Case Report

Malignant Phyllodes Tumor: Report of Two Cases and Review of Literature

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Abstract

Phyllodes tumuor (PT) is a rare biphasic breast neoplasm. It constitutes <1% of the entire tumours of the breast. Based on the World Health Organization's (WHO) proposal, premised on multiple histological features, phyllodes tumour is categorized into benign, borderline, and malignant breast neoplasms. Malignant phyllodes tumor (MPT) is even a rarer neoplasm. It occurs more commonly in older patients. However, it can uncommonly occur in younger individuals. The transformation of benign phyllodes into malignant forms is extremely rare. Here, we present two cases of young females (aged 20 and 27 years, respectively) who individually presented with rapidly progressive breast lumps. The two breast lumps were huge while one was recurrent and under went a malignant transformation in approximately 7 weeks interval following an initial complete excision and histological diagnosis of benign PT. Indeed, even in young females below the modal/peak age of phyllodes, the suspicion should be high. Additionally, breast ultrasonography findings, although not common, can be highly suggestive of PT. Furthermore, every breast lump should be further evaluated, and even more so, histologically, irrespective of the patient's age as our first patient had an excision without histology.

Keywords: Phyllodes Tumour; Young Nigerian Females; Malignant Transformation; Recurrence.

Introduction

Formerly known as cystosarcoma phyllodes, a term first conceived by Johannes Muller in 1838, breast phyllodes tumours are infrequent neoplasms that account for 2.5% of the entire fibroepithelial lesions and around 0.3-0.5% of the whole tumors of the breast.[1-3]

On the basis of distinct histological features which include mitotic figures, stromal cellularity, cellular atypia, overgrowth of the stroma, and tumor margin, PT is classified by the WHO as benign, borderline, and malignant.[4]Furthermore, most PTs are benign (approximately 70%) while only about 10-15% are malignant.[5-7] It is commoner in females between the ages of 35-55 years and not more than 10% of them exceed 10cm in size.[6,8]

Additionally, some of the well-established features of MPT are recurrence, rapid growth, and the less common distant metastasis and malignant

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transformation thus the need for a high index of suspicion among physicians, especially within the young age group to ensure early diagnosis and appropriate intervention with a resultant better outcome. Although mastectomy or local surgical resections with adequate margins are the mainstay of treatments, adjuvant radiotherapy enhances outcomes.[9]

Case Reports

Case 1

A 20-year-old woman presented at our surgical outpatient department with complaints of recurrent right breast lump of 1-month duration. The lesion had rapidly increased in size since onset and was associated with pain. No lump was present in the other breast neither were there swelling in the right armpit, cough, weight loss, or anorexia. She regularly takes alcohol but does not smoke cigarettes. She has had an excision done 1 year, 6 months ago on account of a lump in the left breast in a peripheral hospital for which there was no histological diagnosis, and another excision a month before index presentation on account of a lump in the right breast for which a diagnosis of benign phyllodes tumor was made histologically. (Fig 1)

On clinical examination, she had normal vital signs. There was no palpable peripheral lymphadenopathy. Also, there was no lump felt in the left breast. In the right breast, a subareolar mass, about 12cm, lobulated, not attached to the skin or underlying muscle was felt. Other systems were essentially normal. A working diagnosis of recurrent phyllodes tumour of the right breast was made.

Chest x-ray findings were normal. Computed tomography (CT) of the abdomen and pelvis showed normal findings.

The patient later had nipple-sparing right simple mastectomy. She was discharged 4 days post-op in stable condition while the mastectomy and excised right axillary node samples were subsequently sent for histopathological evaluation.

The gross examination of the breast tissue showed a huge mastectomy specimen with distorted anatomy and no discernible nipple. The surface skin appeared thickened and nodular. It weighed 3.2kg and measured 25.0 x 20.0 x 16.0cm (Fig 2).

