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Malignant Phyllodes Tumor of the Breast with Liposarcomatous Differentiation – A Case Report and Review of Literature For Radiation Therapy

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Abstract: *Phyllodes tumors of the breast are uncommon biphasic fibroepithelial neoplasms that account for less than 1% of breast tumors and 2-3% of the fibroepithelial tumors. Histologically phyllodes tumor consists of epithelial component and mesenchymal or stromal component. Metaplastic malignant stromal transformation in phyllodes tumor is usually in 10-15% of cases mostly as high grade sarcoma NOS type but sometimes may shows areas resembling osteogenic sarcoma, chondrosarcoma, leiomyosarcoma, liposarcoma rarely as MFH. We present here a case of 35 year old female presented with an 8 months history of a palpable lump in left breast without any axillary lymphadenopathy. Simple mastectomy done because of the size of the breast does not permit adequate margins by wide excision. Histopathological examination of lump showed as malignant phyllodes tumor with liposarcoma as a malignant component. Adjuvant radiation therapy was given. We also comment on role of adjuvant treatment (radiation therapy) in malignant phyllodes tumor.*

I. Introduction

Phyllodes tumor of the breast are uncommon biphasic fibroepithelial neoplasms that account for less than 1% of breast tumors and 2-3% of the fibroepithelial tumors(1). Chelius in 1827 first described this tumor(2).The original term cystosarcomaphyllodes coined by Johannel Muller in 1838. It was believed to be benign until 1943, when Cooper and Ackerman reported on the malignant potential of this tumor. In 1981 WHO adopted the term phyllodes tumor described by Rosen. According to WHO criteria it was sub classified histologically as benign, borderline, malignant according to features such as tumor margin, stromal overgrowth, tumor necrosis, cellular atypia and number of mitoses(3). All phyllodes tumor may recur but only malignant and borderline are metastasize. Histologically phyllodes tumor consists of epithelial component and mesenchymal or stromal component (differentiates it from other sarcomas and breast carcinoma). Metaplastic malignant stromal transformation in phyllodes tumor is usually in 10-15% of cases mostly as high grade sarcoma NOS type but sometimes may shows areas resembling osteogenic sarcoma, chondrosarcoma, leiomyosarcoma, liposarcoma rarely as MFH(4). The median age at diagnosis is about 40-45 years. It is difficult to distinguish benign phyllodes tumor from fibroadenoma on cytological (FNAC and core biopsy) and radiological (mammography, ultrasound and MRI) investigatons.

Accurate preoperative pathological diagnosis allows correct surgical planning and avoidance of reoperation and adjuvant treatment(5).The mainstay of treatment is complete surgical removal with wide resection margins >1 cm. lumpectomy or partial mastectomy is the preferred surgical therapy. Total mastectomy is recommended if negative margins cannot be obtained by conservative surgery(6).The role of adjuvant radiotherapy and chemotherapy remains uncertain, but encouraging results using adjuvant radiotherapy in cases of malignant and borderline phyllodes tumors.The role of adjuvant radiotherapy should be more carefully investigated so that treatment approaches can be tailored to the individual patient.There is no proven role of chemotherapy and endocrine therapy.

II. Case Report

We present here a case of 35 year old female present with an 8 months history of a palpable lump in left breast, the lump was progressively increased in last month.She underwent lumpectomy twice in two previous years outside. There was no family history of breast cancer and no history of radiation exposure and trauma. On physical examination there was 10x15 cm lump in left breast which was mobile and non tender. Engorged veins over lump and postoperative scar were present. There was no palpable axillary lymphadenopathy.There was no other radiological abnormalities. Simple mastectomy performed because the size of the breast does not permit adequate margins by wide excision. On gross examination cut section of simple mastectomy specimen showed a tumor with well circumscribed irregular margins occupying almost all

over the breast measuring 18x9.5x8.0cm. Cut section showed gray white solid areas with cleft like space and cystic spaces filled with slimy mucoid material with areas of hemorrhages. Histopathological examination of lump showed as malignant phyllodes tumor with liposarcoma as a malignant component (Figure 1, 2, 3 and 4). Adjuvant radiation therapy was given inveiw of very large recurrent malignant phyllodes tumor and close margins. Adjuvant external beam radiotherapy given a total dose of 50.4 Gy at 1.8 Gy per fraction to chestwall. The patient is on followup, she alive and well with no evidence of either local or distant recurrence.

III. Discussion

Surgery is the mainstay of the treatment but the type of study has been source of debate. Studies have been shown that there is no differences between breast conservation surgery and mastectomy in terms of metastasis free survival or overall survival despite higher incidence of local recurrence with Breast conservation surgery[7]. If diagnosed preoperatively tumor should resected with at least 1 cm margins. Patients with benign phyllodes tumors who have undergone local excision and have histologically positive specimen margins should undergo further surgery or to be followed. Reexcision of borderline and malignant phyllodes tumors identified after local excision should be considered.Despite the complete surgical resection, local failure rates for benign tumors range between 5-15% and 20-30% for malignant tumors rise to haematogenous metastasis[8,9]. In multivariate analysis, the surgical margin is found to be the only independent predictive factor for local recurrence. The role of adjuvant radiotherapy in the treatment of non metastatic phyllodes tumor of breast is uncertain, however some studies have shown better local tumor control.In two recent studies adjuvant radiotherapy was associated with better local control.

