STROMAL CHANGES IN MALIGNANT PHYLLODES TUMOUR- TWO CASE REPORTS OF EXTREME DIAGNOSTIC DIFFICULTY

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ABSTRACT

BACKGROUND

Uncommon large breast tumour with leaf-like stromal proliferation was designated previously as "Cystosarcoma phyllodes," later designated under a broad term phyllodes tumour, qualified as "benign" or "malignant" according to their histological appearance. Most of them are benign. Stromal changes in phyllodes tumour ranges from lipomatous, osseous, cartilaginous, myosarcomatous, angiosarcomatous change in stroma and squamous and apocrine metaplasia of ductal epithelium. They occur in benign Phyllodes tumours, but incidence is much more in malignant ones. FNAC is the first line of diagnosis, but rarer atypical form of stromal changes may limit cytological diagnosis and classification necessitating a biopsy and histopathology for confirmation.

KEYWORDS

Phyllodes Tumour, Epidermal Cyst, Chondrosarcoma, Granular Cell Change.

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BACKGROUND

A distinct fibroepithelial neoplasm characterised by leaf-like arrangement of spindle shaped stromal cell with elongated epithelial component in breast was first named as Cystosarcoma Phyllodes by Johannes Muller in 1838.[1] Among many other names used for this tumour, Phyllodes Tumour (PT) and periductal stromal tumour are still used commonly. The incidence is less than 1% of breast tumours reported worldwide.[2]

The term Cystosarcoma Phyllodes, though considered as a misnomer as majority of the tumour does not present as cyst and most of them are benign in behaviour nevertheless represent a sizable proportion of malignant cases, which present with higher local recurrence and metastasis to distant sites. That is why a diagnosis of phyllodes tumour should always be accompanied by a sub-classification into benign borderline and malignant categories due to largely different behaviour (local spread and metastasis) and prognosis. The distinction is based on histological characteristics of the tumour and predicts the clinical course.[3,4] Malignant phyllodes tumour represents 10 to 30% of all diagnosed phyllodes tumour.

The characteristic findings of PTs include a hypercellular spindle cell stroma having gland-like structures reminiscent of an intracanalicular growth pattern.

Fine Needle Aspiration Cytology (FNAC) of such cases poses a problem as benign phyllodes tumour shares cytological features with sister fibroepithelial proliferative diseases of breast-like fibroadenomas.

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It is easier to differentiate malignant from benign Phyllodes tumour on FNAC.[5] But in the presence of atypical changes in the stroma of a malignant phyllodes tumour, diagnosis can be very difficult. Loss of typical histological features may be misleading when atypical sarcomatous components are present, especially in case of core needle biopsies.

In this case report, we present two such cases of rare stromal changes in malignant phyllodes, which caused immense diagnostic difficulty, investigated cytologically and confirmed histopathologically.

CASE REPORTS

Here, we present cytology and histopathology of two cases of malignant phyllodes tumour; one presenting with squamous differentiation and chondrosarcomatous area which was diagnosed as benign phyllodes tumour with metaplastic squamous cells and another with extremely rare granular change in the stromal component, which could not be diagnosed cytologically and reported as inconclusive for opinion.

Case Report 1

45 years old Hindu female (P_{2+0}) who had a slow growing lump over the right breast for over four years presented with a rapid increase in size over past month. There was also pain, tenderness and discolouration of overlying skin during that period. There was no family history of breast or ovarian tumour.

On examination, a large mass was noticed in the lower inner quadrant of the right breast almost bigger than the size of normal breast tissue, which was pushed to the periphery. It was fixed to skin, had a smooth shiny outer surface with bluish black purpuric lesions over the mass. It was lobulated and firm on palpation. Nipple and areola was normal. The mass was free from chest wall. There was no axillary lymphadenopathy. The other breast was normal.

The chest x-ray was unremarkable along with routine blood works. Ultrasound examination of the right breast revealed a large mass lesion with heterogeneous echotexture of solid and cystic areas.

