



Transformation of a Breast Fibroadenoma to Borderline Phyllodes Tumor in a 20-Year-Old-Girl with Diagnostic Difficulties: A Case Report & Review of Literature

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Authors' contributions

This work was carried out in collaboration among all authors. Author SSK designed the study, wrote the protocol and wrote the first draft of the manuscript. Author TK managed the analyses of the study. Authors HC and BK managed the literature searches. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

We are reporting a rare case of 20 year old girl who presented with lump in the left breast at the age of 18 years. She underwent Fine Needle Aspiration Cytology (FNAC) twice and it was diagnosed as fibroadenoma. Conservative treatment had been advised to her but within next two years, there was gradual increase in the size of the lump to acquire a size of 4x3 cm. Again she underwent evaluation outside with repeat FNAC which was reported as benign breast disease. After consultation with us, we had advised core needle biopsy which was indeterminate. Therefore, we planned wide local excision of the lesion and final pathology turned out as borderline phyllodes tumor. Phyllodes tumor are not true sarcomas. Sometimes they have cystic components also. Their biological behavior and

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cellular origin is different from the origin of true sarcomas. Most commonly they occur in females with median age of presentation of 42 to 45 years. High grade tumors are found in elderly patients. Clinically approximately 20 % of these tumors presents as non palpable lesion which is picked up by screening mammography.

Conclusion: The definitive histopathological diagnosis of phyllodes tumor is possible only after surgical excision and the principle of surgical excision is excision with clear wide margins to avoid local recurrence.

Keywords: Borderline phyllodes tumor; malignant tumor; girl; FNAC; wide excision; core needle biopsy; case report.

1. INTRODUCTION

Phyllodes tumor were originally called "Cystosarcoma phyllodes" by Johannes Muller in 1838 [1]. They are not true sarcomas and occasionally they have cystic components. The pathway of origin of phyllodes tumor is different from that of true sarcomas and they differs in their biological behavior and cellular origin from true sarcomas. These are uncommon fibroepithelial breast tumors with diverse range of biological behavior. When they are least aggressive, they behave like benign fibroadenomas which has a tendency of local recurrence if removed incompletely with positive margins and at the other end they have a potential of distant metastasis. They accounts for less than 1 percent of breast neoplasms [2,3]. They commonly found in women with median age of presentation of 42 to 45 years (Range 10 – 82 years) [4]. High grade tumors are found in elderly patients [5]. Cases of these tumors had been reported in males in association with gynecomastia [6]. Syndromic association has been found in association with Li-Fraumeni syndrome [7]. Clinically approximately 20 % of these tumors presents as non-palpable lesion which is picked up by screening mammography [8]. Other presentations like nipple retraction, ulceration, chest wall fixation, bilateral diseases are rare but have been described for these tumors [9].

We are reporting a case of a girl who presented with left breast lump for the last two years and which had been diagnosed as fibroadenoma on successive FNAC. However, after wide excision of the lesion, final pathology turned out as borderline phyllodes tumor.

2. CASE REPORT

A 20 year old unmarried girl with no comorbidity with Eastern Cooperative Oncology Group (ECOG) Performance Status 1 (PS -1) presented

to our clinic with lump in the left breast for the last two years. She submitted all her previous investigations and reports. There was no positive family history. There was no relevant hospitalization, medical and surgical history in the past. At 18 years of age, she noticed a small lump of size of 2x1 cm in the left breast at upper outer quadrant. She consulted a local clinician who advised her to undergo FNAC (Fine Needle Aspiration Cytology). On microscopic examination of FNAC [Fig. 1] the picture of intracanalicular histologic pattern was found. The stromal connective tissue was invaginated into the glandular component and the compressed ducts had linear branching pattern with slit-like lumens. All findings were in favour of fibroadenoma. Conservative management with observation had been advised by the treating clinician to her. After one year, she noticed that there was an increase in the size of the lump. So she consulted the same clinician and again she underwent FNAC which also reported the same finding of fibroadenoma. Again reassurance had been given to her. Within next one year i.e at 20 years of age, she noticed that there was again an increase in the size of the lump reaching to a size of 4x3 cm. She was advised to undergo repeat FNAC and it was reported as benign breast disease. With this finding she consulted to our clinic. There was no history of pain, nipple discharge, contralateral breast lump and bilateral axillary swelling. On clinical examination, right breast and axilla were normal. Left breast had lump of size 4 x 3 cm at 12 'o clock position. It was a lobulated, hard , freely moving with normal nipple areola complex with no palpable axillary and supraclavicular lymph nodes. Rest of the systemic examination was unremarkable. In view of gradual increase in the size of lump we advised her to undergo ultrasound of both breasts and core needle biopsy from the lesion. Ultrasound [Fig. 2] was suggestive of a well-defined heterogeneously hypo echoic lesion measuring 3.8 x 2.7 cm in size located at 11-12

