Phyllodes tumors are uncommon fibroepithelial neoplasm of the breast, representing 0.3 to 0.5% of all female breast neoplasms. The term “phyllodes tumor” by the World Health Organization (WHO) categorizes it into benign, borderline, and malignant tumors based on histopathological characteristics. Malignant phyllodes tumor is an uncommon but aggressive breast malignancy and accounts for approximately 25% of all phyllodes tumors.

Case Presentation: A 23-year-old female patient Gravida 0 Para 0, previously healthy, with no family history of breast or ovarian cancer was referred to our institution for managing a right breast mass increasing in size over a period of 1 month associated with reddish-brown discoloration of the skin. Breast ultrasound showed an isodense oval mass measuring approximately 16x14x12cm in the right lower outer quadrant of her breast. Core biopsy and FNA done revealed a low grade phyllodes tumor. MRI of breasts showed a huge mass of the right breast occupying all quadrants, measuring 15x14.5 cm in its greatest axis with involvement of the pectoralis major muscle, with no evidence of suspicious axillary lymphadenopathy. Distant metastatic work-up with CT scan of chest abdomen and pelvis and a PET scan did not show distant metastasis. Hence, the patient underwent right total mastectomy with a final pathology compatible with malignant phyllodes tumor. She is on regular follow up and 18 months post-surgery is still disease free.

Conclusion: Management of malignant phyllodes tumor remains debatable, especially when it comes to the effect of adjuvant radiotherapy and chemotherapy. From a surgical perspective, whether phyllodes tumors should be considered as epithelial breast cancers or as soft tissue sarcoma is another debate. On the other hand, although challenging, accurate identification of phyllodes tumor initially may aid in decreased recurrence.
Case Presentation

Our case was a 23-year-old female patient Gravida 0 Para 0, previously healthy, with no family history of breast or ovarian cancer transferred to our institution to receive treatment for a right breast mass increasing in size over a period of 1 month associated with brownish and reddish discoloration of the skin. On physical examination of the right breast a grossly distorted architecture, with reddish-brown discoloration of the skin (Figure 1a, 1b) was observed with no nipple retraction. On palpation of the diffusely hard breast, no nipple discharge and no palpable right axillary lymph nodes were observed. The contralateral breast (left) was normal looking, with no palpable masses, and no left axillary lymph nodes.

The patient underwent investigations with breast ultrasound showing an isodense oval mass measuring approximately 16x14x12cm in the right lower outer quadrant of her breast. Core biopsy and FNA done revealed fragments of myxoid and cellular stroma. These findings were not specific but could indicate a fibroepithelial lesion such as cellular fibroadenoma and low grade phyllodes tumor. MRI of the breasts showed a huge mass of the right breast occupying all quadrants, measuring 15x14.5 cm in its greatest axis with involvement of the pectoralis major muscle, with no evidence of suspicious axillary lymphadenopathy. Distant metastatic workup prior to the surgical intervention with CT scan of chest abdomen and pelvis and a PET scan did not show distant metastasis. Hence, the patient was...
scheduled for right total mastectomy.

The patient went through a right total mastectomy with partial excision of the pectoralis major where the tumor was involved (Figure 3, 4). Primary closure was possible without the need for autologous flap for closure. The final histopathologic result was consistent with features of malignant phyllodes tumor measuring 16.5x15x14cm, with clear negative surgical margins 1.6cm away from the tumor and the deepest surgical margin being 2mm away from the tumor. Post-surgical follow-up showed good wound healing, revealing no flap necrosis (Figure 5). She is on regular follow up and 18 months post-surgery is disease free with no evidence of local recurrence or distant recurrence by PET scan.

