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Case Report

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Malignant Phyllodes Tumour of the Breast with Liposarcomatous Differentiation: A Rare Case Report

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Abstract

Background: Phyllodes tumours (PTs) are rare fibroepithelial neoplasms of the breast, constituting less than 1% of all breast tumours. Among these, malignant PTs with heterologous sarcomatous differentiation, particularly liposarcomatous transformation, are exceedingly uncommon and pose significant diagnostic challenges. ***Case Presentation:*** We report the case of a 55-year-old woman who presented with a painless, mobile breast lump initially suspected to be a benign lesion. Imaging suggested a lipoma, but fine-needle aspiration cytology revealed atypical cells, prompting surgical excision. Histopathological examination confirmed a malignant phyllodes tumour with liposarcomatous differentiation. Immunohistochemistry showed S100 positivity and was negative for MDM2 and CDK4, supporting the diagnosis and excluding primary breast liposarcoma. The patient subsequently underwent a left mastectomy, with no residual tumour detected and remains under close follow-up without recurrence. ***Conclusion:*** This case underscores the importance of integrating clinical, radiological, histopathological, and immunohistochemical findings in diagnosing rare variants of malignant PTs. Recognizing liposarcomatous differentiation within PTs is critical, as it influences prognosis and helps differentiate them from primary breast sarcomas.

Keywords: ***Malignant phyllodes tumour, Liposarcomatous differentiation, Immunohistochemistry, Breast.***

Introduction

Phyllodes tumours (PTs) are uncommon fibroepithelial tumours of the breast and constitute less than 1% of malignant breast lesions [1]. They are rapidly growing tumours that originate from peri-ductal stroma and are made up of both epithelial and stromal components [2]. These tumours can be classified into benign, borderline or malignant based on the histopathological features such as atypia, mitotic activity or overgrowth in the stroma, however all PTs have the potential to become malignant and their behaviour cannot be predicted based on the histological appearances [3].

PTs are typically solitary lesions, but they may coexist with other breast malignancies. Notably, malignant differentiation may arise from both the epithelial and stromal components. Carcinomas both invasive and in situ can arise from the epithelial component, while the stromal component may give rise to sarcomas such as angiosarcoma, chondrosarcoma, leiomyosarcoma, osteosarcoma, and rhabdomyosarcoma rarely [4]. Malignant PT exhibiting heterologous differentiation is rare, when this occurs, most often is a liposarcomatous differentiation [5]. Primary liposarcoma should be clearly distinguished from liposarcomatous differentiation in a PT.

We hereby present the case of a 55-year-old woman who was diagnosed with a malignant phyllodes tumour of the breast that contained liposarcomatous elements.

Case presentation

A 55-year-old female with no family history of breast malignancy came to us with the complaints of lump in the left breast for the past one month which was non progressive and was otherwise asymptomatic. On clinical examination she was found to have a freely mobile well-defined lump of size 2x2cm in upper outer quadrant of the left breast, right breast and bilateral axilla were unremarkable. Digital mammogram revealed punctate calcification in upper outer quadrant of left breast, small well circumscribed iso to hyperechoic oval mass at 2 o'clock position in the subcutaneous plane with an impression of? lipoma - BIRADS 2 lesion (**Figure 1**). Core needle biopsy done at an outside hospital was reported as? stromal tumour /? lipoma. Patient underwent Ultrasound guided Fine needle aspiration cytology of the lump which showed the presence of atypical cells (**Figure 2**). In view of increased cellularity and nuclear atypia, patient was advised excision. She then underwent Wide local Excision of the left breast lump, which was removed with 2cm margins and sent for histopathological analysis. Grossly, the lump was nodular, and cut surface revealed "cut cabbage appearance". Biopsy report showed Malignant stromal neoplasm suggestive of Malignant phyllodes with liposarcomatous elements, all margins free of tumour with marked stromal cellularity; focal areas of liposarcomatous change with occasional lipoblasts were seen (**Figure 3,4**). Immunohistochemistry showed S100 positive (**Figure 5**), CK, CD34 (**Figure 6**), p63 negative. The tumour cells were also negative for MDM2 and CDK4 which ruled out the possibility of a liposarcoma. Patient had no signs of any distant metastasis. The case was discussed in a Multi-disciplinary Team meeting and the patient then underwent Left mastectomy. Further histopathological analysis revealed no signs of residual tumour and surrounding fibrocystic changes. The patient has been on close follow-up and has no complaints till date.

