Pseudoangiomatous Stromal Hyperplasia (PASH) of the Breast : A Case Report

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ABSTRACT
Pseudoangiomatous stromal hyperplasia (PASH) of the breast is a benign proliferating mesenchymal lesion of the breast. The common presentation of this lesion is usually an incidental microscopic foci & rarely they may present as painless, firm, nodular mass referred to as tumorous PASH. PASH has probable hormonal etiological influence which may mimic Fibroadenoma. We report the case of a 40 year old female with complaints of swelling in the left breast of 6 months duration with clinical diagnosis of fibroadenoma. Radiological & fine needle aspiration cytology (FNAC) studies were suggestive of a benign etiology. Histopathological study & Immunohistochemistry (IHC) showed characteristic features of PASH. We report this unique case to highlight its mimicking presentations clinically, radiologically, cytologically with fibroadenoma & the essentiality of histopathological examination for its correct diagnosis.

KEYWORDS: Pseudoangiomatous stromal hyperplasia, PASH, Benign breast lesion

INTRODUCTION
Pseudoangiomatous stromal hyperplasia (PASH) of the breast was first described in 1986 by Vuitch et al[1]. Leon et al believed it to originate from mammary myofibroblasts & proposed the term nodular myofibroblastic hyperplasia of the mammary stroma to denote its histogenesis[2]. The tumorous presentation of PASH is infrequent & is commonly seen as an incidental finding. PASH clinically & radiologically resembles fibroadenoma & histologically may be confused with Low grade Angiosarcoma[3,4].

PASH of the breast histologically are characterized by the presence of anastomosing slit like spaces in a dense hyalinized fibrous stroma & lined by flat benign spindle cells. The exact etiology & pathogenesis is still not known or clearly understood[3,5]. Proliferative myofibroblastic response to hormonal stimuli have been postulated[3,4,5].

CASE REPORT
A 40 year old woman came to our hospital with complaints of swelling in the left breast for the past 6 months. The swelling was not associated with pain, no history of trauma, fever or any nipple discharge. She gave the history of irregular periods. She was not a known case of Diabetes/Hypertension/Epilepsy/Pulmonary TB or Ischemic heart disease. The swelling was progressive & on examination the mass in her left breast was freely mobile measuring 10x7x6 cm. It was firm & non tender. Her routine Blood, Urine & Liver function tests were within normal limits. Serological studies for HIV & HBsAg was Non Reactive.

Ultrasound(USG) screening & FNAC studies were suggestive of a benign etiology. The patient was taken up for a lumpectomy & the specimen was sent for histopathological examination. On gross examination, the sample received was single gray white tissue mass measuring 11x10x4 cm. The cut section was grey white, homogenous & smooth. (Fig 1) Histopathological examination showed benign ducts & ductules of breast showing mild epitheliosis surrounded by dense hyperplastic stroma with slit like empty spaces. (Fig 2) These spaces resembled blood vessels & were lined by flat fibroblast like spindle cells in a dense collagenised stroma. (Fig 3 & Fig 4). Immunohistochemistry(IHC) studies showed CD34 & Progesterone receptor positivity of the spindle cells lining the slit like spaces & were negative for CD31. The final diagnosis of PASH was given. The patient did well postoperatively & no untoward incidents were reported during follow up.
DISCUSSION

Pseudoangiomatous stromal hyperplasia (PASH) of the breast is a benign tumor & has been reported from various parts of the world with no specific regional preference[6]. PASH usually presents as a unilateral, painless, at times palpable mass in premenopausal women[3,6]. Bilateral involvement is rare & has also been reported to arise in males in recent times[6,7,8].The exact etiopathogenesis is still not well understood & excessive hormonal response of mammary myofibroblasts have been postulated[3,4,7]. Involvement in postmenopausal women on hormone replacement therapy have also been recorded[8]. PASH has been associated with other benign entities including fibroadenoma, non-proliferative fibrocystic changes, gynaecomastia & sclerosing lobular hyperplasias[9].

Clinical presentation of PASH ranges from incidental histological finding in about 23% of breast biopsy specimens to clinically palpable mass or diffuse asymmetric tissue masses referred to as tumorous PASH[3,4,8]. Various radiological studies show a solid, non calcified mass or localized increased stroma on Mammogram & on USG.
studies PASH presented commonly as well defined solid, hypoechoic mass[3,8,9]. These studies found non specific features suggesting an initial diagnosis of fibroadenoma & recommended histological confirmation for the final diagnosis[8]. Grossly the tumor range from microscopic foci up to 18 cm in diameter. The excised tumor are usually round to oval, well demarcated, circumscribed & firm to rubbery in consistency with cut surface appearing homogenous, grey white with or without slit like cystic spaces & typical absence of hemorrhage & necrosis[3,4,8]. Histologically PASH classically shows anastomosing slit like spaces in a dense fibrous like stroma lined by flattened, discontinuous, attenuated benign spindle cells in both intralobular & interlobular stroma. Keloid like wavy hylazined acellular stroma with slit like empty spaces have also been described[3,4,5,8]. IHC staining of myofibroblastic cells in PASH have shown consistent positivity for CD34, Vimentin, Smooth muscle actin & BCL2 & are negative for Cytokeratin, S100, endothelial markers like Von Willebrand factor antigen & CD31[3,8]. Nuclear positivity for Progesterone receptors have been noted in stromal cells[3]. On Ultrastructural studies spindle cells show myofibroblastic features & the cytoplasm contain well developed golgi apparatus & abundant endoplasmic reticulum with consistent lack of Weibel-Palade bodies, pinocytic vesicles & surrounded basement membrane indicating its lack of endothelial features[3,4]. The differential diagnosis of PASH by clinical, radiological & cytological examination can include fibroadenoma in younger women as well as low grade angiosarcoma, myofibroblastoma & mammary hamartoma[3,4]. Angiosarcoma shows slit like spaces dissecting interlobular stroma with invasion of surrounding fat whereas PASH merges gradually with the surrounding stroma. Angiosarcoma are lined by atypical endothelial cells with mild to moderate pleomorphism, nuclear atypia with increased mitotic activity & show red blood cells within vascular channels[3,4]. The spindle cells are positive for CD31, CD34 & Von Willebrand factor antigen, whereas myofibroblasts markers such as CD34 & smooth muscle actin are positive in PASH but are negative for endothelial markers. Myofibroblastomas show bland spindle cells with haphazard fascicular arrangement with interspersed hyalinized collagen bundles. Myofibroblastomas express androgen receptors whereas PASH are positive for Progesterone receptors[3]. Fibroadenoma in comparison to PASH show classically glandular elements in intracanicular or pericanicular pattern with cuboidal to low columnar epithelial lining. Mammary hamartoma show mature adipose tissue with nodular mammary parenchymal aggregates which is absent in PASH[3]. Management requires excision with good safety margins for tumorous PASH in contrast to no additional specific treatment if found incidentally in excised specimen for other reasons[3,4,6]. Diffuse PASH may require mastectomy with reconstruction surgery[4]. Tamoxifen use for hormonal manipulation has been utilized as medical management showing encouraging results[4,6]

**CONCLUSION**

PASH is a benign proliferative mesenchymal lesion with possible etiopathogenesis involving hormonal stimulation. In view of its overlapping clinical, radiological & cytology features with other common benign lesions like fibroadenoma, the histological evaluation for confirmation is essential with the awareness of this entity to interpret the characteristic stromal changes. Wide local excision is considered adequate & rarely mastectomy may be required in cases of PASH with generalized breast enlargement.

**REFERENCES**


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