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# RARE BENIGN AND MALIGNANT LESIONS OF BREAST – A CASE SERIES FROM A TERTIARY REFERRAL CENTRE.

**Pathology**

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## ABSTRACT

Breast lesions are diverse in its presentation, pathology, and clinical course. As its incidence rises, many rare types are identified mainly through case reports and small studies, increasing the risk of misdiagnosis.This series discusses histopathological descriptions of rare breast lesions seen at KIMS, Hubballi's pathology department. We aim to summarize current knowledge on these entities.Patients treated for breast lesions between August 2021 and July 2022 underwent screening for unusual lesions. Cases with rare incidence were identified. Gross, microscopic, and pertinent immunohistochemical details of these specimens were reviewed and detailed.Six cases of uncommon breast lesions were reported. Two were benign, including Pseudoangiomatous Stromal Hyperplasia and benign adenomyoepithelioma. The other four were malignant: primary angiosarcoma, malignant adenomyoepithelioma, invasive ductal carcinoma with apocrine differentiation, and squamous cell carcinoma deposits in the breast.This series aims to highlight histopathological features of rare breast lesions, contributing to current knowledge. It aids pathologists in accurate diagnosis, crucial for treatment and prognosis.

## KEYWORDS

Rare breast lesions Adenomyoepithelioma, PASH, Angiosarcoma

## INTRODUCTION

Breast lesions comprise a family of heterogeneous entities with variable patterns of presentation, morphology and clinical behaviour. The majority of breast lesions are classified traditionally into benign and malignant conditions and their behaviour can, in the vast majority of cases, be predicted with a reasonable degree of accuracy. However, there remain lesions which show borderline features and lie in a grey zone between benign and malignant, as their behaviour cannot be predicted reliably. Defined pathological categorization of such lesions is challenging, and for some entities is recognized to be subjective and include a range of diagnoses, and forms of terminology, which may trigger over- or undertreatment[1]

The aim of our review is to provide a tool for breast lesions caregivers which will enable a better understanding of the disease and its optimal approach to therapy. This may also stand as a clinical framework for a future understanding of these rarer breast cancers when gene analysis work is reported(1)

### Case 1

A 36 year old female presented with bilateral painless breast lumpssince 6 months. She had no family history of breast disease or ovarian cancer, no history of hormonal therapy. Physical examination showed a 10cm mobile, firm lump with well-defined border below left nipple areolar complex and a 3cm mobile, firm lump with ill defined border in the right upper outer quadrant.Mammography showed homogenous soft tissue lesion in left breast and heterogeneous radiodense lesion with few calcifications in right breast suggestive of BIRADS IV lesions.Left side wide local excision and right lumpectomy was performed Grossly, specimen from left breast showed a well defined globular mass measuring 12x10x10 cms with smooth bosselated surface and tan white homogeneous cut surface. Right breast mass measured 2x2x2 cms - globular with grey white cut surface.

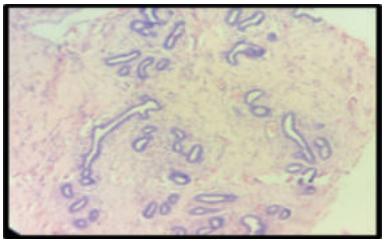

**Figure 1 : Structure Of Breast Showing Glands And Stroma**

Histopathologic findingsof right breast [Fig 1] shows glands and stroma. glands shows features of fibroadenoma showing pericanalicular and intracanalicular arrangement of glands with proliferating stroma

Left breast mass showed few lobules with interlobular stroma consisting of dense collagen and anastomosing slit like channels lined by myofibroblasts. No evidence of atypia noted. [FIG2,3]

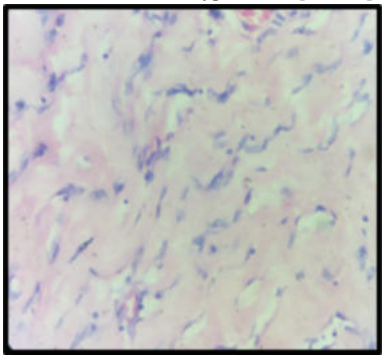

**Figure 2: 40x Interanostomosing Slit Like Spaces Separating Keloid Like Collagen**

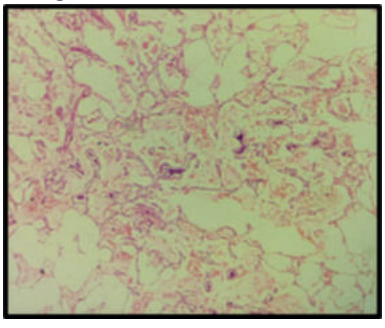

**Figure 3:10x Breast Tissue Showing Anastomising Channels Of Blood Vessels Lined By Plumped Atypical Endothelial Cells.**