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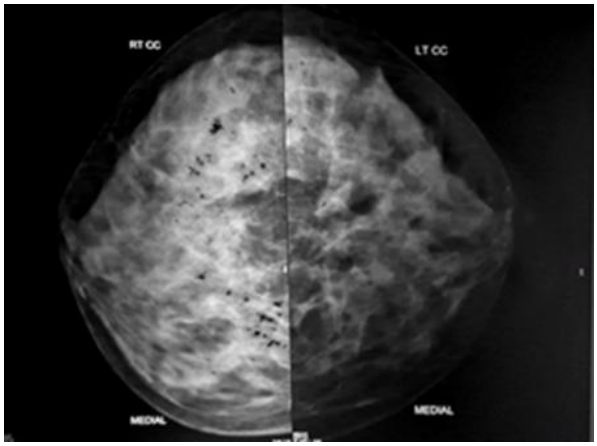

Figure I: X- ray mammogram showing punctate calcifications in upper quadrant of left breast, BIRADS 2 lesion

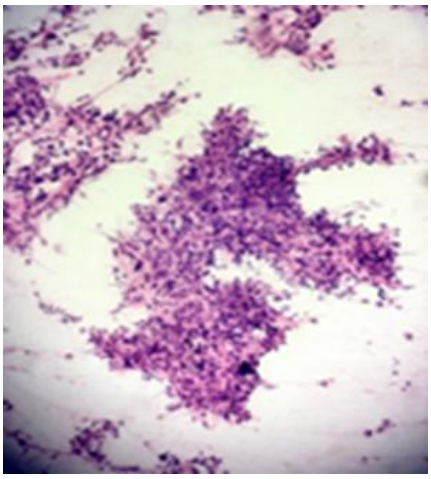

Figure II: Fine needle aspiration cytology showing Atypical cells

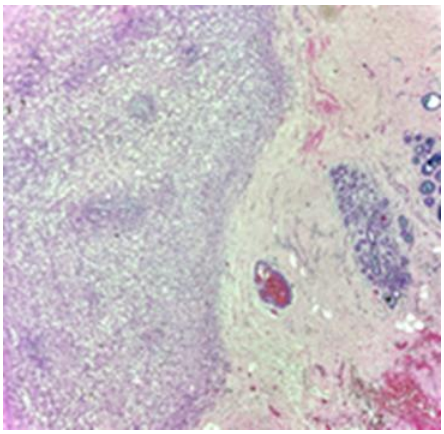

Figure III: Biopsy showing malignant stromal neoplasm with liposarcomatous elements

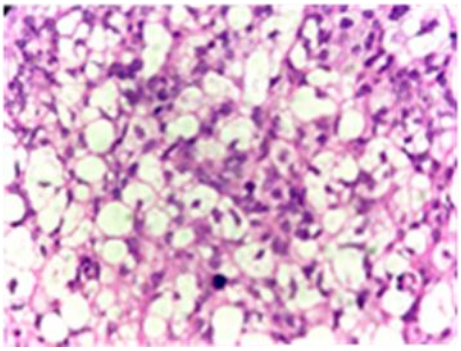

Figure IV: Focal areas of liposarcomatous change with occasional lipoblasts seen

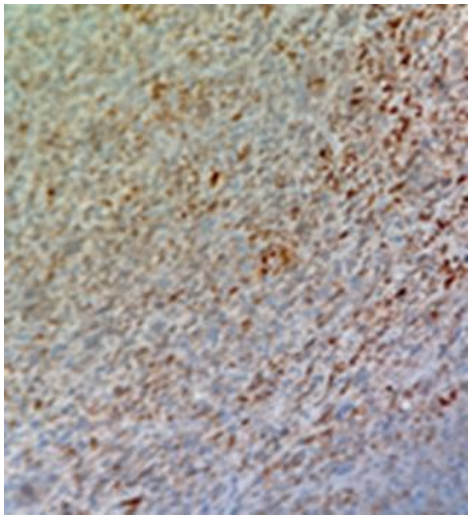

Figure V: Tumour cells stain negative for S100

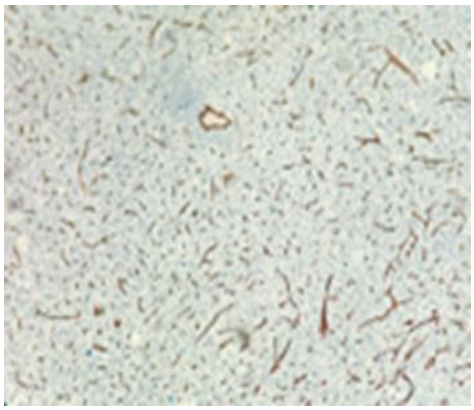

Figure VI: Tumour cells - negative for CD34

Discussion

Phyllodes tumours are rare fibroepithelial neoplasms of the breast, accounting for less than 1% of all breast tumours [1]. These commonly present as rapidly growing painless lumps and are mostly encountered in the upper outer quadrant [9]. Based on histopathological characteristics, such as tumour margins, mesenchymal cell numbers, interstitial cell atypia, mitotic activity, interstitial overgrowth, and malignant heterogeneous elements, the World Health Organization classifies PTs into benign, borderline, and malignant categories [10]. Malignant PTs are quite rare and account for only 0.3-0.5% among all breast tumours and usually occur in women between 35 and 55 years of age. These tumours are characterised by the presence of heterogenic differentiation, stromal cellularity, nuclear pleomorphism, interstitial overgrowth, and more than 10 mitoses figures per 10 high-power fields (HPF) [9]. However, the presence of a malignant heterologous component places the tumour into the malignant category regardless of other histological features [6].

