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Case Report

A Phyllodes Tumor in the Breast: A Case Report

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Abstract

Phyllodes tumor of the breast is a benign tumor with a malignant potential. It is very rare tumor around the world, originate from the rare fibro epithelial neoplasms of the breast, so they are histologically sarcomas. I am reporting a huge phyllodes tumor in Ethiopia on a 63-year-old female patient who presented with a huge breast mass occupying the whole breast with some area of ulceration. Mastectomy with partial resection of the pectoral muscles was done. The resection margin is negative and she is underfollow up and doing well

Keywords: Intermediate, Phyllodes tumor, Prognostic factors

INTRODUCTION

Phyllodes tumors (PTs) of the breast are an infrequent fibro epithelial neoplasm that accounts for less than 1% of all breast neoplasm (Dyer et al., 1966). Phyllodes derive from the Latin Phyllodium which means 'leaf-like' based on a gross pathological description of a leafy, bulky, cystic, and fleshy tumor of the breast (Müller, 1838). PTs were initially described by Muller in 1838 as Cystosarcomaphyllodes are classified as benign, borderline, and malignant based on cellularity of the stroma, the number of mitosis, and degree of stromal atypia (Azzopardi et al., 1979). Most tumors are detected as a palpable mass, and tumor size at presentation is highly variable.

The existing breast phyllodes tumor diagnostic method has a low diagnosis accuracy in general. Preoperative diagnosis uncertainty has hindered the rational development of surgical treatment options. High local recurrence is the most important prognostic feature of this condition, with an overall recurrence rate up to 40% of all histological types of breast phyllodes tumors (Parker and Harries, 2001). Borderline and malignant types have a different degree of malignancy. Without adequate treatment, there will be a tendency of rapid growth and metastasis. The modes of tumor metastasis are primarily via blood, rarely lymph nodes.

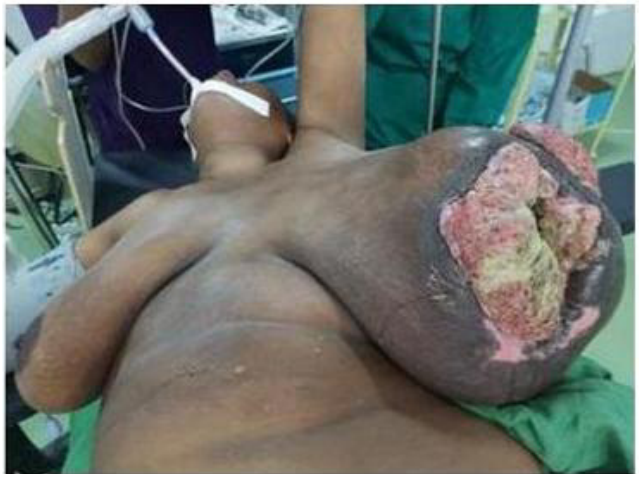
Phyllodes tumor are unpredictable tumor usually they increase in size rapidly, but there are cases where slowly growing over the years and then suddenly accelerate the rate of growth and gain the ability to metastasize after malignant transformation (White and Irvine, 2013).

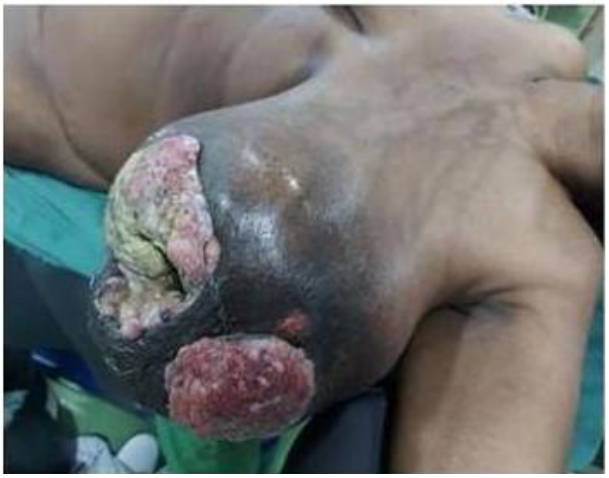
CASE REPORT

I am presenting a 63 years old lady from Ethiopia with diagnosis of phyllodes tumor of the left breast. She is married and a mother of three children. She has well control hypertension, with Body mass Index (BMI) 30.8 Kg/m^2. No History of any other chronic illness in the past.