Repeated fine needle aspiration from different sites revealed fragments of benign ductal epithelial cell in monolayer sheets in a background of abundant mature nucleated and anucleated squamous cells with occasional dysplastic squamous cells (Figure 1A and 1B). The case was reported as benign phyllodes with a focus of metaplastic squamous cells (Cytological Category C4: Suspicious of Malignancy).[6] Urgent mastectomy was advised to confirm metaplastic breast carcinoma.

A modified radical mastectomy was performed after 3 days. The specimen received contained a large heterogeneous breast mass measuring 14 x 11 x 7 cm^3 with involvement of deep resection margin (Figure 1C). Representative sections were taken. Histopathological examination after Haematoxylin and Eosin staining revealed it as a malignant phyllodes tumour characterised by extensive stromal overgrowth, sheets of malignant stromal cells with scanty trapped leaf-like arrangement of benign ductal epithelial cells (Figure 1D). Along with that there was prominent chondrosarcomatous areas (Figure 1E and 1F) and extensive squamous metaplasia with formation of numerous epidermal cysts of keratinous type (Figure 1G).

A final histopathological diagnosis of malignant phyllodes tumour with chondrosarcomatous differentiation and squamous metaplasia was given.

The patient underwent a barrage of tests and ultimately through a PET scan from a different institute, which showed multiple metastatic deposit in liver and lungs. Chemotherapy helped her to live four more months until she died of sepsis.

Case Report 2

In the other case, 38 years' Muslim female (P_{3+0}) patient presented with a discrete palpable firm lump in left breast for past 21 days. She had no history of previous breast lump. She had 3 children who have been exclusively breastfed. There was no positive family history too.

On examination, there was an ovoid mass about 4 cm in greatest dimension in the upper inner quadrant of breast. It was fixed to the breast tissue, but free from skin and chest wall. Nipple areola was within normal limit and there was no axillary lymphadenopathy.

Routine chest x-ray was within normal limit along with routine blood works. On ultrasonography, an irregular lump with heterogeneous echotexture was reported as suspicious of malignancy.

FNAC finding was inconclusive with scanty cellularity and occasional degenerated cells forming poorly cohesive clusters. The cells had fragile cytoplasm with poorly defined cell border and anisonucleosis. Repeated aspiration revealed similar morphology and was reported as 'Inadequate for opinion' (Category C1).[6] Excision biopsy was suggested as next investigation.

A Lumpectomy was planned in view of suspicious ultrasonography and inconclusive FNAC; 2 days later, the mass was completely enucleated with wide excision of margins. On gross examination, it was a lobulated tumour (4.5 x 5.5 x 2 cm^3), grey-white in colour, soft-to-firm in texture, myxoid in appearance with focal homogeneous fleshy white areas and chink-like clefts on cut section (Figure 2A).

Histopathological examination after H and E staining revealed frond-like projections of pleomorphic hypercellular stroma covered by thin layer of epithelium (Figure 2B). There was marked granular cell changes of stroma, having compact population of polygonal to spindle cells, anisonucleosis and abundant eosinophilic granular cytoplasm with distinct margins (Figure 2C). Mitotic activity was 05/10 h.p.f. in stromal component. Epithelial cells had blunt nuclear chromatin, no mitotic activity and preserved myoepithelial component.

A final diagnosis of Malignant Phyllodes Tumour with marked granular cell change of stroma was given.

The surgeons converted the lumpectomy into a modified radical mastectomy without prophylactic radiation or chemotherapy. The patient recovered uneventfully and two whole body PET CT scan of this patient has not revealed any metastatic deposit 1 month and 11 months after surgery.