Cut section showed a diffuse greyish white to reddish-brown multilobulated mass involving all the breast quadrants with areas of necrosis and haemorrhage. The mass measured 20.5 x 16.5 x 10.0cm. The tumour was less than 1cm from the deep margin of resection. Furthermore, the axillary lymph node grossly showed a piece of yellowish-brown tissue, soft in consistency, weighed less than 10 grams, and measured 3.5 x 1.5 x 1.0cm. The cut section showed a greyish white appearance. Microscopically, sections of the breast tissue revealed a malignant mesenchymal neoplasm composed of a markedly cellular stroma. The stromal cells were markedly pleomorphic and disposed predominantly in sheets. The component cells had oval to polygonal hyperchromatic to vesicular nuclei, prominent nucleoli, and moderate eosinophilic neoplasm. Mitosis was brisk with many atypical forms and mitotic count >20 per 10HPF. There were extensive areas of necrosis and haemorrhage (Fig 3). The margins of resection were involved by tumor cells. The accompanying axillary lymph node revealed reactive follicular hyperplasia. A histopathologically confirmed diagnosis of malignant phyllodes was made.

Follow-up visits showed good wound healing. There are plans for radiotherapygiven the involved tumour margins and for a possible breast reconstruction post-treatment.

Case 2

A 27-year-old woman presented to our general surgery clinic on account of left breast swelling of 14 months duration. The swelling has progressively increased in size, from pear-sized to that of a watermelon. There was an associated pain that began 1 month before presentation. No history of dizziness, dyspnea, cough, or chest pain.

On examination, general examination findings and vital signs were normal. Right breast findings were normal. However, the left breast showed erythematous skin with visible superficial veins. Also found was a firm, mobile mass measuring 20.0 x 15.0cm, not fixed to the overlying skin or underlying muscle. There was no palpable axillary lymphadenopathy. Other systems were essentially

normal. A diagnosis of phyllodes tumor of the left breast was made.

A requested sonomammogram revealed a huge mixed echogenic mass occupying all four quadrants of the left breast with loss of the normal fibroglandular breast pattern, measuring 13.5 x 11.5 x 10.6cm, with a volume of 855mls. Increased vascularity was seen on color Doppler. There was no axillary lymphadenopathy seen bilaterally. Diagnosis based on the breast ultrasonography findings was phyllodes tumor of the left breast (BIRADS category IV) with multiple right breast cysts (BIRADS Category II). In addition, chest x-ray and abdominal ultrasound scan showed normal findings.

Also, a core biopsy of the left breast sent for histopathological examination showed on macroscopy astiny strands of greyish white tissue measuring 3.0 x 1.5cm each. On microscopy, highly cellular lesions composed of moderately to markedly pleomorphic mesenchymal cells disposed in sheets and fascicles were seen. The component tumor cells had oval to elongated hyperchromatic nuclei and moderate eosinophilic cytoplasm. Additionally, several large bizarre cells were seen in areas. Also seen were atypical mitosis with a mitotic count >10 per 10HPF. (Fig 4). A definitive diagnosis of malignant phyllodes was made. The patient was counseled on the histology result and has been scheduled for a left mastectomy.

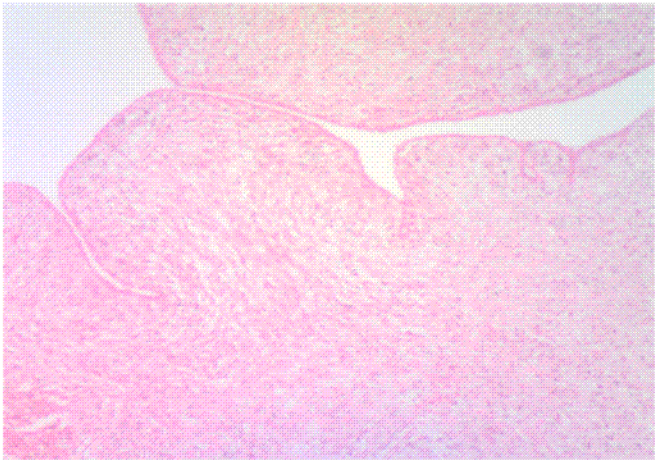

Figure 1: Breast biopsy showing mild stromal cellularity with minimal atypia and mitosis <5 per 10HPF consistent with the diagnosis of benign phyllodes tumour (H & E X 40).

