Case Report

rare tumors

Rare Tumors
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Phyllodes tumor with metastases to the skull managed with local excision: A case report

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Abstract

The behavior of phyllodes tumors is unpredictable and can behave as benign fibroadenomas or malignant neoplasms mimicking the course of aggressive sarcomas, characterized by distant metastases and a high short-term mortality. The malignant forms are treated with surgery and adjuvant chemotherapy, but often with poor outcomes. We examine the first reported case of an aggressive osteosarcoma subtype of phyllodes tumor that recurred in the skull after total mastectomy and adjuvant chemotherapy. The skull lesion was treated with excision, and the patient currently remains disease-free.

Keywords

Phyllodes, phyllodes tumor, skull, calvarium, breast cancer

Introduction

Phyllodes tumors are rare tumors of the breast which are capable of a wide range of disease activity. The benign tumors are often labeled as fibroadenomas and are managed with wide resection. However, the malignant types are aggressive, often with distant metastases to sites such as brain, liver, lung, adrenals, and rarer sites such as duodenum, heart, and parotid glands.[1] The skull is a well-known place for metastases, with breast cancer the most common primary site.[2] However, this is the first known case report of a patient with phyllodes tumor of the breast metastasizing to the skull. This patient is disease-free 49 months after surgical resection of her skull metastases, which is unusual considering the high recurrence rates of phyllodes tumors.[3]

Case

The patient is a 45-year-old woman who initially presented in 2012 with a 3-month history of a painful mass in the right breast that had been rapidly growing. A diagnostic mammogram done a few weeks later showed a BIRADS 4C lesion. A subsequent ultrasound showed a 15-cm lobulated mass of mixed echogenicity with areas of necrosis. US-guided biopsy showed a malignant spindle cell neoplasm with extensive necrosis. The criteria used to classify this tumor as a phyllodes tumor were stromal overgrowth, nuclear pleomorphism, high mitotic rate in stromal cells, infiltrative border in surrounding breast tissue, benign breast epithelium, and pericanalicular pattern of stromal growth. Phyllodes tumors which exhibit a percanalicular and infiltrative pattern are also called periductal stromal sarcomas, thus placing our tumor in this category (Figures 1–7). Multiple immunostains were negative including pancytokeratin (CK AE1/AE3), CK5/6, and EMA, thus

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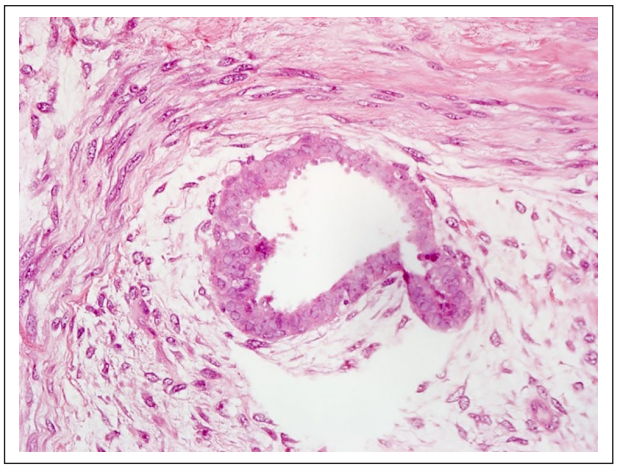

Figure 1. Pathology: Neoplastic stroma.
H&E stained image demonstrates benign breast epithelium with apocrine metaplasia. The surrounding stroma represents the neoplastic stroma of the phyllodes tumor.

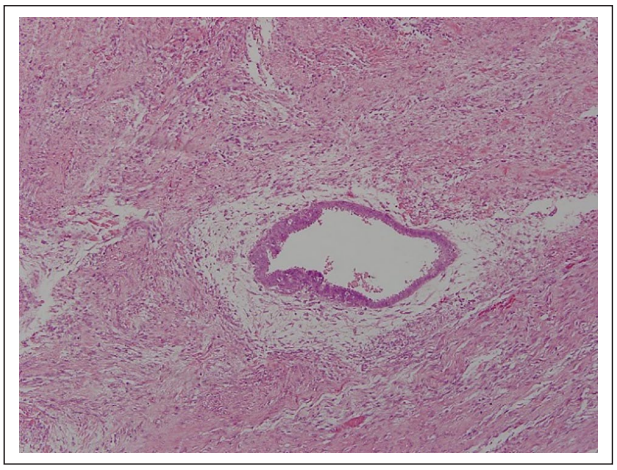

Figure 3. Pathology: Pericanalicular growth, 100×.
Pericanalicular growth: H&E stained image demonstrating a pericanalicular overgrowth of spindle-shaped stromal cells (magnification 100×).