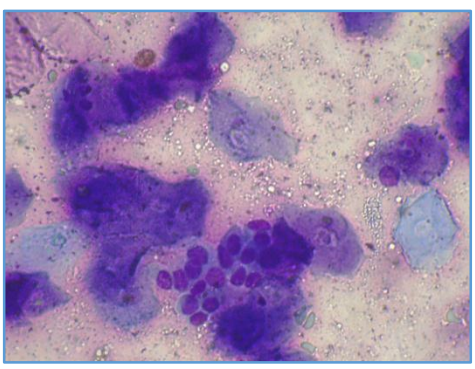

Figure 1A. Metaplastic Squamous Fragments with Mature Nucleated and Anucleated Squamous Cells (LG x 400)

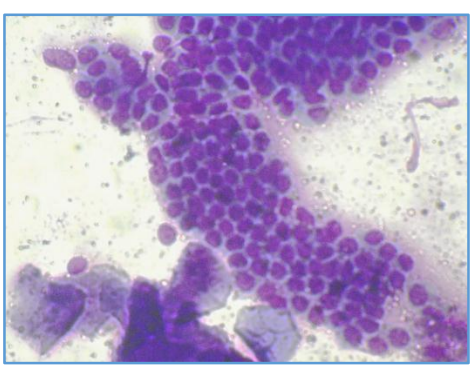

Figure 1B. Ductal Component in a Background of Mature Squamous Cells (LG x 400)

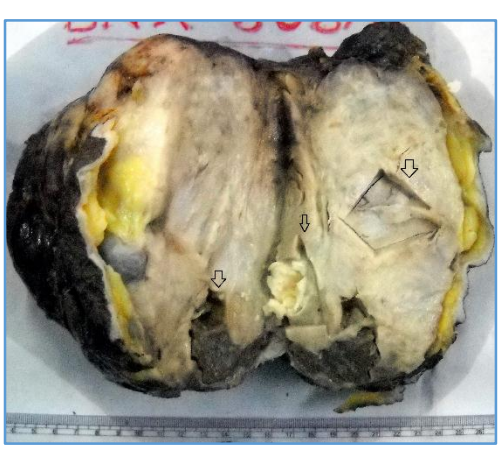

Figure 1C. Gross Specimen shows a Variegated Mass with Solid and Spongy Areas; Arrows marking the Areas of Sections Taken

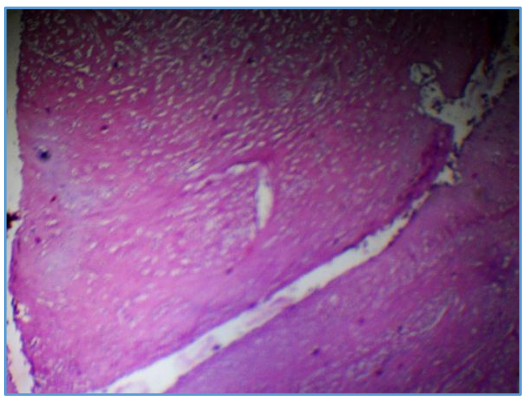

Figure 1D. Stromal Overgrowth with Leaf-like Fronds of benign Ductal Epithelial Cells (H & E x 100)

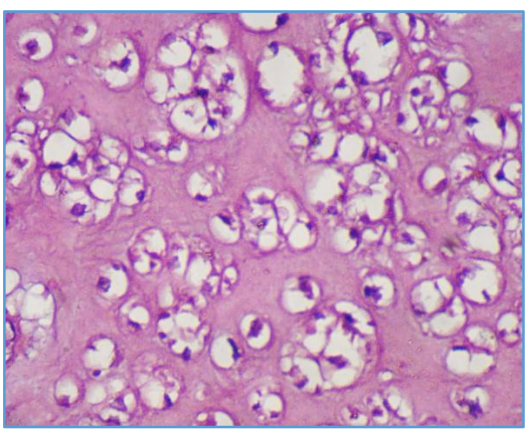

Figure 1E. Chondrosarcomatous Area (H & E x 100)

