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CASE REPORT

Malignant Phyllodes Tumour in a Pregnant Woman Masquerading Clinically as an Abscess: A case report

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ABSTRACT

Phyllodes tumors (PT) are rare breast tumours comprising of < 1% of all breast tumours that arise from the stromal connective tissue of the breast. These tumors usually affect the adults of fifth and sixth decade and are rarely found in the pediatric or young age group. PT presents as a rapidly growing discrete palpable mass. Histologically, they are classified as benign, borderline, and malignant on the basis of histological features, mitotic index, necrosis, and infiltrative growth pattern. Malignant PT is a rare entity in pregnancy. We present a case of 27-year-old multigravida with one live male child and a term still born who presented to the outpatient department during antenatal visit with a rapidly growing breast lump early in the 25th week of gestation. Malignant PT becomes difficult to diagnose in a pregnant woman as lactation changes and clinical appearance can mask this diagnosis. A multidisciplinary approach is needed in such cases because there is a high recurrence rate and metastases when tumors are large, bulky with involved surgical margins.

Keywords: malignant, phyllodes, breast, pregnancy, abscess.

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Introduction

PT is a rare subset of fibroepithelial breast neoplasms with epithelial and stromal proliferation comprising 0.3 to 1% tumors that occur in female breast[1,2]. Characterized initially in 1838 by Johannes Muller as 'cystosarcomaphyllodes', the current endorsed designation is PT by the World Health Organisation (WHO)[3,4]. PT demonstrates heterogeneous behavior dictated by underlying pathological features and is classified into benign, borderline, and malignant categories. Benign PT simulates fibroadenoma and is prone to recurrence if not excised with wide margins, while malignant PT can exhibit distant metastasis via haematogenous route[3, 5, 6]. Usual presentation in PT is a breast lump. Higher incidence is reported in women of 4th to 5th decade, though they occur from puberty to menopause. Rapid enlargement mimics breast carcinoma, particularly if there is coexistent skin ulceration, nipple retraction, or fixation to the chest wall or overlying skin. Presentation during pregnancy is a rare event associated with marked increase in size.

Biopsy is the recommended tool for diagnosis, though occasionally immunohistochemistry may be required. Treatment of choice is wide surgical excision; however, revision surgeries may be required due to involved margins at initial excision[1,3].

Case Report

A 27-year-old female with G3P2, having a live male child aged seven and a term still born three years earlier, on a routine antenatal visit was referred to surgery OPD with a rapidly growing breast lump early in her 25th week of gestation. Four months ago, the patient had noticed a small lemon-sized lump in her left breast that had enlarged rapidly involving her entire breast causing immense discomfort. On examination a markedly enlarged left breast, firm to cystic on palpation, bearing shiny overlying skin and engorged superficial vessels measuring 22 X 18 centimetres was documented. No nipple retraction-inversion, skin ulceration, or fixation to the underlying tissues was evident. Axillary soft tissue was unremarkable on palpation. There was leucocytosis (13,880/mm^3) with neutrophilia (84%) and hypochromic microcytic anemia, probably due to multiple pregnancies and poor socioeconomic status of the patient leading to iron deficiency (haemoglobin: 8.6 g / dl, MCV: 62.5 fl, MCH: 21.7 pg) on hemogram. On ultrasonography a large loculated lesion with areas of organized component, low level echoes within lesion identified in left breast at 9 o'clock to 4 o'clock region. Radiologist suggested the possibility of galactocele or abscess (Fig. 1a). The surgeons performed incision and drainage (I&D), whereby 20-30 ml of serous fluid was drained and sent for pus culture. Although the patient had temporary relief following

I & D, the culture was sterile. Gram stain was not performed. Fine needle aspiration cytology (FNAC) showed cellular smears with sheets and clusters of atypical cells that were large in size, had high N: C ratio, hyperchromatic nuclei with prominent nucleoli, and vacuolated cytoplasm. These cells were admixed with stromal cells, hemosiderin macrophages, and red blood cells suggestive of malignancy (Fig. 1b & 1c). A core biopsy performed in the interim was suspicious of a phyllodes tumor, and a mastectomy with wide surgical margins was promptly performed.

The gross specimen received in surgical pathology was 19 x 16 x 6 centimetres. Serial sectioning identified solid cystic areas, the latter were filled with mucoid reddish fluid. The solid areas bore a tan appearance (Figs. 1d & 1e).

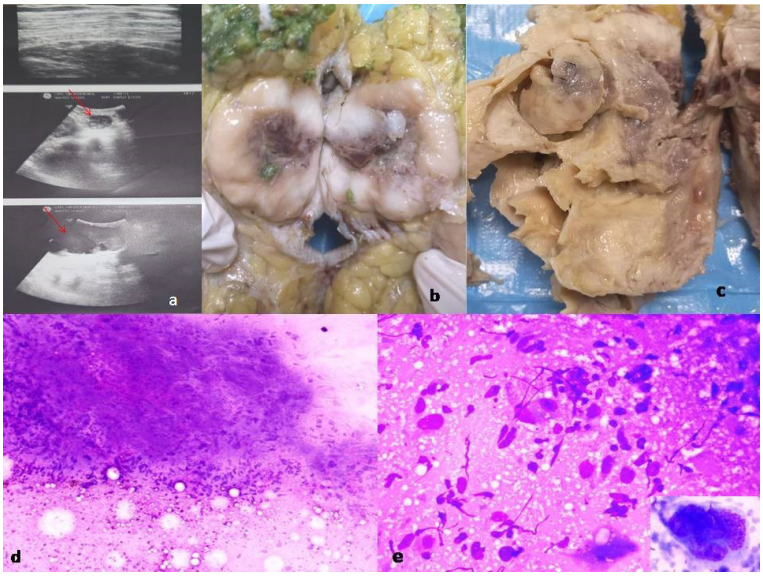

Fig. 1.

