

Case Report

Diagnosis and management of liposarcomatous differentiation in a phyllodes tumor: a rare clinical conundrum

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ABSTRACT

The solitary variant of rapidly growing large breast masses consisting of both epithelial and stromal components with no nodal involvement is called a phyllodes tumor and they are rare neoplasms of the breast. They constitute about 1% of all breast masses, with a slightly higher incidence in the Asian population. Although 10-30% of phyllodes tumors eventually undergo malignant transformation, which can either be in the epithelium or the stroma. However, heterologous transformation of phyllodes is an extremely rare entity. Here, we reported the case of a 60-year-old woman with an expeditiously growing breast mass for six months, which on biopsy raised a suspicion of malignant mesenchymal neoplasm. The patient underwent mastectomy with axillary sentinel lymph node biopsy (SLNB) and the final histopathological and immunohistochemistry examination revealed a phylloides tumor with a pleomorphic variety of liposarcomatous differentiation. Even with a typical mammographic appearance, liposarcomatous differentiation in phyllodes tumors can present a diagnostic dilemma on histopathology. Axillary sentinel lymph node biopsy (SLNB) forms a middle path in such cases of diagnostic challenge, which not only avoids the unnecessary morbidity of axillary lymph node dissection but also, at the same time, addresses the axilla in case the final histopathology shows evidence of invasive carcinoma.

Keywords: Cystosarcoma phyllodes, Liposarcomatous differentiation, Malignant transformation, Sentinel lymph node biopsy

INTRODUCTION

The term 'cystosarcoma phyllodes' was used for the first time by Johannes Muller in 1838 to describe a neoplasm of breast comprising of a double-layered epithelial component arranged in clefts surrounded by hypercellular mesenchymal tissue to form a structure organized like a leaf.¹ Phylloides tumor is a rare neoplasm of the breast, comprising approximately 0.3% to 1.5% of all breast neoplasms in the western population, with Asian women having an increased incidence of 6.92%.² They present as a locally aggressive, rapidly growing large

breast mass without any axillary node involvement and are classified into benign, borderline, and malignant types on the basis of histological features.³ Usually they present as solitary, benign lesions composed of both epithelial and stromal components originating in the peri-ductal stroma and presence of both types of cells is necessary for diagnosis.⁴

About 10-30% of phylloides tumors can undergo malignant transformation, which is commonly seen in the stromal component that routinely follows fibrosarcomatous differentiation.⁵ The malignant

transformation of the epithelial component demonstrating both invasive and in situ carcinoma is also known. Heterologous differentiation in a phylloides tumor is a rare entity, which can have an associated lobular or ductal carcinoma component also. It therefore becomes very difficult for the clinician to decide whether to go for axillary dissection along with the mastectomy or not.

Here, we reported the case of a 60-year-old woman who presented to us with a rapidly growing breast mass with an initial histopathology dilemma between a lobular carcinoma and a malignant mesenchymal neoplasm, and by doing so, we also opined on how to approach this clinical conundrum.

CASE REPORT

A 60-year-old woman presented to the department of surgical oncology with complaints of a progressive, painless right breast lump for the past six months without any nipple discharge, skin changes, other lumps in the same or opposite breast, or history of weight loss. On clinical examination, a firm, non-tender, well-defined mass of size 5×3 cm was present in the lower inner quadrant of the right breast, which was not fixed to the underlying muscle or to the overlying skin without any nipple discharge or skin changes. There was no palpable breast lump elsewhere or axillary lymph nodes. Bilateral mammography suggested a large, well-circumscribed, hyperdense oval lesion in the lower inner quadrant of the right breast with smooth margins and a surrounding halo. Contrast-enhanced computed tomography (CECT) of the abdomen was grossly unremarkable. A core biopsy with subsequent histopathological examination revealed variably sized adipocytes, signet ring cells and bizarre looking spindle cells and bands of fibrotic stroma containing enlarged, hyper chromatic nuclei, thus suggesting either a signet ring cell/pleomorphic variant of lobular carcinoma or a malignant mesenchymal neoplasm. After a thorough pre-anaesthetic check-up, the patient underwent a right mastectomy with wide local excision of all the involved skin, along with SLNB of the axillary lymph nodes using methylene blue dye intraoperatively. Three lymph nodes were detected on SLNB and sent for frozen section analysis. All three lymph nodes were found to be reactive in nature. No further axillary lymph node dissection was done. The final histopathology revealed a phyllodes tumor with liposarcomatous differentiation without any evidence of metastatic spread to any of the resected axillary lymph nodes after SLNB (Figure 1). As shown in Figure 2, immunohistochemistry (IHC) evaluation revealed the positivity of the epithelial component for PanCytoKeratin. Also, few lipoblasts and the mature adipocytic component in the stroma showed positivity for S-100, which is consistent with the pleomorphic variety of liposarcoma. So, the final diagnosis of a liposarcomatous differentiation in a phyllodes tumor without any axillary metastasis was established. The patient was discharged in healthy condition without any