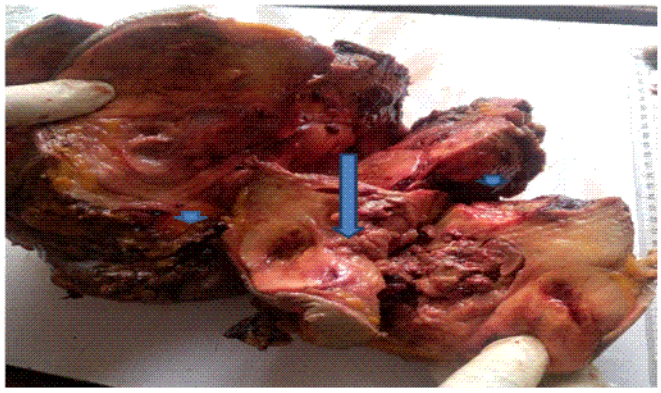

Figure 2: Gross appearance of the huge mastectomy specimen with the cut surface showing a diffuse greyish white to reddish brown multilobulated mass with areas of necrosis (long arrow) and haemorrhage (short arrows).

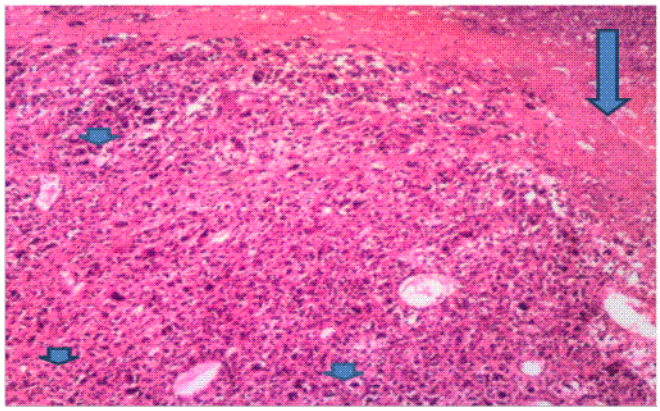

Figure 3: Breast biopsy showing a markedly cellular stroma composed of pleomorphic mesenchymal cells with occasional atypical mitosis (short arrows) and an area of necrosis (long arrow) consistent with the diagnosis of malignant phyllodes. (H & E X 100).

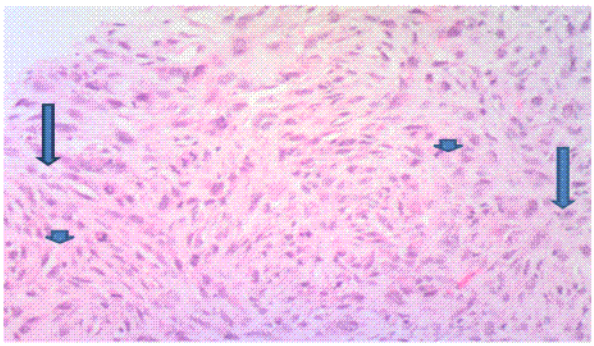

Figure 4: Breast biopsy showing a highly cellular stroma composed of fascicles of pleomorphic mesenchymal cells with some large bizarre cells (long arrow) and occasional atypical mitosis (short arrows) consistent with the diagnosis of malignant phyllodes tumour (H & E X 100).

Discussion

Phyllodes tumor (PT) is an infrequent and sometimes aggressive breast neoplasm. It represents <1% of the whole tumors of the breast, 2.5% of the fibroepithelial breast lesions and has an annual incidence of approximately 2 per million women with a predilection for Latino women.[1-3,10]

The WHO classifies PT into 3 categories namely, benign, borderline, and malignant with histological features such as stromal overgrowth, cellular atypia, tumor margin, mitotic activity, and stromal cellularity serving as the criteria.[4]Malignant phyllodes tumor (MPT) is the rarest of the spectrum of PT consisting of about 10-15% of the tumors.[5,7]PT is commoner in females between the ages of 35-55 years and has 40 and 45 years as its mean and median ages of occurrence respectively[6, 11, 12]. Though rare, it can occur in young women [13] as was seen in our patients who were 20 and 27 years respectively.

Malignant transformation of PT is an extremely rare occurrence and only a few cases have been reported in the literature.[14]In a single case described by Pornchai et al, the malignant transformation time was 36 months.[14]In our first case which showed malignant transformation, it took approximately 7weeks for transformation from benign PT to MPT following the previous excision.

PTs usually present as unilateral, painless, well-circumscribed, mobile breast lumps with some showing distension of the superficial veins of the overlying skin.[6, 12] It can however present with pain.[12]Our patients had unilateral, mobile breast lumps associated with pains with one of them having distention of the veins of overlying skin consistent with findings in the literature.