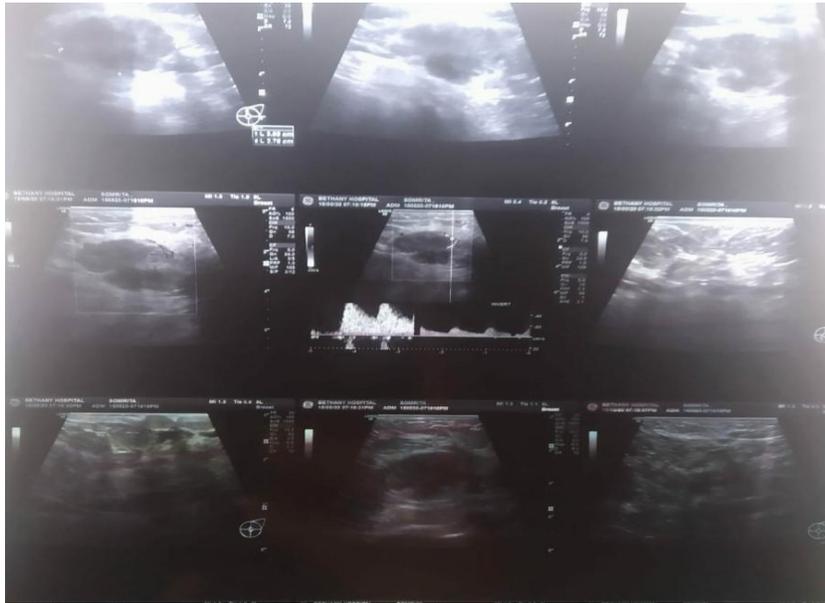


Fig. 1. Ultrasound images of left breast lesion

12 o'clock position with no significant axillary lymph nodes on either side possibility of fibroadenoma. Core needle biopsy was indeterminate. Clinical examination, pathology results and unexpected progress of the lesion in a young girl were not in favor of benign breast disease or fibroadenoma. Hence we advised her to undergo wide local excision of the lesion. Patient and her parents were also keen to remove it surgically. Hence, we planned her surgery with wide local excision of the lesion.

architecture with intracanalicular growth pattern and pushing borders. It comprises slit-like and branching ducts, having a preserved myoepithelial layer, which are surrounded by a stromal proliferation with no necrosis. The noteworthy feature was the presence of a prominent myofibroblastic stroma. Final histopathology report was suggestive of borderline phyllodes tumor with tumor size 3.9 x 3.7 x 3.7 cm with all margins more than 1cm and free from tumor.

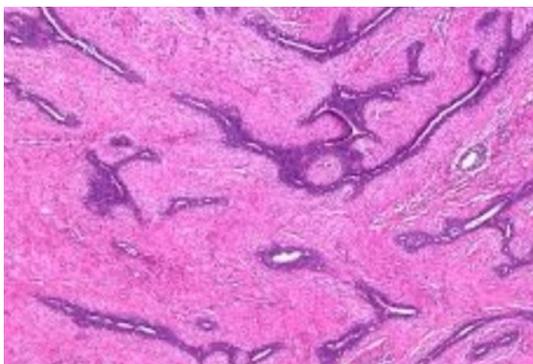


Fig. 2. Intracanalicular Fibroadenoma

With circumareolar incision she underwent wide local excision of the lesion with macroscopic adequate margins. She was operated in the morning hours and discharged in the evening. On histopathological examination [Figs. 3 & 4], there was a tumour composed of a leaf like

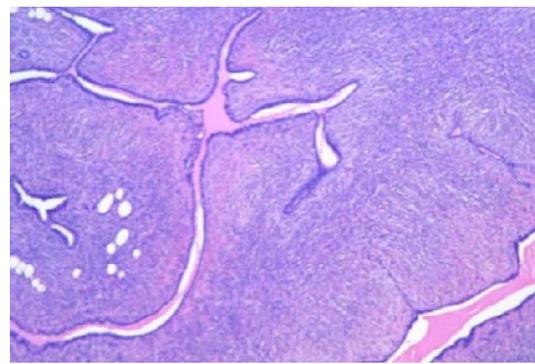


Fig. 3. Microscopic view of borderline Phyllodes Tumor (Low magnification)

The next question was whether adjuvant radiation is advisable or not to this girl. The case was discussed in our institutional multidisciplinary tumor board for the role of adjuvant radiation therapy. In view of borderline

nature of the tumor the board's final decision was no adjuvant treatment, only surveillance. She is on periodic follow up with us according to our institutional follow up protocol and after one year of completion of surgery, there is no recurrence.

