Unique Presentation of Pseudoangiomatous Stromal Hyperplasia

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Background
A 46-year-old female with no prior cancer diagnosis presented with an enlarging right breast mass over the past year. Imaging demonstrated a 26 cm mass occupying most of the right breast, and ultrasound-guided core needle biopsy showed pseudoangiomatous stromal hyperplasia (PASH).

Summary
Based on the rapid enlargement, lobulated nature, and size of the mass, there was high suspicion for underlying malignancy. Our differential included phyllodes tumor, angiosarcoma, or benign lesions such as hamartoma or giant fibroadenoma. Our patient was managed surgically with palpation-guided enucleation yielding a 26 cm encapsulated mass with heterogeneous architecture weighing 6 lb. 15 oz. Final pathology confirmed the initial diagnosis of pseudoangiomatous stromal hyperplasia, and the patient has had an uncomplicated postoperative course.

Conclusion
Although the typical size for PASH associated with a mass is reported to be 0.3–7.0 cm, PASH can present as a mass large enough to encompass and distort the entirety of the breast. Based on the heterogeneous texture and well-defined, lobulated capsule of the mass, ruling out malignancy is crucial in these cases as it is now evident that atypical presentations of PASH can resemble high-risk lesions.

Key Words
pseudoangiomatous stromal hyperplasia; PASH; segmental mastectomy; breast mass
**Case Description**

Pseudoangiomatous stromal hyperplasia (PASH) is a benign mesenchymal breast lesion that typically presents clinically as a mass. Since this rare pathology was initially described in 1986 by Vuitch et al., less than 200 cases have been reported in the literature.\(^1,2\) It was initially thought to be a variant of mammary hamartoma but is now considered a proliferation of stromal myofibroblasts expressing CD34, vimentin, smooth muscle actin, BCL-2, and desmin.\(^3\) Prior literature predicts that hormonal changes play a role in the development of PASH; however, this is unclear due to the rarity of these cases. Tumor-forming PASH is thought to represent a proliferative response of myofibroblasts to estrogen and progesterone and predominantly presents in premenopausal or perimenopausal women as a mobile, firm breast mass.\(^4\)

We present a 46-year-old female with no significant medical/oncologic history who presented to our clinic with a one-year history of an enlarging right breast mass (Figure 1). Family history was significant for breast cancer of unknown etiology in the patient’s maternal aunt, who died at age 55. The patient was a premenopausal G2P2 who underwent menarche at age 12, first live birth at age 14, and had no use of oral contraceptives or hormonal replacement therapy. The patient denied any associated symptoms such as breast pain, erythema, nipple discharge, or nipple changes. However, she was unable to wear a bra due to the massive asymmetry between her breasts. She described back pain and the inability to engage in many of her usual activities. She was evaluated with breast ultrasound and mammogram, which revealed a 26 × 22 × 26 cm solid, heterogeneous mass with internal cystic spaces occupying all quadrants of her right breast and bilateral lymphadenopathy, with the largest right-sided lymph node measuring 3.5 × 0.9 × 3.3 cm. Ultrasound-guided core needle biopsy of the right breast mass was performed and was consistent with PASH, which was discordant with clinical and imaging findings. Left axillary lymph node biopsy revealed a benign, reactive lymph node. The patient was thoroughly counseled regarding the need for excision and the differential diagnosis included: PASH, phyllodes tumor, sarcoma, hamartoma, or fibroadenoma, and surgical excision was recommended.

The patient was scheduled for surgery and underwent a palpation-guided excisional breast biopsy. A lateral hockey stick incision was made along the inframammary fold, and an anterior skin flap was developed. Using palpation as guidance, we continued with dissection, and thick adhesions were taken down. The capsule of the mass was bluntly and sharply dissected until the mass was only attached to the subcutaneous tissue of the medial superior breast (Figure 2).

The breast skin was everted, and the primary surgeon delivered the mass through the incision with the help of two assistants (Figure 3). The mass was dissected free, passed to the back table to be weighed, and sent to surgical pathology for permanent section.

The surgical cavity was irrigated, and hemostasis was achieved. A closed-suction (JP) drain was placed, and the incision was closed. The mass demonstrated heterogeneous texture and color with a well-defined, lobulated capsule (Figure 4).

