhibiting lung metastases.[11] Kapiris *et al.* found an increased incidence of local recurrence (12-65%) and metastatic spread (up to 27%), especially in tumors with large sizes and inadequate surgical margins.[12]

There is no consensus on the optimal management of MPT. NCCN 2020 guidelines recommend excision with a margin of ≥10 mm for borderline and malignant phyllodes tumors (MPT) to reduce the incidence of tumor recurrence.[13] Tumor size and a negative margin status are considered to be the most reliable predictors of recurrence.[10]

Lymph node involvement is relatively uncommon in MPT; thus, axillary lymph node dissection is not routinely performed for such patients which was similar to our case. The role of adjuvant therapy for cases displaying heterologous sarcomatous elements remains controversial due to limited evidence.[10,12] Our patient opted for surgery with regular follow-up using imaging studies and has not reported recurrence or metastasis to date.

A summary of clinicopathological characteristics of cases diagnosed as MPT with osteosarcoma differentiation in the last three years is provided in Table 1.

CONCLUSION

MPT with osteosarcomatous transformation is a rare and challenging entity associated with a poor clinical outcome. The aggressive nature of this subtype underscores the importance of a multidisciplinary approach involving breast surgeons, pathologists and radiologists to optimize patient care and prognosis. A careful histopathological examination and immunohistochemistry evaluation aid in accurate diagnosis of high-grade PT. We presented a unique case of MPT with osteosarcomatous differentiation and osteoclast-like giant cells diagnosed on a wide local excision specimen. Close surveillance is crucial in such patients for timely detection of tumor recurrence and metastasis.

ETHICAL CONSIDERATIONS

The patient provided written informed consent to publish the information and images contained in the case report.

CONFLICT OF INTERESTS

None to declare.

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None.

DATA AVAILABILITY

All data relevant to the study are included in the article

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