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MALIGNANT PHYLLODES TUMOUR OF BREAST WITH SOLITARY BONE METASTASIS IN FEMUR : A CASE SERIES AND REVIEW OF LITERATURE

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ABSTRACT:
Breast cancer is the most commonly diagnosed neoplasm in women worldwide [1]. Phyllodes tumor is a very rare tumor of the breast, incidence being 0.3–0.9% of all breast tumors. (2,3).
Distant metastases occur in about 2 percent of phyllodes tumours and are seen almost exclusively in malignant phyllodes tumours. They usually occur within 5-8 years of diagnosis.(4,5)
We present 3 cases of women in their late 3rd and early 4th decade of life who were diagnosed with a malignant phyllode tumour of breast and underwent standard surgical and adjuvant treatment with curative intent. However presenting in their at mid term follow up with a solitary metastasis to bone .
All three cases had presentation in femoral bone and underwent surgical management . One of the patients denied chemotherapy while the other two received standard Ifosphamide and adriamycin based chemotherapy.
All three females were mobile independent with no local or distant metastasis at last follow up.

Key words: Malignant Phyllodes Tumour,solitary Metastasis,Whoops Surgery,Breast cancer,Immunohistochemistry

INTRODUCTION:

Breast cancer is the most commonly diagnosed neoplasm in women worldwide [1]. Phyllodes tumor is a very rare tumor of the breast, incidence being 0.3–0.9% of all breast tumors. (2,3).
Phyllodes tumour (PT) arises from intralobular stroma of breast. They are classified into benign, borderline, and malignant phyllodes tumours (MPTs) based on histologic characteristics (4).

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The rarity of this malignancy contributes to the difficulty in defining the most appropriate treatment. This uncertainty is even more marked for recurrent and metastatic MPTs, for which prognosis is significantly affected, and evidence is limited concerning their optimal management.(6,7)
The incidence of phylloid tumour is higher in Asian women (2.5%) compared to women of European decent (0.3-1%) . Phyllodes tumours occur predominantly in older women (average age: 40- 50 years).(8)

CASE SERIES:

CASE 1:
36 years old woman presented to us with history of pain and swelling in her left thigh and knee for 4 weeks. The patient noted diminished ability to use her left lower extremity due to worsening left hip pain. Clinical examination revealed a tender distal femur with gross limitation of right lower limb movements.

In her past, she had malignant phyllodes tumour in right breast diagnosed 4 years ago in 2021 .The lump was initially small about 1.5cm which was present since 2016. She only sought medical attention during phase of rapid growth in size of the lesion covering the whole breast .Biopsy revealed a malignant phyllode tumour .She subsequently underwent Wide excision in the form of Right mastectomy and local flap transposition in 2021. She also received adjuvant radiotherapy .

At her recent presentation a Magnetic resonance imaging (MRI) of the femur was acquired to evaluate disease extent and to aid in surgical planning (Figure 2) It Showed a well-defined osteolytic lesion in distal femoral metaphysis appearing central in location with perilesional oedema. The lesion appears hypo to isointense on T1W images and mildly hyperintense on T2W Images surrounded by a hypointense rim. There was narrow zone of transition and continuous periosteal reaction with break in posterior cortex of distal femur extending posterior along distal femur suspected of pathological fracture and extending into soft tissue. There was subtle cortical erosion and endosteal scalloping in anterior and medial femoral cortex. Internal foci of nodular / linear blooming was seen. The lesion measured approximately 65 x 41 x 38 mm (CC x AP x TR).
Computed tomography and FDG-PET Scan revealed meta diaphyseal lytic lesion in distal femur with pathological fracture and pathological FDG uptake of the left distal femur without other suspicious lesions.

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Subsequently, a CT guided bone biopsy was performed (which confirmed the presence of a spindle cell tumour consistent with the patient's known history of malignant PT.
Microscopic examination showed sections of spindle cells in interlacing fascicles exhibiting high-grade atypia and brisk Mitosis.(Figure 1)
On immunohistochemistry (IHC), the tumour cells tested positive for Vimentin while negative for CK, SATB2, H3F3A, TRPS1, SMA, MYOD1, MUC4, S100, DESMIN, ER, CD34, CDK4, SS18 and MDM2.
Thus, a diagnosis of metastatic malignant PT was made.
She underwent wide resection of the distal femur and mega prosthesis reconstruction but denied any chemotherapy.
She is doing well without any evidence of progression on her imaging follow-up at 6 months.