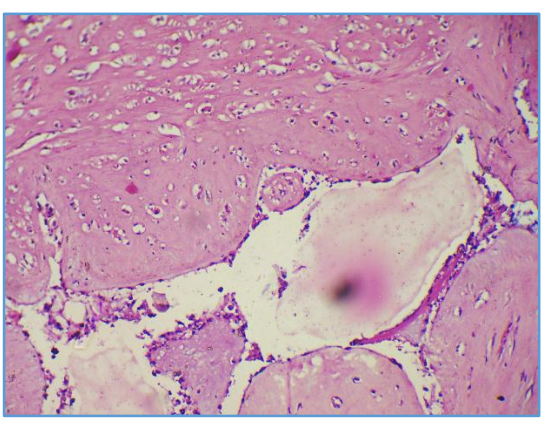

Figure 1F. Chondrosarcomatous Area (H & E x 400)

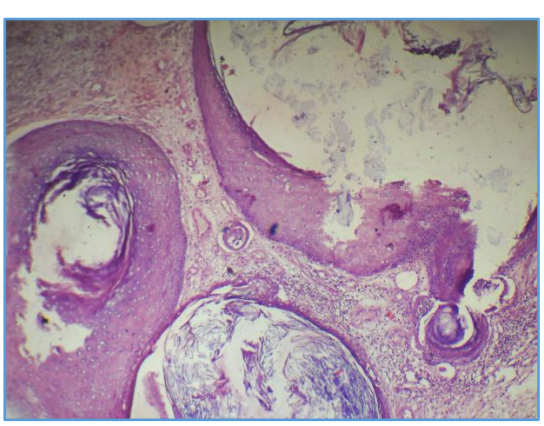

Figure 1G. Squamoid Areas with Epidermal Cyst Formation (H & E x 100)

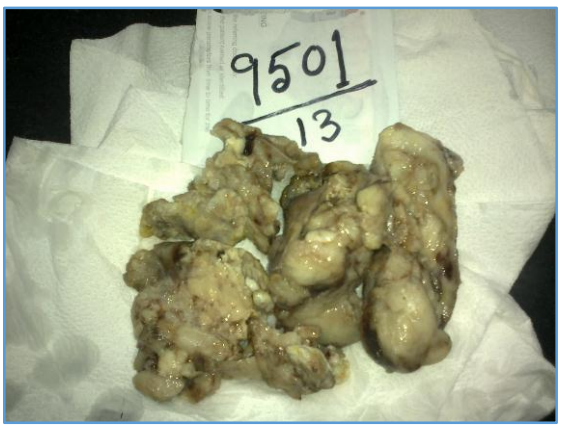

Figure 2A. Cut Surface of the Gross Lumpectomy Specimen shows Lobulated, Gray-White, Homogeneous, Soft-to-Firm in Texture with Fleshy White Areas and Chink-like Clefts

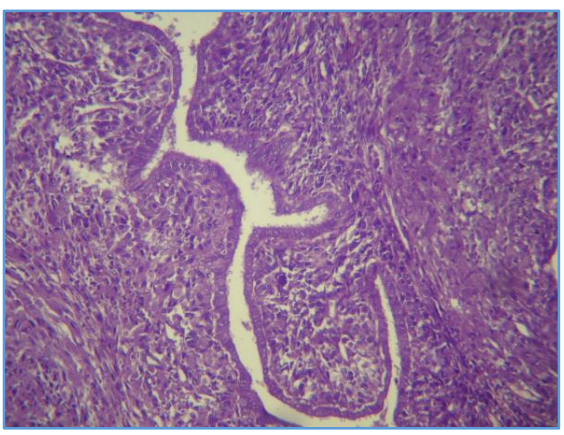

Figure 2B. Low Power View (H & E x 100) of Tumour showing Cleft-like Spaces Lined by Blunt Epithelial Component and Cellular Stroma