plan for further adjuvant therapy. The patient had been kept on active surveillance since six months after surgery and was asymptomatic without any radiological evidence of disease recurrence.

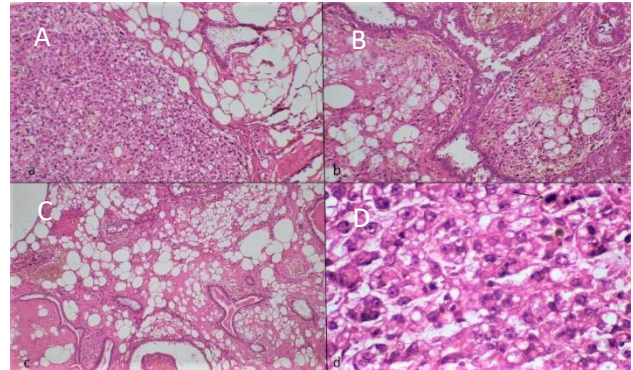


Figure 1: (A) sections show prominent stromal hypercellularity, atypia and over growth (H and E, ×4); (B, C) sections show mild epithelial hyperplasia and stromal hypercellularity with lipoblasts (H and E, ×10); (D) black arrow depicting mitosis (H AND E, ×40).

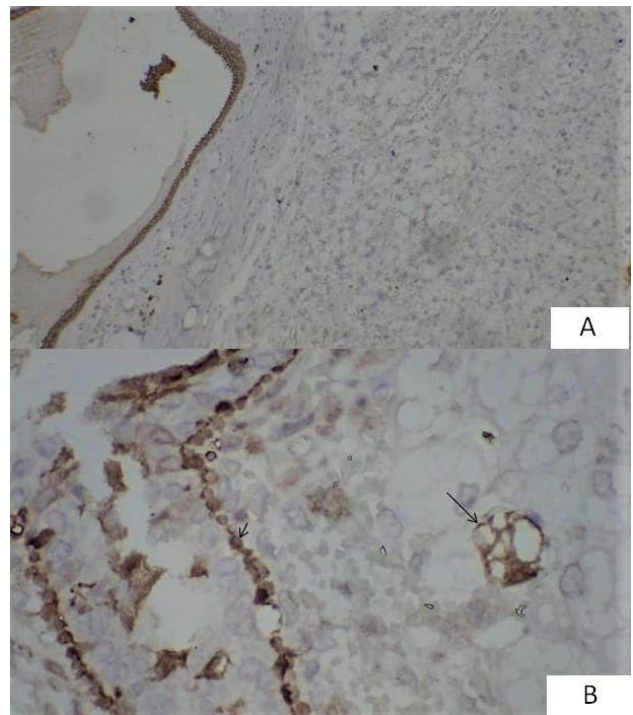


Figure 2: Immunohistochemistry showing (A) PANCK positivity in the epithelial component (PANCK, ×40). (B) S-100 positivity in lipoblasts and the myoepithelial component of the lining epithelium (S-100, ×40).