1a: Ultrasonographic imaging showing a large loculated lesion measuring approximately 23 x 19 cm in size with areas of organised component (low level echoes) (⇧)

1b: Cut surface of gross specimen of left breast showing grey white, firm solid, hemorrhagic area.

1c: Gross specimen of left breast showing grey white to tan, solid and cystic areas. The latter filled with mucoid reddish fluid

1d: Fine needle aspiration cytology (FNAC) of the lesion showing hypercellular smears displaying abundant stromal cells mixed with pleomorphic tumour cells (MGG; 40x).

1e: Fine needle aspiration cytology (FNAC) of the lesion showing scattered pleomorhic, hyperchromatic cells with scant amount of cytoplasm admixed with stromal cells in haemorrhagic and necrotic background. Inset showing a large, markedly plemorphic cells with prominent nucleoli. (MGG; 400x).

Representative sections examined demonstrated a markedly cellular tumor showing stromal overgrowth, nuclear and cellular pleomorphism, high mitotic index (33/10 high-power fields or 22/millimetre^2), bizarre giant cells, and focally present epithelial elements. Osseous metaplasia and myxoidsarcomatous changes were identifiable along with areas of necrosis (Figs. 2a, 2b, 2c, 2d). A diagnosis of malignant PT was rendered. Three of the four resected margins were involved. Tumor reached upto but did not affect the posterior resected surface. No lymph nodes were identified. The tissue resected bore fibroadenomatous foci in areas farther away from foci of phyllodes. The surgeons decided to wait for the patient to deliver the growing fetus at term before pursuing further surgery. The patient had confirmed a family history of breast cancer in her paternal grandmother who died one year after diagnosis and subsequent breast surgery, but due to lack of knowledge was not able

to share further details. Following sepsis due to severe urinary tract infection, the patient was induced and delivered a healthy male at 8 months of gestation. Breast surgery was re-performed three months after delivery with wide local excision repaired through latissimus dorsi flap. The posterior margins were affected in the frozen section, confirmed in histopathology. The patient received three cycles of Adriamycin-I-phosphamide post-surgery. Subsequently, she was referred to radiation oncologist. However, after 25 cycles of radio therapy, she returned to OPD with recurrence at the surgical margin. In the follow-up, the patient was not taking any treatment at the time of writing the article.

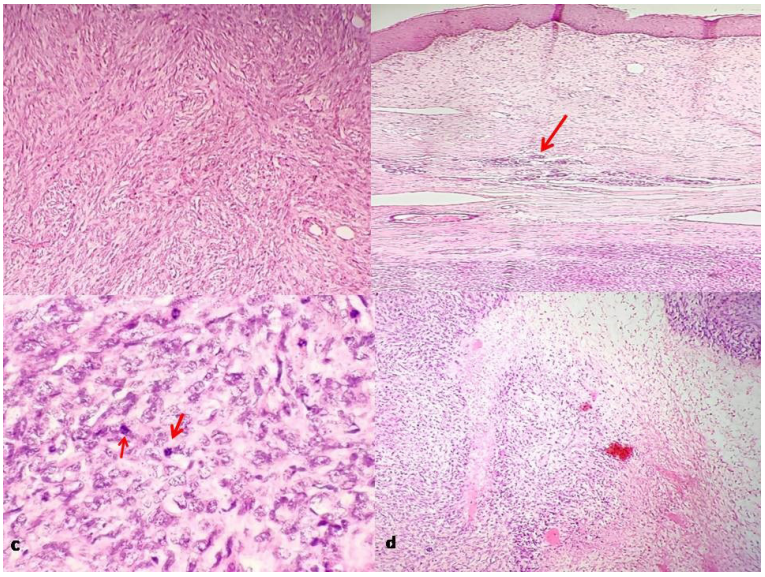

Fig. 2.

2a: Low power view of markedly cellular tumour showing stromal overgrowth arranged in fascicles and haphazardly with dilated and congested thick blood vessel (H&E; 100x).

2b: Normal breast acini (⇧) seen below the skin, beneath it highly cellular tumour seen with infiltrating pattern (H&E; 40x)

2c: spindled tumour cells displaying pleomorphism, hyperchromasia and vesicular chromatin with atypical mitosis (⇧) (H&E; 400x)

2d: Tumour cells with myxoid areas and necrosis (H&E; 100x).