She presented to our oncology department with history of painless left breast mass of 4 years duration which started to increase in size last one year and recently developed ulceration with minimal bleeding from the lesion. She gave history of back pain and mild abdominal discomfort.

On physical examination ECOG -2, Stable vital sign, the pertinent finding was left huge breast mass almost involving the whole breast ulcerated lesion more on the left upper quadrant destroyed the left nipple. No axillary or supraclavicular LN, right breast is normal, Chest/CVS/and abdomen grossly normal. On laboratory CBC/RFT/LFT – WNL, Chest x ray PA and Lateral show's left anterior chest mass; Ultra sound of abdomen and pelvic – normal no sign of organo-megaly, no sign of





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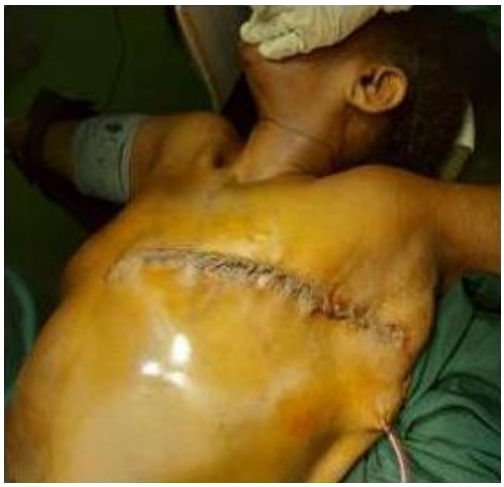

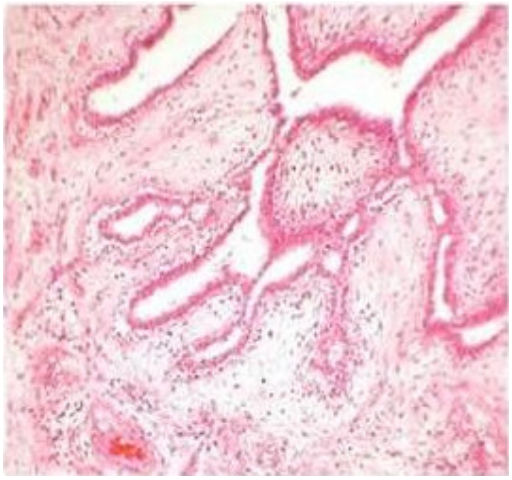

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primary or metastatic disease, no ascites Core Biopsy – Phyllodes tumor? Malignant potential Figure 1

Primary surgery Mastectomy with partial resection of the pectoral muscle was done. She tolerated well the procedure without any complication. She had smooth post-operative period and had regular follow up.

Histopathology report

Biphasic fibro epithelial lesion characterized by leaf-like phyllodal epithelial pattern Moderate graded of differentiation with stromal infiltration heterologous sarcomata's differentiation. All margin are negative for malignancy No neuro or vascular invasion No sign of LN invasion Assessment: Phyllodes tumor with malignant potential. Figure 2

Immune histo-chemstry was done and show's positive forCD34 while negative for CK BGL2, SMA Desmin, p53, S100 and B Catonin, Ki 67 is 10-12% in the highest proliferating area, Mitosis 7-8/10HPF and over all diagnosed Consistent with phyllodestumor – Borderline type.

DISCUSSION

Phyllodes tumors are rare fibroepithelial lesions. They make up 0.3 to 0.5% of female breast tumors an incidence of about 2.1 per million, the peak of which occurs in women aged 45 to 49 years (Rowell et al., 1993). The majority of phyllodes tumors have been described as benign (35% to 64%), with the remainder divided between the borderline and malignant subtype (Salvadori et al., 1989). Based on different literatures and WHO the characteristics of a phyllodes tumor can be divided in to three major groups as listed below (Abe et al., 2011; Gullett et al., 2009). Table 1

Table 1. World health organization (WHO) classifies phyllodes tumors

	Benign	Borderline	Malignant
Stromal hypercellularity	Minimal	Moderate	Marked
Cellular pleomorphism	Minimal	Moderate	Marked
Mitosis	0–4/HPF	5–9/HPF	>10/HPF
Margin	Pushing	Pushing or infiltrating	Infiltrating
Stromal pattern	Uniform	Heterogeneous	Marked