The patient was successfully discharged home that day. She had an uncomplicated postoperative course, and the JP drain was removed on postoperative day 16. She had significant excess skin on the anterior aspect of her right breast, for which she was referred to plastic surgery for possible reconstruction (anticipating partial but not complete skin retraction over time).
Figure 2. Views of Breast. Published with Permission

A) Right Craniocaudal View of Breast on Mammogram; B) Right Upper Inferior Quadrant View of Breast on Long Axis

Figure 3. Intraoperative Dissection of Right Breast Mass. Published with Permission

Figure 4. Delivery of Right Breast Mass after Extensive Dissection. Published with Permission
Final surgical pathology revealed a right breast mass weighing 3150 g (6.94 lb) and measuring 26.5 × 26.0 × 8.5 cm. Histologic sections showed scattered benign ductal epithelium in a dense collagenous (keloid-like) (Figure 5A) stroma. Slit-like anastomosing spaces were lined by elongated bland-looking lesional cells within the stroma (Figure 5B). These features are sufficient for diagnosing pseudoangiomatous stromal hyperplasia (PASH). In addition to the classic PASH-looking areas, focal areas showed glomeruloid formations scattered within the stroma (Figure 5C), some associated with entrapped capillaries. Immunohistochemical stains (Figure 5D), CD31, and ERG highlighted the small, entrapped capillaries but were negative in the lesional cells. CK AE1/AE3 highlights only benign ductal epithelium (not shown) but negative in the lesional cells. CD34 was positive both in the lesional cells and capillary endothelial cells. The presence of positive CD34 and negative CD31/ERG supported the myofibroblastic nature of the lesional cells. The morphological and immunohistochemical features supported PASH, and the negative ERG and CD31 excluded a vascular neoplasm. None of the PASH cases in the literature mention glomeruloid formations, the significance of which is unknown but may be related to the chronicity and mass-forming nature of this lesion.3
Discussion

This is the first case of mass-forming, encapsulated PASH in the literature of this size and weight. Typically, PASH presents on mammography as a well-demarcated, oval, or round hypoechoic mass with interspersed cystic spaces. In the preoperative setting, discussion of differential diagnoses despite benign biopsy results is crucial. The main differentials are fibroadenoma, Phyllodes tumor, low-grade angiosarcoma, and hamartoma.

In the case of our patient, the well-circumscribed, encapsulated appearance of the mass with heterogeneous echogenicity made hamartoma the most likely differential diagnosis due to the classic hamartoma “breast-within-breast” appearance, followed by phyllodes tumor or giant fibroadenoma.

Histologically, the slit-like channels lined by spindle-like myofibroblasts can be mistaken for the vascular spaces of low-grade angiosarcoma, the most feared diagnosis. Angiosarcomas exhibit infiltrative anastomosing vascular channels with blood without collagenous stroma. Further, the lack of leaf-like architecture, stromal cellularity/nuclear pleomorphism, and overgrowth made the phyllodes tumor unlikely. PASH is a known component in a subset of mammary hamartoma cases. But we did not encounter any combination of adipose, fibrous tissue interspersed between the mammary lobules and ducts. Immunohistochemistry was necessary to distinguish between angiosarcoma, Phyllodes tumor, and PASH. On immunohistochemistry, angiosarcoma stains CD34+/CD31+ and negative for ERG, PASH stains CD34+/CD31-, and a malignant phyllodes tumor generally range from 37-57% in CD34 positivity. The final diagnosis was PASH based on histopathology of complex, anastomosing, slit-like spaces throughout the stroma and CD34+/CD31-staining. Our patient followed an uncomplicated postoperative course and has no additional interventions planned at this time. We recommend biannual clinic visits and breast exams due to the recurrence risk of 12.5%. There is no increased risk for breast cancer development though if there is a recurrence of the mass, then mastectomy is recommended for definitive treatment and pathologic diagnosis.

This unusual presentation of PASH yields many teachable points that should be considered when seeing a patient with an enlarging breast mass. Though initial pathology may show a benign lesion such as PASH, it is possible to upstage to a higher risk or malignant lesion. Based on a previously published retrospective analysis of 988 breast core needle biopsies, there was a 2.23% false negative rate, with 64% of these particular biopsies being upstaged. Furthermore, it is also possible for PASH to present as a large, encapsulated mass, resembling a hamartoma with heterogeneous features. Even if another diagnosis is not highly suspected, patient symptoms and the cosmetic appearance of the mass asymmetric breasts should prompt surgical intervention. Palpation-guided excision for a mass this large is the recommended treatment option with JP drain placement and possible plastic surgery reconstruction for excess skin removal after initial skin retraction. Should excision reveal a benign diagnosis, negative margins are unnecessary to prevent a recurrence, and preservation of normal breast tissue will maximize cosmesis postoperatively. Re-excision is always possible to achieve negative margins if the final pathology reveals a malignant diagnosis.

Conclusion

This case demonstrates the atypical presentation of PASH, a rare, benign mesenchymal proliferation with a mass measuring 26 cm long and nearly 7 lbs. An operative approach of excision/enucleation is preferred. The possibility of upstaging to malignancy should always be considered when dealing with an enlarging breast mass.

Lessons Learned

Benign lesions such as pseudoangiomatous stromal hyperplasia may appear more like a hamartoma, fibroadenoma, or phyllodes tumor. Due to the rarity of this diagnosis, it may be easily ruled out; however, its diagnosis should be considered when facing an enlarging breast mass.

References