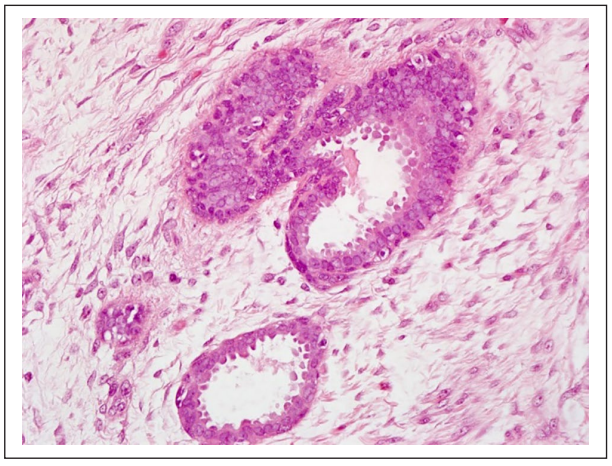

Figure 2. Pathology: Benign breast epithelium.
H&E stained image demonstrates benign breast epithelium with apocrine metaplasia and usual ductal hyperplasia. The surrounding stroma is neoplastic.

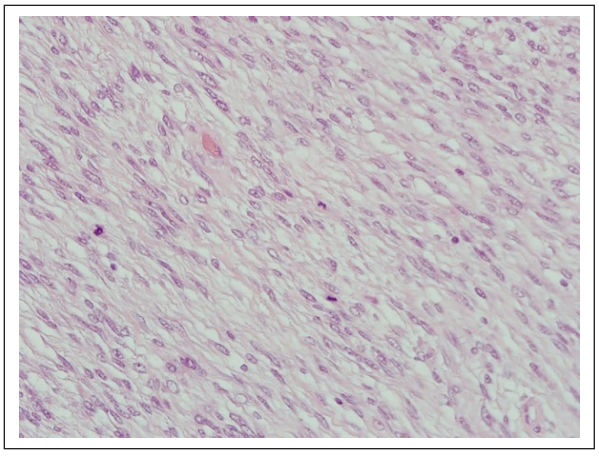

Figure 4. Pathology: Phyllodes mitoses, 400×.
Phyllodes mitoses: H&E stained image exhibits three mitotic figures and overgrowth of spindle-shaped stromal cells. Mitotic count was 32 per 10 high power fields in the most proliferative area. (magnification 400×).

eliminating metaplastic carcinoma (Figures 8 and 9). Furthermore, the presence of a heterologous element such as osteosarcoma in a breast stromal tumor is more likely a part of phyllodes tumor than primary breast sarcoma. Breast sarcoma is a very rare neoplasm which is a diagnosis of exclusion. Since this tumor fits within the phyllodes tumor based on the aforementioned criteria, the tumor cannot be classified as a primary breast sarcoma. The case was presented at sarcoma tumor board and was deemed high risk for recurrence and development of metastatic disease given tumor histological characteristics and a significant component of osteosarcomatous dedifferentiation. In March 2012, the patient underwent a total mastectomy with flap reconstruction. Final surgical pathology showed a 22.8-cm mass with histologic features consistent with phyllodes sarcoma with osteosarcomatous dedifferentiation. The mitotic rate was 32/10 HPF, 25% necrosis, negative margins, and a final pathologic stage of pT2aNxMx. A CT scan of the chest, abdomen, and pelvis showed no evidence of metastatic disease. She underwent four cycles of adjuvant Cisplatin 100 mg/m^2 and Adriamycin 60 mg/m^2 from May to July 2012 followed by radiation therapy consisting of 5040 cGy in 180-cGy fractions from August to September 2012. Annual surveillance CT scans of the chest showed no evidence of metastases through the early part of 2015. The patient reported to her oncology appointment in April 2015 complaining of a lump on the right side of her head associated with headache and eye pain. A PET CT scan showed a metabolically active soft-tissue lesion on the skull extending from the right parietal bone that was concerning for a