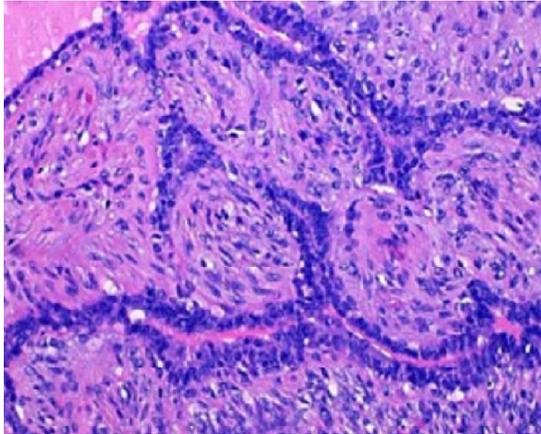


Fig. 4. Microscopic view of borderline Phyllodes Tumor (high magnification)

3. DISCUSSION

Phyllodes tumors are usually diagnosed on pathology. The imaging features of these tumors are in favor of fibroadenoma but history of rapid growth and large size indicates otherwise. The present case was also diagnosed as fibroadenoma on imaging and FNAC until its wide excision. The different imaging modalities available are ultrasound, mammogram and MRI of breast. On ultrasound, they appear primarily as solid, hypoechoic and well circumscribed mass. When there are cystic areas within the breast mass, the differential diagnosis of phyllodes tumor should be considered as first priority [10]. On mammography they appear as smooth, polylobulated mass which resembles a fibroadenoma. Routine use of breast MRI for phyllodes tumor is not supported by data. Malignant phyllodes tumor does not show rapid enhancement on MRI which is opposite to adenocarcinoma of breast. However, benign phyllodes tumor shows rapid enhancement on MRI [11].

The tissue diagnostic methods available are FNAC, core needle biopsy and excision biopsy. FNAC is associated with high false negative rate and low overall accuracy for the diagnosis of phyllodes tumor [12]. Core needle biopsy is typically diagnostic and the additional features

which distinguishes from FNAC are increased cellularity, mitosis, stromal overgrowth and fragmentation. If the result of a core biopsy is indeterminate, an excision biopsy is required. But core biopsy has a 25- 30 % false negative rate when used to diagnose phyllodes tumor [13]. If a core biopsy proven solid benign breast lesion rapidly increases in size or becomes symptomatic, an excision biopsy is indicated. The index case had undergone thrice FNAC which were suggestive of fibroadenoma and our core needle biopsy was indeterminate in spite of three cores from the lesion. Clinical course of the lesion was contradictory to the course of fibroadenoma, hence we advised her to undergo wide local excision of the lesion.

Histological classification of phyllodes tumors includes benign, borderline, or malignant based upon the assessment of four features [14,15]:

1. Mitotic activity
2. Infiltrative or circumscribed tumor margins
3. The degree of stromal cellular atypia
4. Presence or absence of stromal overgrowth

Out of all these features, stromal overgrowth is most consistently associated with aggressive behavior [16]. Benign tumors are characterized by increased stromal cellularity with mild-to-moderate cellular atypia, circumscribed tumor margins and low mitotic rate (less than 5 mitoses per 10 high-power fields), and lack of stromal overgrowth. Borderline tumors have a greater degree of stromal cellularity and atypia, a mitotic rate of 5 to 9 mitoses per 10 high-power fields, microscopic infiltrative borders, and lack of stromal overgrowth. Malignant tumors are characterized by marked stromal cellularity and atypia, infiltrative margins, high mitotic rate (more than 10 mitoses per 10 high-power fields), and the presence of stromal overgrowth [17,18, Table 1]. In case of malignant or metastatic phyllodes tumors, one or more sarcomatous elements had overgrowth. Benign phyllodes tumor have better local control and disease free survival as compared with borderline and malignant phyllodes tumor [19]. The recurrence rate is very low with benign and borderline phyllodes tumor after wide excision [20].