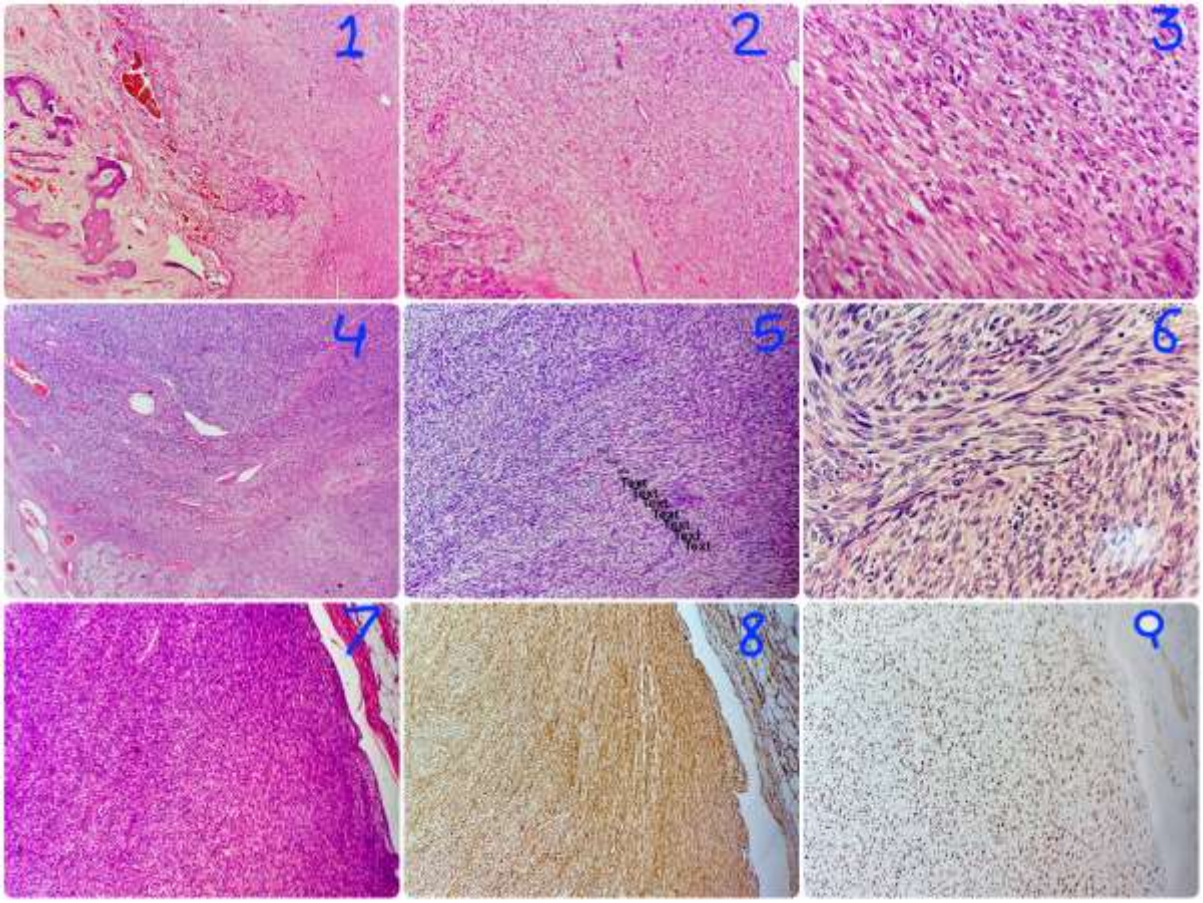

Figure 1: Photomicrograph shows a malignant spindle cell tumour consistent with a metastatic phyllodes tumour in bone and adjacent soft tissue. Images 1 & 4 (H&E 40X); Images 2, 5, & 7 (H&E, 100X); Images 3 & 6 (H&E 400X). Image 8 shows that the IHC stain is positive for vimentin (IHC, 100X). Image 9 shows high Ki67 proliferative index (30-35%), (IHC, 100X)

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Figure 2 : Showing MRI image and extent of lesion in distal femur

CASE 2:

45 years old woman presenting with pain and swelling of her right lower limb. She had suffered a pathological fracture of her right proximal femur 2 months ago. An inadvertent whoops procedure was performed elsewhere with proximal femoral nailing for fracture stabilisation 2 months ago. She also received radiotherapy to right femur after this surgery. She complained of persistent pain and swelling of her right thigh and hip with gross restriction of limb function and was completely bed bound.
Clinical examination revealed swelling extending from her right inguinal region to lower leg.