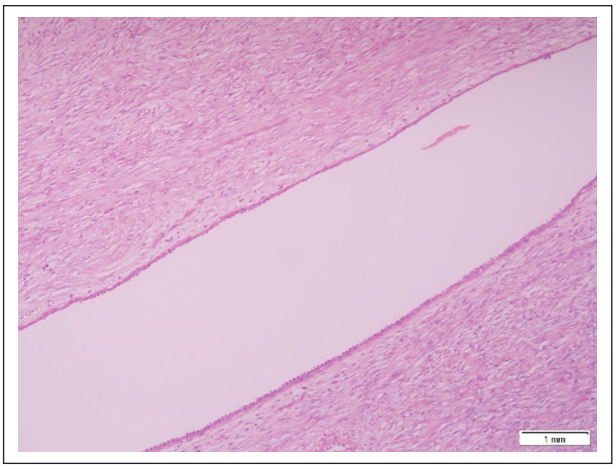

Figure 5. Pathology: Pericanalicular growth.
Pericanalicular pattern of stromal overgrowth with retained benign breast epithelial component.

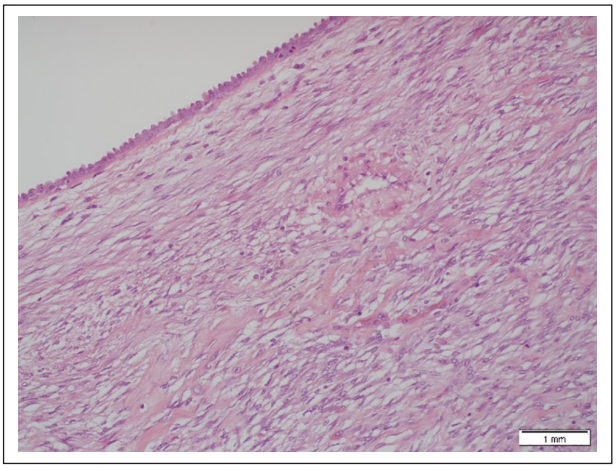

Figure 6. Pathology: Pericanalicular growth.
Pericanalicular pattern of stromal overgrowth with retained benign breast epithelial component.

solitary metastasis. MRI of the brain showed a 3.6-cm right parietal and frontal bone mass with minimal extension into the adjacent extra-axial space favoring metastases (Figure 11). Neurosurgery was consulted and the mass was resected (Figure 12) with the final pathology showing phyllodes tumor with osteosarcomatous elements and clear margins consistent with her original breast diagnosis (Figure 10). The case was discussed at a multi-disciplinary tumor board with a plan for adjuvant chemotherapy with a standard relapse regimen consisting of Ifosfamide and Etoposide. However, after presenting the patient with this plan at the next follow-up, she declined and elected to continue with serial scans and consider treatment in the future if her disease were to return. Subsequent follow-up with regular radiological and clinical surveillance confirmed the patient being free of disease 4 years after relapse.

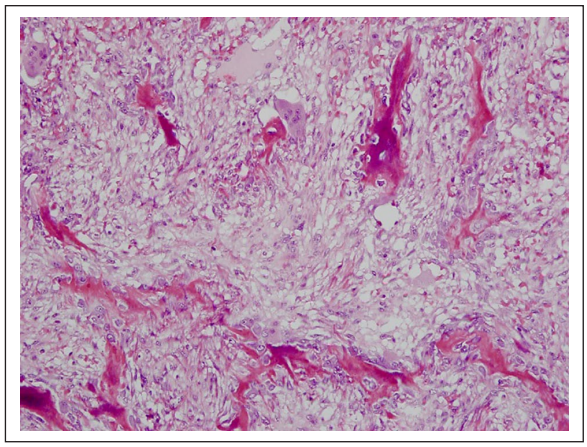

Figure 7. Pathology: Malignant osteoid.
Malignant osteoid: H&E stained image shows spindle cells, scattered giant cells, and malignant osteoid representing the heterologous element of osteosarcoma in the setting of a malignant phyllodes tumor.

