Case Report

Malignant phyllodes tumor with chondro and osteosarcomatous differentiation and secondaries in lungs

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ABSTRACT

Phyllodes tumor is a rare breast tumor, with neoplastic epithelial and stromal components for <1% of all breast neoplasms. Phyllodes tumors form a spectrum from benign tumors, similar to fibroadenomas, of malignant tumors with a propensity for rapid growth and metastatic spread. High-grade malignant phyllodes tumor is a very rare, but aggressive breast malignancy and forms approximately 25% of all phyllodes tumors. We report a case of a 44-year-old female who presented with a painless left breast lump for 4 months duration. The mass was >10 cm in size and firm in consistency. She underwent left mastectomy. The histopathology revealed a malignant phyllodes tumor with sarcomatous stromal overgrowth and heterogeneous chondro and osteosarcomatous differentiation. At 2 months after surgery, she reported to us with secondaries in bilateral lungs. We planned palliative chemotherapy in view of good general condition of the patient and lung metastasis. Chemotherapy included ifosfamide, adriamycin and cisplatin as per standard regimen every 3 weekly. After three cycles, her lung metastasis cleared completely. It was planned to continue same chemotherapy for six cycles.

Key words: Breast cancer, chondromatous, malignant, osteosarcomatous, phyllodes tumor

INTRODUCTION

Phyllodes tumor is a rare breast tumor, with neoplastic epithelial and stromal components for <1% of all breast neoplasms. The terminology phyllodes tumor was given by World Health Organization and classifies it into benign, borderline, and malignant tumors according to histopathological features malignant phyllodes tumor with high-grade features is a very rare, but highly aggressive subgroup of this tumor.[1] It has neoplastic epithelial and stromal components. The stromal component may show homologous and heterologous sarcomatous elements, including chondrosarcomatous and osteosarcomatous differentiation.[2] As such tumors may present with an almost exclusively sarcomatous component, a pathologist should include this entity in the differential diagnosis of fine-needle aspirations of breast neoplasms showing sarcomatous differentiation. Such differentiation of a malignant phyllodes tumor is rare, accounting for 1.3% of phyllodes tumors in the breast.[3] This differentiation is also believed to increase the aggressiveness of the neoplasm manifold, particularly when large (>5 cm) or associated with an osteoclastic or osteoblastic osteosarcoma. We report a case of a 44-year-old female in which the histopathology revealed a malignant phyllodes tumor with sarcomatous stromal overgrowth and heterogeneous chondro and osteosarcomatous differentiation.

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CASE REPORT

A 44-year-old perimenopausal woman had a painless left breast lump for 4 months duration which enlarged rapidly in last 2 months. She had no past history of malignancy or prior irradiation to the breast or thoracic region. Family

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history was also not significant. The lump was >10 cm and firm in consistency. The axillary lymph nodes were not palpable. Left sided mastectomy was done at a peripheral hospital. The histopathological specimen's cut surfaces showed irregular grey brown friable growth measuring 15 cm × 9 cm × 7 cm, reaching up to the distal resected margin. It was grey white glistening with slit-like areas. Grossly, the growth was close to all peripheral margins and 1 cm below the skin surface. No lymph node was identified. Microscopically, it was suggestive of malignant phyllodes tumor with sarcomatous stromal overgrowth and heterogeneous chondro and osteosarcomatous differentiation [Figures 1 and 2]. The mitotic rate was 28/10 high-power field (HPF) and remnants of benign phyllodes tumor were also seen. She reported to us after 2 months of surgery. Her computed tomography scan chest revealed bilateral lung metastasis. We planned palliative chemotherapy in view of good general condition of the patient and lung metastasis. Chemotherapy included ifosfamide, Adriamycin, and cisplatin as per standard regime of day 1-22. After three cycles, her lung metastasis cleared completely. She was planned to continue same chemotherapy for six cycles.

DISCUSSION

Phyllodes tumors are uncommon neoplasm that account for <1% of all breast tumors.[1,4] High-grade malignant phyllodes tumor is a very rare, but aggressive breast malignancy and forms approximately 25% of all phyllodes tumors.[5] Most of the cases present between the ages of 35 and 55 years in women who haven't yet been through the menopause; adolescent and elderly women are also affected. There are no predisposing factors and the etiology of a phyllodes tumor is unknown.[6] However, its incidence is higher in whites in general, in Latin whites and East Asians in particular. Clinically it appears as a round, mobile, and painless mass. Axillary lymph nodes are usually not palpable at presentation, because metastatic spread of these tumors is primarily hematogenous; lungs, pleura, and bone have been the most common sites of metastasis. Metastasis to axillary lymph nodes is observed in only 2% cases.[7]

Histologically, the phyllodes tumor consists of epithelial cells and connective tissue with more stromal proliferation than that of fibroadenoma, often accompanied by cellular atypia. For malignant phyllodes tumor, they are further divided into borderline, low-grade, and high-grade on the basis of the following histological criteria: Tumor borders, mitotic activity, stromal atypia, and stromal overgrowth. Only the stromal cells have the potential for metastasis. The malignant character of the phyllodes tumor is therefore confirmed by the microscopic appearance of the stroma.[8]