Discussion

From its initial description by Johannes Muller in 1838 as "Cystosarcoma Phyllodes" derived from the Greek word phyllon to signify the macroscopic leaflike appearance, this entity has been subjected to various nomenclatures, the currently accepted term by WHO being PT[7]. Constituting < 1% of all breast tumors, PT are categorised into benign, borderline and malignant[8]. PT can be detected accidentally on ultrasound (US) examination or present as painless breast lumps of variable size (median range of 4-5 centimeters)[3]. According to the literature, PT occurs in older females (40-50 years of age) and malignant PT occurs even 2-5 years later than benign PT, the index case reported here is of a young female with malignant phyllodes[7]. Malignant PT is associated with rapid growth in pregnancy and can attain huge dimensions as highlighted in prior case reports[9].

Malignant PT accounts for approximately 6.5-27% of all PT[10]. Tumours of large sizes exhibit cystic changes and frequently areas of necrosis and hemorrhage, in the present case, cystic areas filled with mucoid material and hemoorhage were evident. However, areas of necrosis were not evident grossly[11]. Secondary changes like nipple retraction, discharge or tumour involvement of chest wall may occur simulating other breast carcinomas[3, 12]. Axillary lymph nodes are seldom involved and when palpable are in lieu of reactive causes[12]. Malignant PT are exceedingly rare and there occurrence in the breasts of pregnant women is even a rarer event. They may erroneously be misdiagnosed as benign and at times a delayed diagnosis due to apprehension regarding fetal outcomes can adversely affect management as in the present case report.

The literature has documented the rapid growth of all types of PT in pregnancy supporting the notion that they are hormone dependent[2,9]. Rapid growth of breast lump was recognized in present case yet erroneously misdiagnosed due to radiological, clinical and laboratory parameters unlike any of the previously cited case reports. This delayed the time excision of the mass. However, once excised and evaluated, the histopathology diagnosis was straightforward.

Histopathology is gold standard for diagnosis requiring diffuse and excessive stromal overgrowth along with marked nuclear pleomorphism and absence of epithelial elements in one low power microscopic field visualised by a 10x eyepiece 40 x magnifications and 4x objective[7]. Mitosis should be in excess of ≥ 10/10HPF of 0.5mm diameter, ≥ 5mitosis/mm^2 [7, 13].

The common differential diagnosis of phyllodes tumors includes fibroadenoma (intracanalicular pattern), sarcomas, periductal stromal tumor (PST), and metaplastic carcinoma. Both the fibroadenomas and phyllodes tumor show epithelial and connective tissue stromal elements, but higher stromal cellularity in PT helps to distinguish these two[14,15]. Primary breast sarcomas show high heterogeneity. Malignant PT is commonly misdiagnosed as pure breast sarcomas and vice a verse[14,16]. Desmoids fibromatosis, Angiosarcoma, inflammatory myofibroblastic tumor, leiomyosarcoma, liposarcoma and malignant fibrous histiocytoma are the most common mesenchymal tumors of breast. Distinguishing them from each other may require collaboration of clinical features with histopathology and panel of immunohistochemistry (IHC) in some cases[7]. PT and PST share overlapping histological features, and the difference lies in the absence of leaflike fronds in PST. PST is characterized by proliferating spindle cells around open tubules and also, it is not circumscribed. Metaplastic carcinoma is another important differential diagnosis of malignant PT, but spindle cells in metaplastic carcinomas are positive for high molecular weight /basal cytokeratin such as 34 βE12 and CK 5/6 helps in resolving the problem[14, 17]. Diagnosis of PT can sometimes be arduous as overlap exists between benign PT and fibroadeoma and malignant PT with spindle cell sarcomas and metaplastic carcinomas. Intermediate PT can be confounding by itself due to lack of stringent diagnostic criteria and interobserver variation. When in doubt IHC can be resorted to. Cytokeratins CK 5/6, CKAE1/AE3, Cam 5.2 and 34 βE12 and p53 show variable positivity with sarcomatoid carcinoma while malignant PT is negative[18]. Markers for prediction of the outcome namely p53, EGFR, Ki 67 and PDGF are not particularly useful[2, 13].

Complete surgical excision is the standard treatment of choice (excision margins >1cm)[13]. Cases of malignant and borderline PT may additionally require adjuvant options like radiation and chemotherapy[2, 13]. The risk of recurrence and metastasis in tumors with involved resected margins is a potential possibility and hence a constant challenge to the surgeon. A lack of uniform guidelines in the management of pregnant malignant PT patients is an existing lacunae given the rare nature of the disease and should be addressed. However, rapid enlargement in size of PT has been documented in pregnancy. The present case has been reported to highlight its presentation as an mistaken diagnosis of an abscess both radiologically and clinically, leading

to the delayed treatment.

Conclusion

A high index of suspicion in pregnant women with rapidly enlarging breast masses will help in the timely diagnosis and management of malignant PT, as wide uninvolved resected margins are the end point that significantly improves prognosis for the patient. Delayed diagnosis, involved resected margins will subsequently require adjuvant techniques that may have financial and emotional consequences for the patient in the addition to worsening outcome as in present case.

Potential conflicts of interest

The authors declare no conflicts of interest.

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