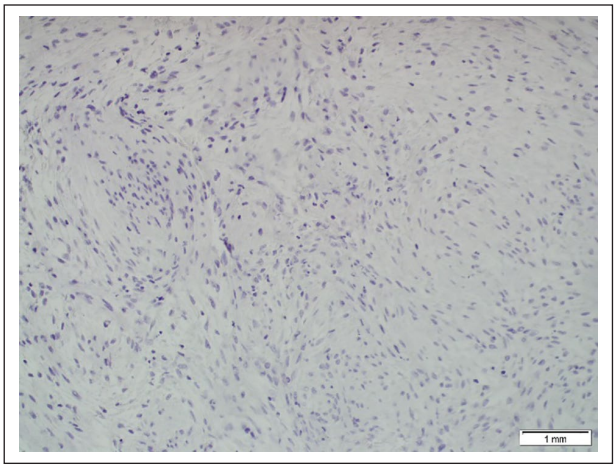

Figure 8. Pathology: IHC stain, EMA.
Immunohistochemistry stain for epithelial membrane antigen, negative.

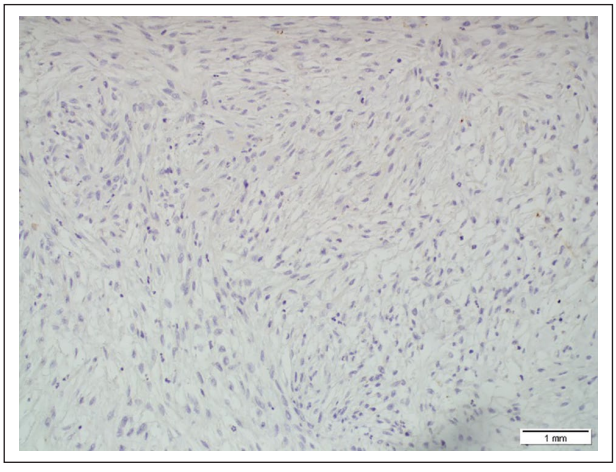

Figure 9. Pathology: IHC stain, pancytokeratin.
Immunohistochemistry stain for pancytokeratin, negative.

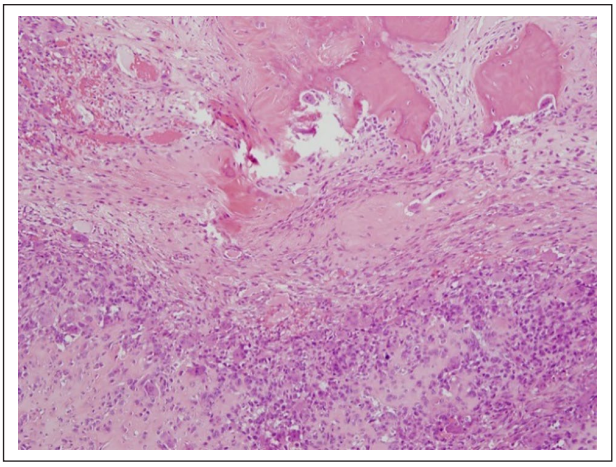

Figure 10. Pathology: Skull metastases.
Skull mets: H&E stained image displays numerous atypical spindle and epithelioid cells with mitosis and malignant osteoid, invading the bone. This is consistent with metastatic osteosarcoma, to the skull.

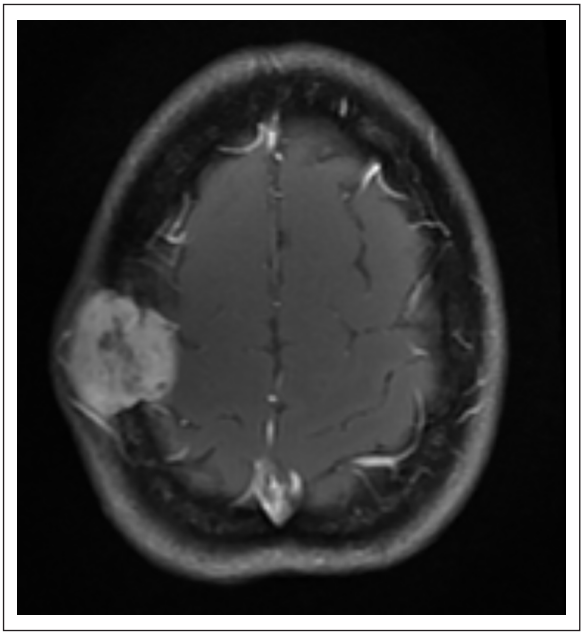

Figure 11. Imaging: MRI axial T1 pre-op.
Axial T1-weighted post-contrast image, from 29/4/2015, shows an avidly enhancing 3.6-cm right parietal calvarial mass with minimal extension into the adjacent extra-axial space. There are no additional enhancing lesions.