Discussion

Extensive studies have been done regarding the treatment of common breast malignancies. However, the optimal management for rare breast tumors including phyllodes tumor has not been well established. Due to its rarity, the current medical literature lacks a sound treatment plan, especially when it comes to the effect of chemotherapy or radiotherapy on managing malignant phyllodes tumor of the breast. Most management protocols depend on retrospective case series. Irrespective of their histologic classification, phyllodes tumors have an unpredictable clinical outcome. Age, tumor size, surgical approach, mitotic activity, stromal overgrowth and surgical margin have been found to be important factors in diagnosis and prediction of recurrence. Kaprisi et al. found that tumor size and surgical margins were predictive of local recurrence, which is very important for treatment of phyllodes tumors to be successful. A review of the literature reveals a low recurrence rate >40% for all pathological types. On the contrary, different studies showed a local recurrence rate of less than 20% depending on the tumor subtype. Furthermore, a delay in treatment increases the possibility of distant metastases. Metastasis usually occurs via the bloodstream and lymphatic metastasis occurs rarely. The most frequently reported sites for metastases are the lung, soft tissue, bone, and pleura. The rate of metastases is 25%–31% for malignant and borderline tumors, whereas it is 4% for all types of phyllodes masses. Guidelines for cases of malignant phyllodes tumor by National Comprehensive Cancer Network include complete surgical resection with negative margins of at least 1 cm and preferably 1 to 2 cm due to the morphologic characteristic of the tumor. The presence of a pseudo capsule containing finger-like or pseudopodia-like projections around the phyllodes tumor tissue is likely, which, if not surgically excised, leads to a local recurrence. Therefore, the tumor with 1–2-cm width of normal tissue should be removed including these pseudopodia of tumors. Total mastectomy is in general not suggested due to poor cosmetic outcomes, unless negative margins cannot be conducted or if the tumor is too large to be completely excised. Adjuvant radiation therapy is debatable in preventing tumor recurrence. Radiation has been found to prevent recurrence of borderline and malignant phyllodes tumor after surgical interventions (breast-conserving surgery and mastectomy) with no impact on disease-free survival. Furthermore, adjuvant radiation therapy is suggested for recurrent and malignant phyllodes tumor. Patients with high risk for recurrence, including those with histological margin less than 5 mm may be candidates for radiotherapy. On the other hand, routine adjuvant systemic therapy after initial excision is not recommended. Chemotherapy for locally recurrent tumor is contentious. Burton et al. reported effective palliation for patients suffering from metastatic disease with chemotherapy based on cisplatin and etoposide. As far as we know, this is the youngest reported case of malignant phyllodes tumor of the breast with this size. In our case, despite the large size of the tumor negative surgical margins of 1.6 cm were achieved by total mastectomy, with no recurrence at 18 months of follow-up. In our
review of the English medical literature we identified 16 cases of large malignant phyllodes tumors of the breast, above 10cm in largest dimension (Table 1), with a size range of 10 to 40cm, with a mean age of 44 years old. Table 1 shows that the most common site of metastasis is lungs 6/16 (37.5%), followed by brain 3/16 (18.7%). Hence, appropriate surgery is the cornerstone and the first step towards successful treatment of phyllodes tumor.