In her significant past history, she had Malignant phyllodes of her left breast 2 years ago for which she underwent breast conservation surgery. Tumour size was 9.5 X 5.6 X 4 cm and surgical margins posteriorly were close approximately 0.3cm ,0/21 lymph node positive. Radiotherapy was started on 16.10.2023 and completed Radiotherapy on 28.11.2023 (Dose - 50 Gy in 25 Fractions + 10 Gy in 4 Fractions - Boost) by IGRT Technique

Magnetic resonance imaging (MRI) of the femur was acquired to evaluate disease extent which revealed a large ill-defined heterogeneously enhancing solid cystic lesion involving proximal thigh, femoral neck and metaphyseal region, extending superiorly along iliopsoas muscle, without extension into the hip joint space, with

heterogeneous enhancing solid component and diffuse oedematous changes in subcutaneous, intramuscular and intermuscular planes and vascular encasement in anterior thigh region.(Figure 4)

PET CT scan revealed an FDG avid soft tissue density intramuscular mass lesion (18.0cm x 18.0cm x 23.0cm with SUV max of 11.9 involving muscles of right proximal thigh. causing lytic destruction in right proximal femur and no other focus of activity anywhere else in body.

Subsequently, a CT guided bone biopsy was performed and sections showed oval to spindle cell arranged in sheets and focal fascicular pattern. There was increased cellularity, marked atypic and significant mitosis. (14-16/HPF).(Figure)

On Immunohistochemistry tumour cells were positive for CD34, TRPS1, SMA while negative for S100, SATB2, TLE1, CK, DESMIN, MYOD1 CD68 and CD163 with numerous osteoclasts like giant cells in the background.

Thus, a diagnosis of a metastatic malignant Phyllodes tumour was made.

She underwent external hemipelvectomy and subsequent chemotherapy.

She is doing well without any evidence of progression on her follow-up at 8 months.

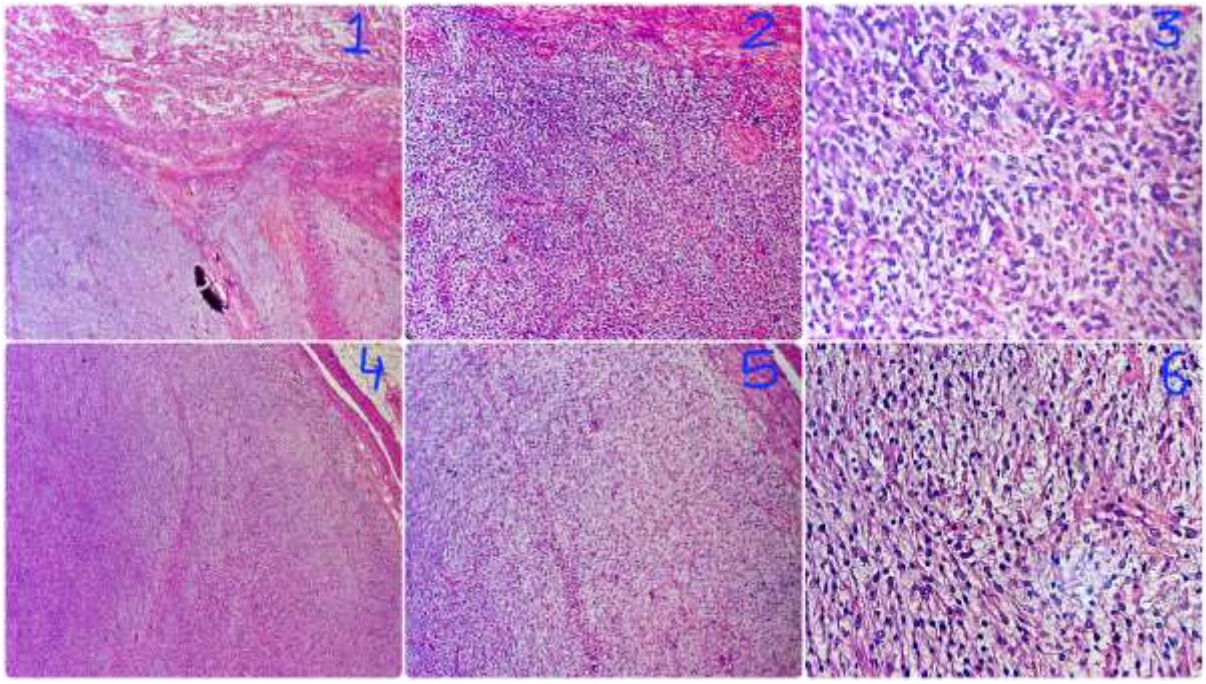

Figure 3 : Photomicrograph shows a malignant spindle cell tumour consistent with a metastatic phyllodes tumour of soft tissue around the proximal femur. Images 1 & 4 (H&E 40X); Images 2 & 5 (H&E, 100X); Images 3 & 6 (H&E 400X).