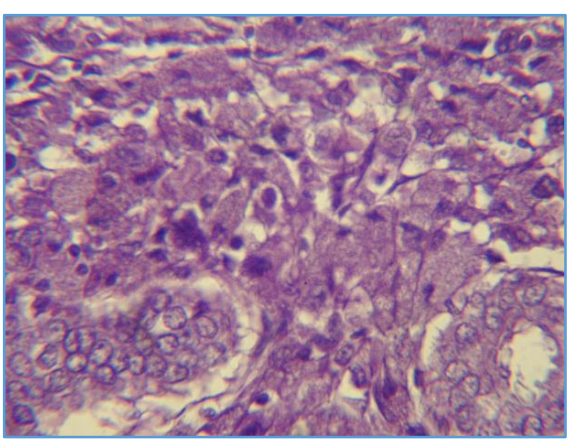

Figure 2C. High Power View (H & E x 400) of Compact Stromal Component showing Large Polygonal Granular Cells with Distinct Cell Boundary, Eosinophilic Granular Cytoplasm, Anisonucleosis and Mitotic Activity with Entrapped Duct lined by Single Layer Benign Epithelial Cells

DISCUSSION

The term Phyllodes Tumour first appeared as an entity in WHO classification of 1981.[7] A clear majority of the cases (35 - 64%) are benign[8] and amenable to cure after wide excision or mastectomy. Patients are usually

postmenopausal, median age of diagnosis being 45 years. This is sharply in contrast with fibroadenomas, which tends to happen in young women. The diagnosis of PT is fraught with difficulty. Clinical signs of a unilateral rapidly growing breast tumour often alerts the surgeon of the possibility of a phyllodes tumour. There is no specific radiological feature. After detection of a breast lump, FNAC from the lesion is a routine procedure in most parts of the world, usually associated with ultrasonography and/or mammography. The role of a cytopathologist is to confirm the suspicion of the PT and grade it benign, low grade or high grade which corresponds to histological classification of benign borderline and malignant defined by WHO.[9] Histopathology following biopsy or surgery is still gold standard in diagnosis and classification of PT.

Microscopic diagnosis of phyllodes tumour rests on two basic principles of stromal hypercellularity and the presence of benign glandular elements as an integral component of the neoplasm.[4] Malignant PT is diagnosed by sarcomatous stroma, high mitotic index and stromal overgrowth along with an invasive margin on histopathology. Metastasis and tumour necrosis are important feature of this subtype. In the sarcomatous area various stromal changes are found; most notable of them are angiosarcoma, liposarcoma, chondrosarcoma, myosarcoma or osteosarcoma.[3] The diagnostic difficulty with these stromal changes are two-fold. Firstly, they are sometimes very prominent so as to obscure the typical phyllodes morphology. Secondly, they are not always of the usual types mentioned above. There may be a myriad of changes ranging from squamous metaplasia to atypical ductal and lobular cells, even frank carcinoma,[10] which when arising in conjunction with a malignant phyllodes tumour get counted as a carcinosarcoma.

FNAC can suspect a presence of phyllodes morphology in most cases, but overgrowth of an atypical sarcomatous element can give a different diagnosis ranging from inadequate for opinion to primary sarcoma (ranging from C1 to C5 in cytologic scale of behaviour).[7]

Biopsy and histopathology should always be attempted in case of 'inconclusive' cytology in a rapidly growing unilateral breast mass.

CONCLUSION

Malignant phyllodes Tumour usually runs a fatal course due to rapid growth of the tumour and metastasis. Pathologists should be aware of the atypical changes in the stroma and limitation of FNAC in such cases. Clinicians should be conversant with such changes in stroma, which will help them to manage similar cases by early biopsy and a more adequate surgery.

Abbreviations

1. PT - Phyllodes Tumour.
2. FNAC - Fine Needle Aspiration Cytology.
3. H and E - Haematoxylin and Eosin Staining.
4. LG - Leishman and Giemsa staining.
5. PET Scan - Positron Emitting Tomography CT scan.
6. WHO - World Health Organisation.

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