Phyllodes tumors are clinically similar to fibroadenomas and both have common mammographic and sonographic characteristics. On ultrasound examination, they are lobulated with heterogeneous internal echoes and intramural cysts while mammographic finding is described as a sharply defined round or oval mass with lobulation.[9]

Difficulties with diagnosis of phyllodes tumor by fine-needle aspiration cytology (FNAC) have been reported, but when these tumors present with an almost exclusively sarcomatous component, it is important for the pathologist to include this entity in the diagnostic considerations of fine-needle aspirations of breast neoplasm showing sarcomatous differentiation. The cytologist reported phyllodes tumor in only 23% of cases where FNAC was done at the time of diagnosis. In cases where core biopsy was done, phyllodes tumor was correctly diagnosed in 65% of the cases.[7]

Surgical treatment is generally accepted as the most important and primary therapy for phyllodes tumors,

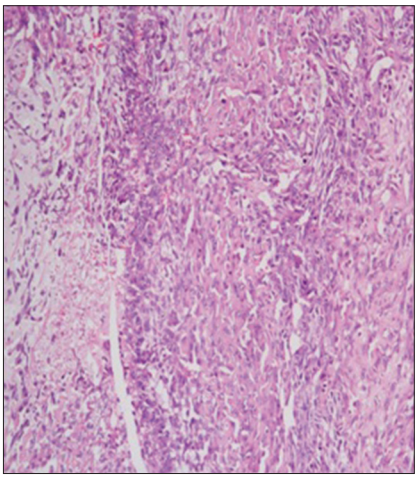

Figure 1: Microscopic view demonstrating osteosarcomatous components (H and E, ×4)

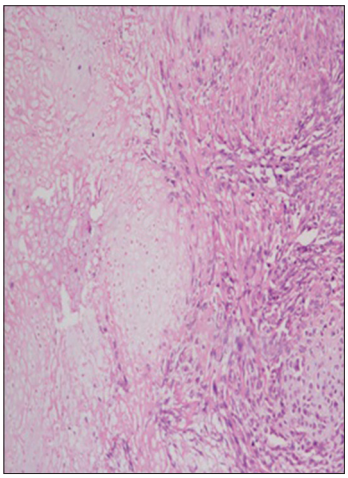

Figure 2: Photo micrograph demonstrating chondrosarcomatous components (H and E, ×4)

regardless of its histological type. A lumpectomy with clear margins (more than 1-2 cm) is recommended for small lesions (up to a size of 3 cm). A segment resection also with clear margins is recommended for larger lesions (over 3 cm in size). A mastectomy should be performed in the case of even more extensive, borderline or infiltrative areas. An axillary lymphadenectomy should only be performed in clinically conspicuous cases, as phyllodes tumor has predominantly hematogenous metastases and axillary metastases occur in <10% of cases.[8,10]

The role of radiotherapy remains unclear from published reports because of small patient numbers and a lack of controlled data. Pandey *et al*. suggested that adjuvant radiotherapy also improved the disease-free survival. August and Kearney recommended that adjuvant radiotherapy be considered for high-risk phyllodes tumors, including those >5 cm, with stromal overgrowth, with >10 mitoses/HPF, or with infiltrating margins.[7] If only local recurrence (LR), then repeat surgery once/twice may be considered. The role of external beam radiotherapy is limited to the condition only when surgery has been done twice/thrice and still recurrence occurs.

Different chemotherapy regimens have been applied in malignant phyllodes tumors. Doxorubicin and ifosfamide-based chemotherapies have shown some efficacy in women with metastatic spread of phyllodes tumors. In one study of 101 patients, 4 patients were treated with chemotherapy and a role for adjuvant chemotherapy in patients with stromal overgrowth was considered. This recommendation has so far not been confirmed in literature. Altogether, there is no clear indication for adjuvant chemotherapy for patients with phyllodes tumors.[10]

Local recurrences are a common complication of high-grade lesions with a reported frequency of approximately 26% (12-65%).[3] Stromal overgrowth, larger tumor size, and involved margin were all significantly correlated with LR. Stromal overgrowth increased the probability of LR seven-fold, whereas if the margin was <1 cm, the risk of LR increased five-fold, and if tumor size was >10 cm, then the prevalence of LR was 4 times greater than for smaller tumors. The 5 and 10 years survival rates for malignant phyllodes tumor range from 54% to 82% and 23% to 42%, respectively.[7,10]

CONCLUSIONS

High-grade malignant phyllodes tumor with sarcomatous stromal overgrowth and heterogeneous chondro and osteosarcomatous differentiation is a very rare, but aggressive breast malignancy. Stromal overgrowth carries a grave prognosis. Either wide local excision with adequate margins or mastectomy is an appropriate treatment for such patients. Metastatic tumor may be benefitted from chemotherapy. When systemic therapy is used for malignant phyllodes tumor, treatment is based on guideline for treating sarcomas.

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