Belkacémi et al conducted a retrospective study that included a total of 443 patients with phyllodes tumor of the breast with no residual disease.Benign tumors have a good prognosis after surgery alone. In borderline and malignant tumors, Simple Mastectomy had better results than Breast Conservation Surgery. Thus, in these forms adjuvant RT should be considered according to histological criteria (surgical margins, size, and pathologic criteria of the tumor, such as mitotic index, stromal overgrowth, cellular atypia, and tumor necrosis). There is a need for future studies to identify novel biologic markers (such as p53 expression and the MIB-1 index) that may more accurately predict the behaviour of this rare neoplasm.

A study done by Richard J. Barth et al demonstrated that margin-negative resection combined with adjuvant radiotherapy is an effective therapy for local control of borderline and malignant phyllodes tumors. Chaney et al found adjuvant radiotherapy to be beneficial in patients with adverse features (e.g., bulky tumors, close or positive surgical margins, hyper cellular stroma, high nuclear pleomorphism, high mitotic rate, presence of necrosis, and increased vascularity within the tumor and tumor recurrence) but the use is controversial. Another retrospective study done by Renata et al recommends postoperative irradiation on the chest wall in patients with malignant phyllodes tumor, because adjuvant radiotherapy decreased the incidence of local relapse.MD Anderson Cancer Centre recommends that the phyllodes tumor of the breast is benign or borderline histology, radiation therapy not routinely recommended after excision. If the tumor has malignant features, it is treated like other high grade sarcomas as follows – 1) If mastectomy is performed and margins negative, do not recommend XRT. 2) If mastectomy was performed and margins were concerning/close, tumor involved the fascia or chest wall, or tumor was very large (greater than 5 cm), then recommend XRT to chest wall. 3) If partial mastectomy only is performed, recommend adjuvant XRT after surgery.

NCCN guidelines recommend that there is no prospective randomized data supporting the use of radiation therapy with phyllodes tumor. In the setting where additional recurrence would create significant morbidity (Example – chestwall recurrence following salvage mastectomy) radiation therapy may be considered following the same principles that are applied to the treatment of the soft tissue sarcoma. here is no clear role of adjuvant chemotherapy in nonmetastatic PTB. A study conducted by Morales-Vazquez et al., adjuvant chemotherapy with doxorubicin and dacarbazine did not affect patients survival.

Figure1: Photomicrograph of phyllodes tumor showing biphasic epithelial and stromal components. Thick capsule surrounding tumor is present. Native breast tissue seen outside (H&E – low power)

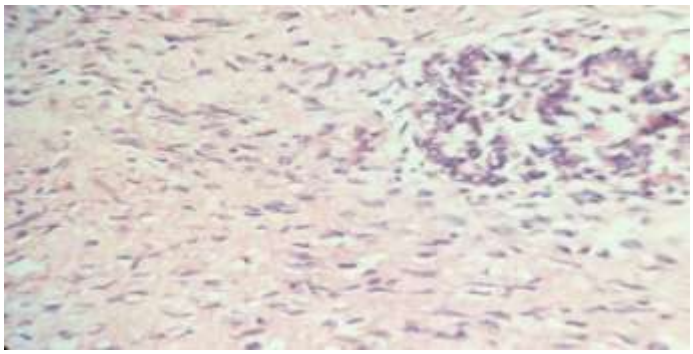

Figure2: photomicrograph of phyllodes tumor showing glandular and stromal components (H&E – low power)

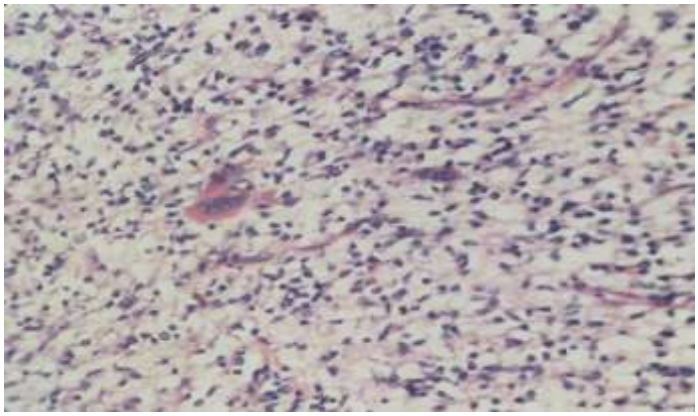

Figure 3: Malignant Phyllodes tumor, composed of sheets of cells with vacuolated cytoplasm interspersed with numerous blood vessels showing chicken wire pattern and multinucleated giant cells (H&E – high power).

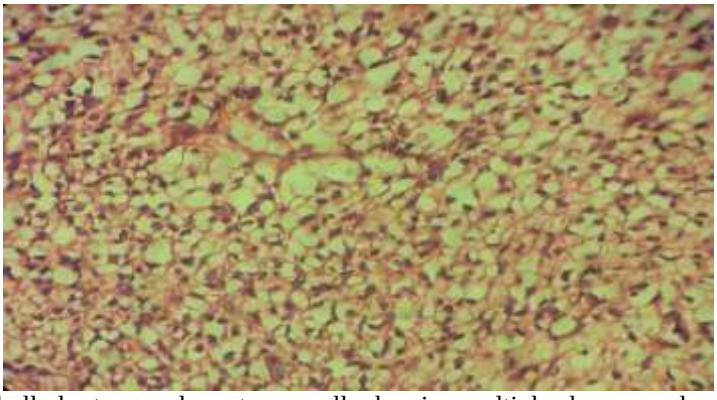

Figure4: Malignant Phyllodes tumor - large tumor cells showing multiple clear vacuoles producing indentation of nucleus suggesting their lipoblast nature (H&E – high power).

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