There have been reports of rapidly developing PT over 2 months period.[2,16] Indeed, our first case had an overt rapid progression in a space of 1 month prior to her first presentation which even makes it more interesting. Furthermore, in about 15% of cases, local recurrence is encountered and usually occurs within a few months to 2 years following previous excision.[2, 11, 14, 15]

Although PTs have a median size of about 4cm, one case measuring 50 x 50cm in size, the largest thus far, has been previously reported.[8,17] Indeed, generally,<10% of PT exceeds 10cm in growth [8]. In our cases, one grossly measured 20.5 x 10.5 x 10.0cm while the other on clinical examination estimated 20 x 15cm in size. Additionally, in only around 20% of cases, palpable lymphadenopathy can be detected. In line with literature that supports the uncommon occurrence of axillary lymph node swelling in MPT, none of our patients had palpable axillary lymphadenopathy.

Radiologically, it is near unattainable to usea sonogram or mammogram to distinguish benign PT from MPT, or even draw a distinction between PT and fibroadenoma, one of its differentials, owing to the paucity of specific findings. [6, 18]In addition, the only findings suggestive of PTs include the swift rate of growth with or without an extremely huge size resemblance of a fibroadenoma thus making a preoperative diagnosis of PTs very challenging [6]. Furthermore, on sonography MPT appears as smooth masses with multiple lobules similar to a fibroadenoma. However, PT should be put into consideration if lengthened spaces occupied by fluid or a firm mass with clefts are observed in this imaging technique.[6]

Additionally, on ultrasound, certain MPT characteristics, also commonly seen in complex fibroadenoma can be observed and these include heterogeneous or well-circumscribed hypoechoic mass with lobulation, microcalcification, and poorly defined margin.[19] Also, on mammography, differentiating PTs from other tumors are difficult as the findings which include oval or round mass with poor-or well-defined margins are non-specific.[20]

However, there are suggestions that magnetic resonance imaging (MRI) could be more useful in diagnosing PT than sonography or mammography.[20] PTs are heterogeneous neoplasms that have both epithelial and stromal components, although histologically, the stromal element distinguishes it.[15] As previously stated, according to the WHO, PT is classified into 3 categories based on several histologic characteristics.

The microscopic features of benign PT are well-defined tumor margin, mild stromal atypia, and cellularity, mitosis <5 per 10HPF, and absence of stromal overgrowth while MPT is characterized histologically by tumor margin infiltration, stromal overgrowth >10 mitoses/10HPF, nuclear pleomorphism and marked stromal atypia and cellularity [21]. In our first case, in line with literature, the diagnosis of benign PT was made on her first presentation based on our histological findings of mild stromal cellularity with minimal atypia with mitoses <5 per 10HPF (Fig 1). Furthermore, our subsequent diagnosis of MPT (following malignant transformation) in our first patient and in our second patient as described in Figs 3& 4 agreed with literature.

Indeed, two important differentials diagnoses of PTs are fibroadenoma (FA) and myxofibrosarcoma (MFS).[20, 21]However, the well-developed leaf-like pattern, hypercellularity, and marked stromal overgrowth distinguish PTs from FAs. On the other hand, MFS lack the leaf-like pattern seen in PTs and it's often observed on microscopy to be made up of a group of large fascicles containing spindle cells separated by mucin-like matrix, adipocytes, and collagen fibres.[20, 22]Malignant transformations have been postulated to originate from mutation of residual cells of the tumour for which its risk and that of recurrence can be reduced by complete and adequate margin excision.[23] p53 is the most culpable gene mutated in these lesions.[14] With a proven low recurrence rate, benign PTs are locally excised with appropriate margins in the majority of cases with the aim of conserving the parenchyma of the breast.[7,14] Taking cognizance of literature and her young age, this was what we offered our patient on initial presentation as it was impossible at the time to forecast the subsequent malignant transformation due to the general unpredictable nature of the tumor.

Adjuvant radiotherapy can improve outcomes even though mastectomy or local surgical resection with an adequate margin of 1-2cm are the treatments of choice.[2, 9, 14, 24] It is also beneficial in controlling disease locally, metastasis prevention and should be recommended following R1 resection.[24, 25] Indeed, there are plans for radiotherapy for our first case following mastectomy considering microscopic tumour margin infiltration, local recurrence history, and the huge tumour size. Additionally, she will also have reconstructive surgery afterward for cosmetic purposes.

Declaration of conflicting interests

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