Recent data have revealed that malignant PTs tend to display features of mesenchymal stem cells with the ability to be induced to or may spontaneously undergo differentiation to other lineages [8]. Several theories have been proposed to explain the pathogenesis of malignant phyllodes tumours with heterologous components. One hypothesis suggests that these tumours arise from the differentiation of pluripotent stem cells, accompanied by a loss of stromal dependency on the epithelial component. Additionally, malignant transformation within the metaplastic stromal component has also been implicated as a potential mechanism for heterologous differentiation in Malignant PTs [12]. Heterologous sarcomatous

transformation is extremely rare and very few cases have been reported, which included liposarcoma, angiosarcoma, osteosarcoma, rhabdomyosarcoma, fibrosarcoma, etc [13]. Clarifications in the pathological diagnosis and classification of this complex group of tumours have facilitated more accurate categorization by distinguishing them from other, even rarer, breast tumours such as spindle cell metaplastic carcinoma and primary breast liposarcoma which are two of the most challenging differential diagnoses [7].

Distinguishing between phyllodes tumours and fibroadenomas can be challenging, requiring a thorough pathological evaluation that integrates histologic features, immunohistochemical staining, and precise clinical information to achieve an accurate diagnosis; as in our case where our patient presented with a freely mobile lump in the upper outer quadrant which clinically pointed towards a fibroadenoma or a subcutaneous lipoma. Studies have demonstrated that fibroadenomas typically appear homogeneous and hypoechoic on ultrasound, while PTs present as complex and heterogeneous masses. Notably, 50-77% of PTs exhibit posterior acoustic enhancement on ultrasound. Furthermore, the high density of these lesions observed on mammography are often associated with larger tumour size and may serve as a useful indicator suggestive of PTs.

There are only few published reports describing the differentiation of malignant PT combined with liposarcoma, highlighting the significance of our case. The mainstay of treatment for malignant PT remains Wide local resection with adequate margins or Total mastectomy. However, in recent years, breast conservative surgery has proven to be a suitable option. Surgical margins were found to be an important factor for predicting recurrence and most studies suggest 10 mm as the optimal margin [11]. There is no consensus on the role of adjuvant radiotherapy for such cases and previous studies have shown no added benefit with RT when adequate surgical excision has been performed.

Malignant PTs with liposarcomatous changes may be confused with primary liposarcoma of the breast. Despite the similarity in clinical presentation, phyllodes tumours with liposarcomatous differentiation generally have a more favourable prognosis compared to primary breast liposarcomas which are extremely rare. In distinguishing malignant PT from primary breast liposarcomas, the presence of a characteristic leaf-like architecture is a key histological feature. Recent studies have emphasized the diagnostic value of immunohistochemical markers such as MDM2 and cyclin-dependent kinase 4 (CDK4). Malignant phyllodes tumours with liposarcomatous differentiation generally lack amplification of these markers, in contrast to primary breast liposarcomas, which often demonstrate amplification of both. Consistent with these findings, our case also showed negative immunostaining for MDM2 and CDK4, supporting the diagnosis of malignant phyllodes tumour with liposarcomatous differentiation.

Liposarcoma may arise de novo, although this is less common than liposarcomatous overgrowth associated with phyllodes tumours. In malignant phyllodes tumours, the lipomatous component often exhibits morphological features resembling well-differentiated and pleomorphic liposarcoma subtypes seen at extramammary sites [6]. Liposarcomatous differentiation in phyllodes tumours may consist of well differentiated, myxoid, round cell, and pleomorphic liposarcomatous elements [14]. To avoid misdiagnosis, a diagnosis of primary liposarcoma should only be considered after thorough histological sampling has excluded an underlying phyllodes tumour. While differentiating between these two entities can be histologically challenging, current evidence suggests their clinical behavior is largely comparable [5].

Conclusions

We present a rare case of malignant PT with liposarcomatous differentiation diagnosed and surgically managed in our Institute. Diagnosis of this tumour should be established using a combination of clinical, pathological, and immunohistochemical staining results. The main treatment for malignant PT is extensive local resection or total mastectomy. This case highlights the need for awareness of such rare histological variants and reinforces the role of complete surgical excision with negative margins as the cornerstone of management.

Abbreviations

PT: Phyllodes tumour
CK: Cytokeratin
CD34: Cluster of Differentiation 34
MDM2: Murine Double Minute 2
CDK4: Cyclin-dependent kinase 4
HPF: High Power Fields

Declarations

Ethics approval and consent to participate

Written informed consent was obtained from the patient. Ethics committee approval was not required.

Consent for publication

I on behalf of all co-authors, hereby give my consent for publication of the manuscript in your esteemed journal.

Availability of supportive data

If needed, we give consent to provide supplementary Data.

Competing Interests

None

Funding Statement

None

Author’s contributions

Kirthika Arunachalam was involved in data collection and drafting the manuscript, Prof Mohanapriya Thyagarajan and Dr Kishor were involved in reviewing, editing and finalising the manuscript

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None

Conflict of interest

The authors have no conflicts of interest to declare

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