In conclusion, management of malignant

Table 1. Comparison the studies evaluated malignant phyllodes tumor

<table>
<thead>
<tr>
<th>Author/year</th>
<th>Age</th>
<th>Pre-operative work-up</th>
<th>Size(cm)</th>
<th>Tumor Site</th>
<th>Type of Surgery</th>
<th>Adjuvant treatment</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>O.ECW*, K.CK, 2017**</td>
<td>53</td>
<td>Core biopsy inconclusive CT chest and abdomen: large tumor with extension to rib and pleura</td>
<td>40x38x16</td>
<td>Right</td>
<td>Radical mastectomy (tumor dissected off with right 6th rib and pectoralis major) (primary closure not possible)</td>
<td>None</td>
<td>1. All margins involved 2. Post-op PET scan: tumor infiltrating the 5th and 6th ribs 3. 6 weeks post-operative: re-admitted for pleural effusion deceased due to pulmonary complications</td>
</tr>
<tr>
<td>A. Testori et al., 2015**</td>
<td>33</td>
<td>PET: positive ALN Skeletal &amp; lung xray normal</td>
<td>40x30x10</td>
<td>Right</td>
<td>Modified radical mastectomy (1/9 LNs)</td>
<td>Chemotherapy (adriamycin and ifosfamide)/radiotherapy</td>
<td>Free of recurrence at 18 months follow up</td>
</tr>
<tr>
<td>R.Krishnamoorthy et al., 2014*</td>
<td>35</td>
<td>FNA: borderline phyllodes Core biopsy: biphasic neoplasm with malignant stromal component CT brain and chest &amp; US abdomen no metastasis</td>
<td>33x32x22</td>
<td>Right</td>
<td>Simple mastectomy</td>
<td>Chemotherapy (doxorubicin and ifosfamide) Radiotherapy</td>
<td>Free of recurrence at 1 year follow up</td>
</tr>
<tr>
<td>AP.Gregston et al., 2019**</td>
<td>32</td>
<td>Chest CT scan: large solid mass occupying the entire left breast</td>
<td>32x32x17</td>
<td>Left</td>
<td>Radical mastectomy with split thickness graft</td>
<td>6 cycles (AdriamycinVR, ifosfamide, and mesna) 4 cycles (gemcitabine and doceetaxel)</td>
<td>1. 3 weeks post-op: complaint of headache Right parietal tumor – right craniotomy: metastatic malignant phyllodes tumor 2. 7 weeks post-op: Right parietal tumor – right craniotomy: metastatic malignant phyllodes tumor 3. 2.7 weeks post-op: Right parietal tumor – right craniotomy: metastatic malignant phyllodes tumor 4. Patient deceased before any therapy could be initiated</td>
</tr>
<tr>
<td>N. Roberts, D.M. Runk, 2015*</td>
<td>50</td>
<td>Core needle biopsy: malignant neoplasm with carcinomatous and sarcomatous elements, the cells showed focal marked pleomorphism (10 mitoses/10HPF) with focal necrosis (ER/PR positive; HER2 negative) CT of chest positive for bilateral chest massesPET Scan: result not mentioned</td>
<td>31.5x15.6</td>
<td>Right</td>
<td>Simple mastectomy</td>
<td>Patient deceased before any therapy could be initiated</td>
<td>1.3 weeks post-op: complaint of headache Right parietal tumor – right craniotomy: metastatic malignant phyllodes tumor 2. 7 weeks post-op: Right parietal tumor – right craniotomy: metastatic malignant phyllodes tumor 3. Patient deceased before initiating treatment</td>
</tr>
<tr>
<td>I. Albalawi, 2018*</td>
<td>41</td>
<td>True cut biopsy malignant phyllodes tumor CT scan chest, abdomen and pelvis normal isotopes scan normal</td>
<td>30x20x13</td>
<td>Left</td>
<td>Simple mastectomy</td>
<td>Radiotherapy</td>
<td>Free of recurrence 1 year after surgery</td>
</tr>
<tr>
<td>MA. Sbeih et al., 2015*</td>
<td>41</td>
<td>Core biopsy: fascicular pseudoangiomatous stromal hyperplasia or phyllodes tumor Left ALN biopsy: chronic lymphadenitis without neoplastic cells CT chest and abdomen: no metastasis</td>
<td>20x20x25</td>
<td>Left</td>
<td>Simple mastectomy with left chest wall defect was covered temporarily with INTEGRA replaced with split thickness skin graft 5 weeks later</td>
<td>None</td>
<td>NA</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Case</th>
<th>Procedure</th>
<th>Follow-up</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>M. Takenaka et al., 2011</td>
<td>Radical mastectomy with pectoralis major excision + axillary lymph nodes dissection (no positive ALNs)</td>
<td>No LR 17 months after surgery</td>
<td></td>
</tr>
<tr>
<td>Our Case, 2020</td>
<td>Total mastectomy with partial excision of pectoralis major (with primary closure of defect)</td>
<td>No LR after 18 months follow-up PET scan: no distant metastasis</td>
<td>Free of LR at 3 years follow-up and free of distant metastasis (lung metastasis resolved)</td>
</tr>
<tr>
<td>SH Moon et al., 2019</td>
<td>Modified Radical Mastectomy + TRAM flap (1/32 ALNs)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T. Saito et al., 1998</td>
<td>Simple mastectomy</td>
<td>Radiotherapy (50Gy), Chemotherapy (Cyclophosphamide)</td>
<td>1. After 9 months Lung metastasis 2. Died of disease after 18 months of primary diagnosis</td>
</tr>
<tr>
<td>S. Khanal et al., 2018</td>
<td>Modified Radical Mastectomy</td>
<td>None</td>
<td>3 months' post-op: No LR - Huge cystic nodule in the brain - Contrast enhanced computed tomography (CECT) of chest, abdomen and pelvis showed lesions in lower lobe of left lung of 3.9 × 3.6 cm of +40 (HU) in posterobasal segment and right adrenal gland of 5.8 × 5.1 cm of +30HU - 20 days' later patient succumbed to disease</td>
</tr>
<tr>
<td>J. Kaya, A. Betensley, 2013</td>
<td>Simple mastectomy</td>
<td>Radiotherapy</td>
<td>19 months post-op: left pleural effusion/pleural mass - Patient deceased of disease 21 months after diagnosis</td>
</tr>
<tr>
<td>J. Alves et al., 2011</td>
<td>Simple mastectomy without ALND</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>A. Abdulkareem, 2019</td>
<td>Partial mastectomy</td>
<td>Radio</td>
<td>1. Free margins but &lt;1mm: re-excision margins 2. CT scan and bone scan negative for metastasis</td>
</tr>
<tr>
<td>M. Sani et al., 2008</td>
<td>Modified radical mastectomy</td>
<td>None</td>
<td>Post-op CT chest and abdomen scan; no liver or lung mets Follow-up NA</td>
</tr>
<tr>
<td>S. Suzuki-Uematsu, 2010</td>
<td>Simple mastectomy + ALN excision</td>
<td>4 cycles (FEC therapy: cyclophosphamide, epirubicin, fluorouracil)</td>
<td>1. Lung metastasis increased in size (progressive disease) 2. Patient died 4 months post-surgery due to respiratory failure</td>
</tr>
</tbody>
</table>
Phyllodes tumor remains debatable, especially when it comes to the role of adjuvant radiotherapy and chemotherapy. From a surgical perspective, whether phyllodes tumors should be considered as epithelial breast cancers or as soft tissue sarcoma is another debate. On the other hand, although challenging, accurate identification of phyllodes tumor initially may aid in decreasing the rate of local recurrence. Finally, due to rarity of such a disease, combining the observations of clinicians treating malignant phyllodes tumor in an international database will be beneficial to patients.

Acknowledgements
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Ethical Consideration
A written informed consent was obtained from the patient to publish the case as well as any associated images.

Conflict of Interest
None.

References