Clinical Presentation

Clinically, phyllodes tumors tend to present as unilateral firm, enlarging painless breast masses that stretch the overlying skin with striking distension of superficial veins. The size may range from 1 to 45 cm and may occupy the entire breast. They tend to grow large fairly quickly, and they often stretch the skin. Sometimes these tumors are seen first incidentally or on an imaging test like an ultrasound or mammogram, in which case they're often hard to tell apart from fibro adenomas. History of previous fibro adenoma, been age above 35, history of trauma (surgery – incisional or excisional scar), lactation and pregnancy listed down among common history in phyllodes tumor. Bloody nipple discharge caused by spontaneous infarction of the tumor has been described. Ulceration and nipple retraction are uncommon in early stage of the illness. Palpable axillary lymphadenopathy can be identified in up to 10–15% of patients but <1% had pathological positive nodes (Gullett et al., 2009). Significant proportion of patients have history of fibro adenoma and in a minority these have been multiple. Our patient presented with history of long standing left breast mass which started to increase on size and developed ulceration within a year. No evidence of clinically as well as pathologically lymph node involvement. Over stretch skin and nipple destruction and ulcerated lesion was observed.

Benign Phyllodes Tumors

This variety comprises 60% to 75% of all phyllodes tumors. In benign phyllodes tumors, the stroma is usually more cellular than in fibroadenomas. The spindle-cell stromal nuclei are uniform, and mitoses are rare, generally less than 5 per 10 high-power fields. Areas of sparse stromal cellularity, hyalinization, or myxoid changes are not uncommon, reflecting stromal heterogeneity. The margins are usually well-delimited and pushing (Correia et al., 2009). The majority of patients with benign phyllodes tumors have indolent course of illness and high tendency of cure with surgery alone (Zhang and Kleer, 2016).

Borderline Phyllodes Tumors

These tumors are diagnosed when the mass does not possess all the adverse histological characteristics found in malignant phyllodes tumors. Borderline phyllodes tumors may have frequent mitoses (5 to 9 per 10 HPF), moderate stromal cellularity, a circumscribed or focally invasive border, and stromal atypia. Stromal overgrowth is often absent.

Malignant Phyllodes Tumors

Malignant phyllode tumors show a combination of marked nuclear pleomorphism of stromal cells, stromal overgrowth defined as the absence of epithelial elements in one low-power microscopic field containing only stroma, increased mitoses (greater than or equal to 10 per 10 HPF), increased stromal cellularity, which is usually diffuse, and infiltrative borders (Zhang and Kleer, 2016).

In malignant phyllodes tumor has high chance of metastasis and most patients with metastasizes die within 3 years of initial treatment. The intent of treatment must be palliation because here is no cures for systemic metastases exist. Roughly 30% of patients with malignant phyllodes tumors die of the disease. In other hand malignant phyllodes tumor have aggressive clinical presentation and the survival rate is reported as approximately 60–80% at 5 years (Chaney et al., 2000; Confavreux et al., 2006).

Over all based on the clinical observation and different

literatures the recurrent malignant tumors seem to be more aggressive than the original tumor (Chaney et al., 2000). The lungs are the most common metastatic site, followed by the skeleton, heart, and liver. Symptoms of metastatic involvement will be dependent on site of recurrence and degree of involvement and it can arise from as early as a few months to as late as 12 years after diagnosis and initial therapy.

Immunohistochemistry

Multiple immunohistochemistry markers have undergone a study in an attempt to improve the classification of PT and predict their outcomes. Studies demonstrate that p53, Ki67, CD117, EGFR, p16, and VEGF (being the lowest in benign phyllodes tumors and the highest in malignant phyllodes tumors) are associated with histologic grades of phyllodes tumors, but none has been proven to be clinically useful (Noronha et al., 2011; Tan et al., 2005; Tse et al., 2009; Karim et al., 2010).

Among these markers, p53 expression and Ki67 index were reported in some studies to be significantly associated with disease-free and overall survivals, but other studies found no association with recurrence or clinical behavior (Yonemori et al., 2006; Niezabitowski e al., 2001). PAX3 and SIX1 expression by immuno-histochemistry and gene expression analysis have recently been identified in borderline and malignant phyllodes tumors and correlate with a poor clinical outcome (Tan et al., 2014).