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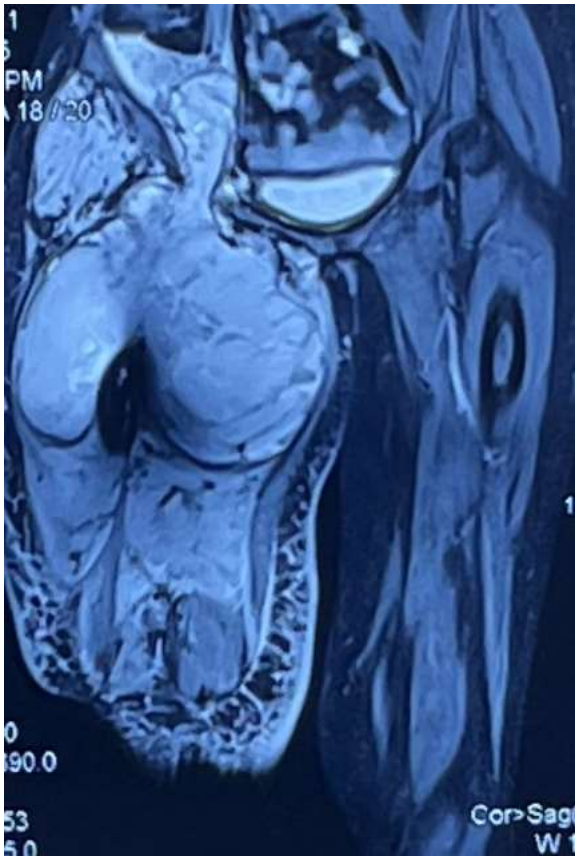

Figure 4: Coronal section of MRI showing the lesion and its extension into pelvis

CASE 3:

A 40 year-old woman presented with four-week history of pain left hip especially on weight bearing and at night which was progressively increasing. She is a known case of Malignant Phyllode tumour of her right breast which was diagnosed in 2023. She underwent right Mastectomy .The tumour size was 12cm x X 5 cm X 4.5 cm. Wide margins were achieved . She also receive radiotherapy to breast as well.

On her recent presentation an imaging studies revealed a lytic lesion of the left femoral head.

Magnetic resonance imaging (MRI) of the femur was acquired to evaluate disease extent which revealed an area of femoral head showing heterogeneously enhancing lesion involving the femoral head and part of neck without extension into the hip joint space.(Figure 7)

A PET CT scan showed a metabolically active lesion with no soft tissue element

The patient underwent core biopsy of his femoral head lesion under CT guidance. Pathological examination shows a proliferation of spindle cells in fascicles with nuclear atypia and high mitotic index (20-24/HPF)

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.Immunohistochemistry demonstrates vimentin,CD34 positivity,smooth muscle actin(SMA), while desmin, S100 protein, , C31, CD99 ,CD68 (Figure 5-6)
Biopsy was consistent with a diagnosis of metastatic malignant phyllodes tumour .
The Patient underwent wide excision and hip reconstruction with megaprosthesis . She further received ifosfamide and adriamycin based chemotherapy. She is doing well without any evidence of progression on her imaging follow- up after 9 months.

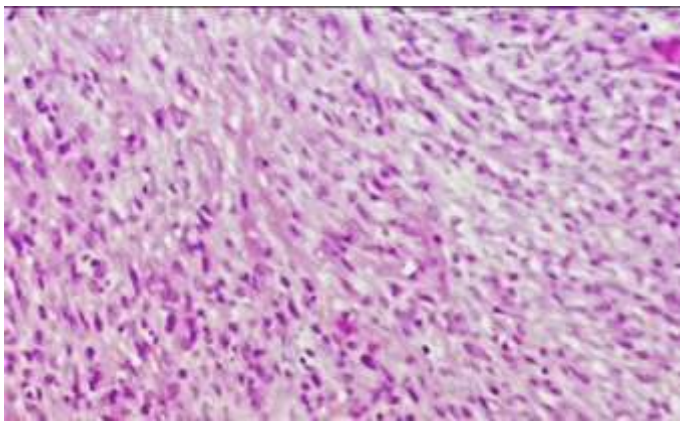

Figure 5: Photomicrograph shows malignant spindle cell tumour consistent with metastatic phyllodes tumour in bone.