There are no prospective randomized trials describing the principles for treating a phyllode tumor. It is based on mainly retrospective series and case reports. A complete surgical excision is

Table 1. Histopathological classification of phyllodes tumor

	Benign	Borderline	Malignant
Stromal atypia	Mild	Moderate	Marked
Stromal cellularity	Mildly increased, can be focal	Moderately increased, can be focal	Markedly and diffusely increased
Stromal overgrowth ¹	Absent	Absent or very focal	Present
Mitotic count	< 5/10 HPF or < 2.5/mm ²	5 - 9/10 HPF or 2.5 - < 5/mm ²	≥ 10/10 HPF or ≥ 5/mm ²
Tumor border	Well defined	Well defined or focally permeative	Diffusely permeative
Malignant heterologous elements	Absent	Absent	Presence directly upgrades to malignant category ²

¹ Defined as absence of epithelial elements containing stroma only in 1 low power field

² Includes chondrosarcoma, liposarcoma (except well differentiated liposarcoma), osteosarcoma, rhabdomyosarcoma, angiosarcoma and leiomyosarcoma

the standard of care for phyllodes tumors. One case series had reported a positive surgical margin was associated with fourfold higher risk of local recurrence [21]. For positive margin, re-excision is the treatment plan. Surgical margins of ≥1 cm have been associated with a lower local recurrence rate in borderline and malignant phyllodes tumor [22]. For benign phyllodes tumor only clear margin is accepted but still there are lots of conflicting statements about margin of phyllodes tumor. A 2019 meta-analysis [17] of 54 observational studies found that a positive margin is associated with higher risk of local recurrence only for malignant phyllode tumor but not for benign and borderline tumors. They had reported overall local recurrence rate of 12 percent (95% CI 10- 14), and pooled local recurrence rates of 8, 13, and 18 percent for benign, borderline, and malignant tumors, respectively. Regardless of all statements, it is safe to accept clear margins for benign tumor and > 1cm margin for borderline and malignant tumors. There is no role of mastectomy for benign phyllodes tumor. The standard of care is wide local excision with clear margins unless indicated when negative margins cannot be achieved or tumor is so large that breast conserving surgery results in cosmetic disfigurement. Axillary lymph node dissection is rarely indicated for phyllodes tumor as it rarely involves axillary lymph nodes [23]. In the present case also, we did not go for axillary dissection as there was no axillary lymphadenopathy.

Radiation Therapy (RT) is considered in the treatment of phyllodes tumor when there is incomplete excision of the tumor or positive surgical margin. In a meta analysis [24] of eight observational studies, it is found that adjuvant RT

clearly reduced local recurrences of borderline or malignant phyllodes tumors after breast-conserving surgery (HR 0.31, 95% CI -0.10 to 0.72) but had no effect on overall or disease-free survival. But National Comprehensive Cancer Network (NCCN) recommends only surveillance upto 3 years and does not recommend adjuvant RT for benign, borderline or malignant phyllodes tumor if it is complete excision [25]. The role of chemotherapy in the treatment of phyllodes tumor is controversial. There are no randomized trials of adjuvant chemotherapy for these tumors. The available data is limited and only retrospective case series had treated these tumors with adjuvant chemotherapy which also does not show any survival benefit. In the same way hormonal therapy does not have any effect on phyllodes tumor [26]. Hormonal receptors are present in the epithelial component of phyllodes tumor and the stromal component expresses estrogen receptor beta instead of receptor alpha which is expressed by breast cancer [27]. The stromal component is considered as the main neoplastic cell population responsible for the metastatic behavior.

Recurrent phyllodes tumors are treated with surgery with or without adjuvant radiation therapy. The target is to avoid re-recurrence and the need for additional surgery. Resectable recurrent disease is treated with re-excision with adequate margins or mastectomy followed by radiation therapy (RT). Unresectable recurrences are treated with palliative radiation alone. The mean survival of patients with metastatic phyllodes tumor is around 30 months [28]. These tumors most commonly metastasize to lungs and resectable metastasis can be considered for metastatectomy or systemic chemotherapy as

per the treatment guidelines of metastatic soft tissue sarcoma. The five year survival rate for malignant phyllodes tumor is around 60-80 % [29].

4. CONCLUSION

Borderline phyllodes tumor is only diagnosed by histopathological examination. Whenever there is suspicion of phyllodes tumor on clinical examination the first choice of investigation is core needle biopsy as FNAC has high false negative rate and low overall accuracy for the diagnosis of phyllodes tumor. If the core needle biopsy comes inconclusive the next choice is its surgical excision. The principle of surgical excision of all types of phyllodes tumor (benign, borderline and malignant) is excision with clear wide margins to avoid recurrence.

CONSENT

An informed consent to publish this case was obtained from the patient.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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