Features are suggestive of (PASH) Pseudoangiomatous stromal hyperplasia

**Case 2**

A 33-year-old lady presented with painful left breast swelling since 3 months. She had no family history of breast or ovarian cancer. Physical examination showed grossly swollen left breast, firm with bluish discoloration of the overlying skin. No palpable left axillary lymph nodes.Ultrasonography showed a large irregular mixed echogenic mass with solid and cystic components within, occupying almost the entire left breast. Multiple large vessels with turbulent flow and pulsations were seen.She underwent left mastectomy Grossly, tumor measured 10.0 × 10.5 × 7.0 cm with firm cut surfaces including foci of hemorrhage, and poorly defined borders.

Histopathological findings showed multifocal, ill-defined vascular tumor consisting of proliferating and anastomosing vascular channels, dissecting through the adipose tissue and lobular stroma. The neoplastic vascular channels were lined by mild atypical endothelial cells with hyperchromatic nuclei, and moderate amount of cytoplasm.Immunohistochemistry studies showed the neoplastic cells were positive for CD31 and CD34 but negative for CKAE1/AE3.

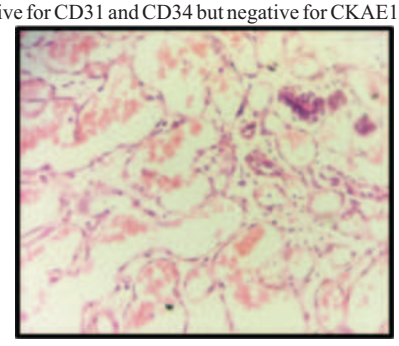

**Fig 4: 40x Image Of Anastomising Channels Of Blood Vessels Features are suggestive of Primary angiosarcoma.**

**Case 3**

30-year-old woman presented with a nodule of the left breast that was accidentally discovered on self-examination. Physical examination showed a well-defined, painless, mobile nodule, located in the inner lower quadrant of the left breast.Ultrasonography showed a solitary lump of hypoechogenic texture, located in the inner lower quadrant, with lobulated margins and no calcifications.Excisional Lumpectomy was done.Grossly it was a grey white firm globular mass measuring 2x2x1.5cm . Histopathological findings showed the inner layer composed of epithelial cells with eosinophilic cytoplasm, round to oval nuclei, bland chromatin, and is bordered with outer myoepithelial cells with clear cytoplasm[fig 5 ,6]

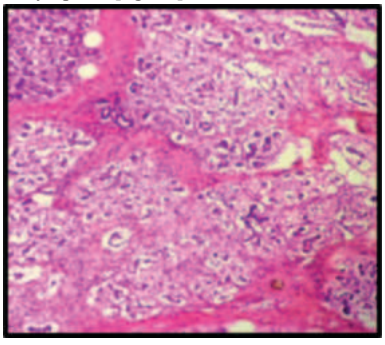

**Figure 5: 10x Breast Tissue Showing Inner Layer Of Epithelial Cells And Outer Layer Of Myoepithelial Cells With Atypical Features**

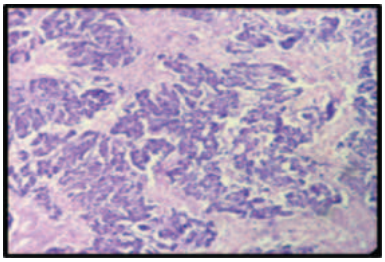

**Figure 6:40x Showing Epithelial And Myoepithelial Cells With Atypical Features**

Features are suggestive of Benign Adenomyoepithelioma

**Case 4**

A 58 year old lady had a painless swelling in right breast for two years. Previous USG of breast suggested a suspicious lesion and core biopsy of the lump revealed an atypical ductal lesion. But patient refused further treatment and discharged. She had developed a wound over the breast swelling with foul smelling discharge and maggot infestation since 10 days. She underwent right sided toilet mastectomy. Grossly, the tumour measured 11x10x7.5 cm with firm consistency, areas of necrosis and haemorrhage are seen.

Histopathological findings showed irregular nodularity with nests of atypical myoepithelial cells[fig 7,8]Features are suggestive of Malignant Adenomyoepithelioma.