The epithelial component demonstrated the expression for ER-alpha (45.6%, 36 of 79), ER-beta (37.2%, 29 of 78), PR (91.1%, 72 of 79), and AR (10.1%, 8 of 79). The stromal component was positive for ER-beta (29.3%, 24 of 82) only. The epithelial expression of ER-beta was found to be significantly correlated with the epithelial expression of AR ($r = 0.352$, $p = 0.002$). No association was found between hormone receptor expression and PT tumor grade. Stromal Ki-67 expression was statistically correlated with epithelial ER-beta, epithelial AR, and stromal ER-beta expression (Kim et al., 2012). There is little evidence of the efficacy of chemotherapy or hormonal therapy, even with estrogen receptor (ER) or progesterone receptor (PR) positivity, in treating MPT. Evidence for favorable effects of systemic therapy for metastatic disease on overall survival (OS) is lacking.

Prognosis

Theprognosis of phyllodes tumor is good with an overall 87% 10-year survival rate (Limaiem and Kashyap, 2022). After wide-margin surgical excision, 98.7% of benign phyllodes tumors and 80% of borderline were cured (Reinfuss et al., 1996). In rare cases where the tumor has metastasized, the prognosis is poor (Limaiem and Kashyap, 2022). This most commonly occurs in cases of malignant grade phyllodes tumor (Limaiem and Kashyap, 2022).

If a phyllodes tumor is benign, the long-term prognosis is excellent after adequate local excision. The possibility for local recurrence after excision always exists in malignant histology. Metastatic disease is typically observed in the lung, mediastinum, and skeleton4.4% distant metastasis, and 3.8% cause-specific death. With respect to individual subgroups, 5-year outcomes for women with benign, borderline, and malignant phyllodes tumors were as follows (Makoto et al., 2011; Rodrigues et al., 2017). Local recurrence - 6%, 9%, and 21%, respectively; Overall survival - 96%, 100%, and 82%, respectively and DFS - 94%, 91%, and 67%, respectively

In another hand the 5-year local recurrence rates after surgery were (Makoto et al., 2011; Rodrigues et al., 2017) 8% for women with negative margins,6% for those with close margins, and 37% for those with positive margins. Our patient has negative margin and borderline grade of illness and already three years after surgery in good performance statues and no sign of recurrence. Almost evidences and observations are promoting positive margins and infiltrative tumor borders were significantly associated with increased local recurrence.

Treatment

The main treatment of phyllodes tumors remains surgical excision. Wide local excision, with a margin of at least 1 cm is the most effective surgery (A prospective, multi-institutional study of adjuvant radiotherapy after resection of malignant phyllodes tumors Ann SurgOncol, 2009) for nonmalignant as well as malignant lesions. Based on the NCCN guidelines, the surgical treatment for malignant phyllodes tumors is a complete surgical excision with 1 cm margins without axillary reection. Re-excision is indicated when necessary to ensure adequate margins as the recurrence rates are unacceptably high following excision with inadequate margins (Macdonald et al., 2006; Barth Jr, 2009). The local recurrence rates following wide local excision are 8% for benign phyllodes tumors and 21–36% for borderline and malignant tumors (A prospective, multi-institutional study of adjuvant radiotherapy after resection of malignant phyllodes tumors Ann SurgOncol, 2009; Barth Jr, 1999). The low incidence of lymph node metastasis in previous studies supports the recommendation to not perform axillary surgery in these cases. The role of adjuvant radiotherapy and chemotherapy remains uncertain, but encouraging results using radiotherapy and chemotherapy for soft-tissue sarcomas suggest that consideration be given for their use in cases of malignant phyllodes tumors. Ifosfamide is considered the most active chem-otherapy agent for metastatic malignant phylliod tumors.

Doxorubcin and dacrbazine have been reported to be effective when administrate with cisplatine and Ifosfamide (Makoto et al., 2011). Now days Apatinib is a small-molecule tyrosine kinase inhibitor targeting vascular endothelial growth factor receptor 2 (VEGFR-2) and has been proven to be effective and safe for multiple solid tumors including MPT (Xiaolu et al., 2021).

CONCLUSIONS

Accurate preoperative pathological diagnosis allows correct surgical planning and avoidance of reoperation. The value of FNAC in the diagnosis of phyllodes tumor remains controversial, but core needle biopsy has high sensitivity value. Surgical management is the mainstay treatment of PT, and local recurrence in phyllodes tumors has been associated with inadequate local excision.

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