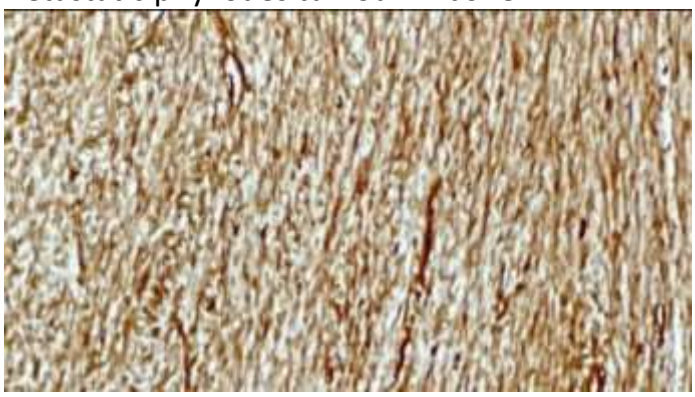

Figure 6: IHC staining positive for viamentin

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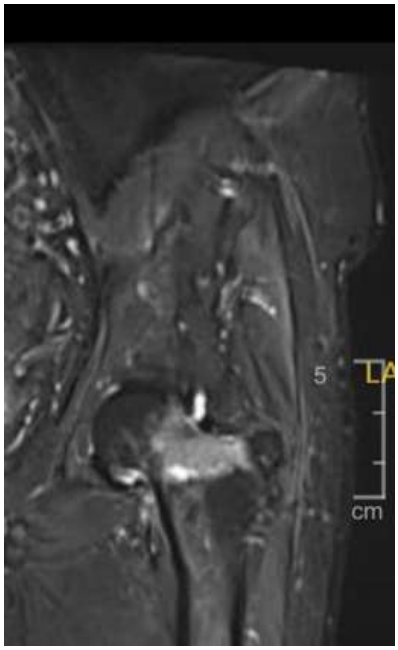

Figure 7: Coronal MRI image showing left femoral head lesion

DISCUSSION:

Metastatic PTs mainly develop from 3 to 10 years after the initial therapy, but they can be delayed or occur as soon as synchronous presentation [9,10].
Only a few cases of PT metastatic to bone have been reported (11,12,13,14)

A study by Kapiris etal looked at the outcome and predictive factors of local recurrence and distant metastases following primary surgical treatment of high grade malignant phyllodes tumour of the breast .In the study the mean patient age was 47 (range 21–85) years and the average tumour size was 7.8 (range 1.5–20) cm. Distant metastasis (DM) occurred in 13 (27%) patients at average time of 25.6 (range 6–120) months. Local recurrence, subsequent metastatic spread and survival following treatment of MPT were related to tumour size and excision margins, but not to other clinical or histopathological characteristics (9)

Up to 20% of malignant phyllodes tumours (PT) metastasize, most frequently to the lungs, bone, and brain. (15).

The clinical presentation of the PT is different compared to that of the breast adenocarcinoma. First, while both the breast adenocarcinoma and PT can occur at any age, the mean age of diagnosis of breast cancer in general in women is 61 [16,17].

In contrast, multiple studies have shown that the diagnosis of the PT tends to occur at an earlier age (18,19,20,21,22) which is consistent with our case series .

In the WHO classification of breast tumours 2019 stromal overgrowth, stromal atypia, and mitotic activity have been deemed to also be important in determining the risk of metastasis(8).All these parameters showed consistency with our cases .

A review of 352 cases of PT (90 malignant) at the Memorial Sloan-Kettering Cancer Center indicated that the 5 patients who developed distant disease composed 71% of patients whose pathological features were aggressive (≥7.0 cm tumour size, infiltrative borders, marked stromal overgrowth, marked stromal cellularity, high mitotic count, necrosis). Tumour necrosis was significantly associated with increased local failure (P=0.006), and was present in all 5 cases of distant disease (23).

CONCLUSION

All our cases also had an aggressive presentation and ,due to the lesion being in a weight bearing femoral bone in relatively healthy middle aged females ,the focus of surgical management was based on wide tumour excision and mechanical stability post-surgery. One of our cases presented with extensive local spread of disease after a whoops surgery with disease extension into pelvis .The limb was non salvageable in this case and she underwent external hemipelvectomy .Rest of the cases were reconstructed using standard oncological principles and megaprosthesis .All three females were mobile independent with no local or distant metastasis at last follow up.

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