Discussion

Phyllodes tumors, derived from the Greek word "phullon," meaning "leaf," account for approximately 0.5% of all breast tumors. They can be either benign, borderline, or malignant with the more aggressive tumors often referred to as sarcomas due to their origin being in the connective tissue of the breast, rather than the terminal duct lobular unit of epithelial tissue. A mammogram and ultrasound are not adequate to differentiate between benign and malignant phyllodes tumors; thus, a biopsy is necessary.[4]

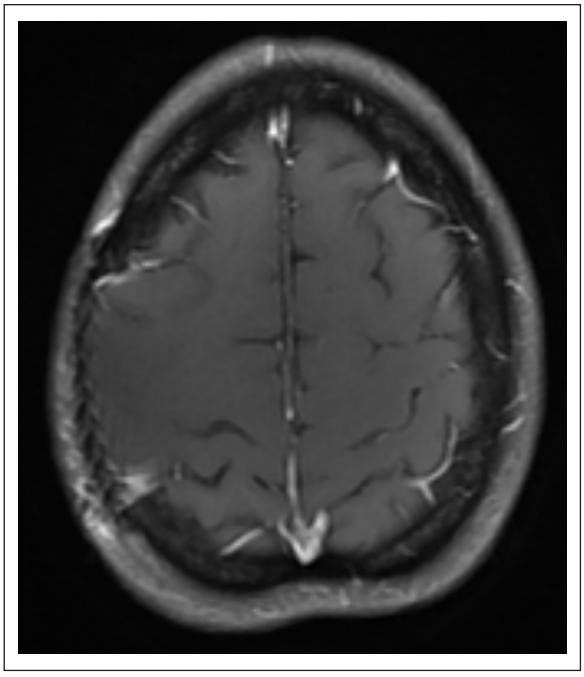

Figure 12. Imaging: MRI axial T1 post-op.
Axial T1-weighted post-contrast image, from 15/7/2015, shows postsurgical changes related to a right frontoparietal cranioplasty, without evidence of nodular enhancement to suggest residual or recurrent tumor.

A study done between September 2002 and March 2008 evaluated 175 patients with skull metastases using MRI. The primary sites of cancer were found to be breast cancer (55%), lung cancer (14%), prostate cancer (6%), malignant lymphoma (5%), and others (20%).[2] There were no reports of breast sarcoma. This is the first known case report of phyllodes tumor metastasizing to the skull.[5–8]

Another unusual feature of this case is the long disease-free interval of a relapsed metastatic solitary metastasis managed with surgery alone. Phyllodes tumors behave aggressively and typically follow the natural history of an aggressive sarcoma with a poor overall survival. In 2001, Kapiris et al. reviewed 48 patients with high-grade malignant phyllodes tumor in an effort to study parameters that influence outcomes. The patients were treated with either local excision (margins <1 cm), wide local excision ($\geqslant 1$ cm), or mastectomy. Distant metastases occurred in 13 (27%) of the patients at a median time of 25.6 months with tumor size and surgical margins being the main risk factors.[9] In 2006, Abdalla et al. reviewed 79 patients with phyllodes tumors and also showed a similar risk of distant metastases (28.6%) in patients with the malignant designation by World Health Organization (WHO). Interestingly, of these patients, 50% had local recurrence prior to distant metastases. Median survival of all patients with distant metastases was 5 months, ranging from 1 to 11 months. All patients with distant metastases were treated with adjuvant chemotherapy with or without radiation.[3]

Conclusion

Phyllodes tumors are aggressive, mesenchymal-based tumors which are known to spread to various locations; of which, this is the first reported case of metastases to skull. The histotype and margin status has been found to be independent predictors of distant metastases and overall survival.[10] The patient in the case had an aggressive subtype with a component of osteosarcoma and was treated with a total mastectomy and chemotherapy directed at osteosarcoma. Even with the removal of all breast tissue and adjuvant treatment, her tumor rapidly recurred. This is the first reported case of an isolated skull metastasis from a phyllodes tumor and osteosarcomatous dedifferentiation. Successful treatment of an isolated skull metastasis should consider full surgical resection with a discussion of appropriate adjuvant systemic therapy.

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Conflict of interests

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