DISCUSSION

Phylloides tumors are usually found in middle-aged women, most commonly detected in the 4th and 5th decades, but can be found in all age groups, even in

adolescents.⁶ Clinically, they present as a firm or hard, painless, rapidly growing mass with an average size of 1-5 cm, but can even grow as big as 20 cm.⁷ They are not encapsulated but are well circumscribed masses. The malignant variant is typically larger and can invade the chest wall or ulcerate the skin.⁶

On mammography, they present as round, circumscribed, high density masses with the margin demonstrated by a lucent halo representing the fat component. Due to rapid growth, calcifications are seldom found in this tumor.⁸ On ultrasonography, they exhibit hypo-echoic internal echo and posterior acoustic enhancement with the detection of cystic spaces, indicating a malignant potential.⁹ Apart from cystic spaces, non-circumscribed margins, irregular shape, and a diameter of more than 7 cm may point towards a more borderline and malignant variety.¹⁰

Most of the grading systems, like the one by Treves et al were three-tiered, classifying these neoplasms as either benign, borderline, malignant or low, intermediate and high grade.¹¹ Histological features which were suggestive of an aggressive phyllodes tumor included higher grade, infiltrative borders, high mitotic count, excessive stromal overgrowth, stromal atypia, tumor necrosis, pseudo-angiomatic stromal hyperplasia, heterologous stromal elements and fibro-proliferation in the surrounding breast tissue.¹² While histological features can point towards malignancy, they cannot conclusively determine the nature of the neoplasm and one parameter alone cannot be relied upon in all cases. In terms of chromosomal aberrations, an increasing frequency of genetic changes has been noticed while progressing from benign to borderline to malignant variants. Most of the previous research had focused on stromal alterations and has demonstrated recurrent copy number gains and losses at +1q, -13q, -6q, +5 and -10p loci, including a probable role of the Wnt2-APC-B-catenin pathway.^{13-15,16}

A variety of malignancies can be associated with phylloides tumors due to the dual population of cells. Mesenchymal malign differentiation can be in the form of angiosarcoma, chondrosarcoma, leiomyosarcoma, osteosarcoma, rhabdomyosarcoma, and liposarcoma, with liposarcomatous differentiation being the most common.¹⁷ Liposarcomatous differentiation can be of three types: well differentiated myxoid, round cell, or pleomorphic type. Similar to our case, in a case of the pleomorphic variant reported by Isotalo et al the histopathology demonstrated lipoblasts, hyperchromatic, scalloped nuclei and vacuolated cytoplasm.¹⁸

Wide local excision with tumor free margins of 1 cm was the recommended treatment for phyllodes tumor with very little evidence documenting the need for chemotherapy or hormone therapy.¹⁹ Also, axillary nodal dissection was not advocated for the management of phyllodes tumor. Post-wide local excision, local recurrence is seen in 10-40% of malignant phyllodes tumours and distant metastases were present in

approximately 20% of malignant phyllodes tumors. To an extent, local recurrences and metastasis were determined by the grade of the tumor.⁴

In our case, due to the diagnostic dilemma between the pleomorphic variant of lobular carcinoma and a malignant mesenchymal tumor as per histopathology, it was imperative to address the axilla. At the same time, axillary SLNB was done along with mastectomy, thus obviating the unnecessary axillary dissection and resultant increased morbidity, but also not leaving the axilla unaddressed.

It is crucial to note that a malignant phyllodes tumor with a liposarcomatous change does not portend a worse prognosis and does not imply a more aggressive tumor. Completely excised tumors with adequate margins have very few recurrences.¹⁹ But prognosis after the diagnosis of metastatic phyllodes is poor when compared with benign entities. In a paper by Reinfusset et al, it was reported that 5-year disease-free survival rates were 96% in benign phyllodes tumor and 66% in malignant phyllodes tumor.¹⁴

CONCLUSION

Liposarcomatous differentiation is a very rare case scenario in phyllodes tumors, which are rare fibro-epithelial neoplasms of the breast. Even with a typical mammographic appearance, there can be a diagnostic dilemma on histopathology. Axillary SLNB forms a middle path in such cases of diagnostic dilemma, which not only avoids the unnecessary morbidity of axillary lymph node dissection but also, at the same time, addresses the axilla in case the final histopathology shows evidence of invasive carcinoma. They are rare tumors, and there is a paucity of data regarding the adjuvant management of such cases.

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