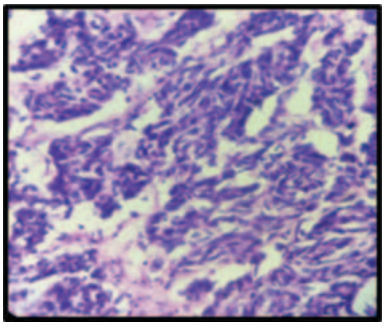

**Figure 7:10x Image Showing Epithelial And Myoepithelial Proliferation**

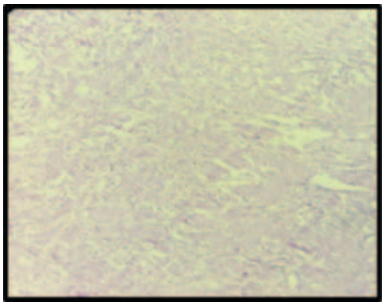

**Figure8:40x Image Showing Cytological Atypia, Nuclear Pleomorphism, Necrosis, And Increased Mitotic Activity.**

**Case 5**

58 year old lady came with lump in the right breast in the central quadrant for 8 months with no relevant family history. FNAC revealed a cellular specimen with numerous sheets of apocrine cells, variable nuclear pleomorphism and myoepithelial cells in the background. She underwent modified radical mastectomy. Grossly, the tumor was well circumscribed, grey white and firm in consistency and measured 4.5x3.5x3cm.

Histopathological findings showed invasive carcinoma composed of solid islands of tumour cells which have abundant eosinophilic cytoplasm and round nuclei with prominent central nucleoli.[fig 9 ,10]

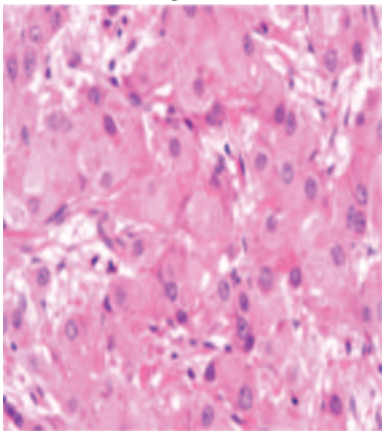

**Figure 9:10x Image Showing Islands Of Tumour Cells**

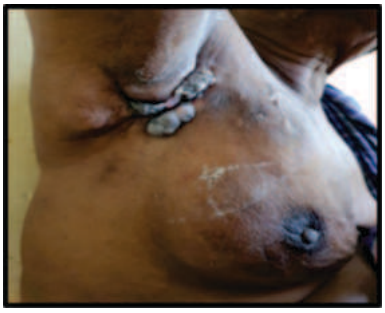

**Figure 10: 40x Image Showing Solid Islands Of Tumour Cells With Abundant Eosinophilic, Granular Cytoplasm And Round Nuclei With Prominent Nucleoli**

Features are suggestive of Invasive ductal carcinoma with apocrine architecture.

**Case 6**

75 year lady presented with lump in right breast since 3 months with supraclavicular swelling and ulcerated right palmar lesion since 4 months.USG breast showed a BIRADS IV lesion with axillary lymphadenopathy.[fig 11] FNA of the lump confirmed malignant cytology and core biopsy showed squamous cell carcinoma with central cystic and necrotic element. She underwent mastectomy, selective neck dissection and resection of palm lesion. Grossly, the breast tumor measured 9x7x4cm, grey white with cystic changes and infiltrative margins.Microscopically, tumor showed epithelial cells arranged in lobules, sheets and nests and at places in cribriform pattern. Cells are pleomorphic with hyperchromatic nucleus and prominent keratinisation, areas of necrosis noted. Features are suggestive of squamous cell carcinoma – well differentiated (metastatic deposits Supraclavicular mass and palmar lesions also showed features of squamous cell carcinoma. [fig 12,13]

**Figure 11:Gross Image Of Swelling In Axilla And Breast Lump**

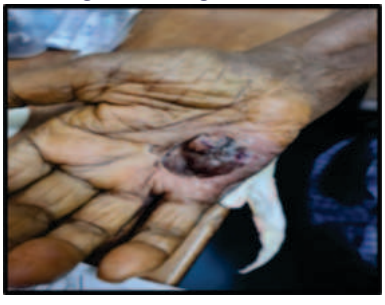

**Figure 12: Gross Image Of Supraclavicular Swelling**

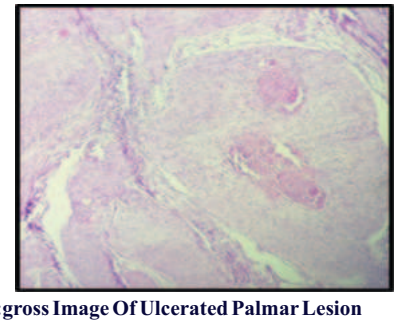

**Figure 13:gross Image Of Ulcerated Palmar Lesion**

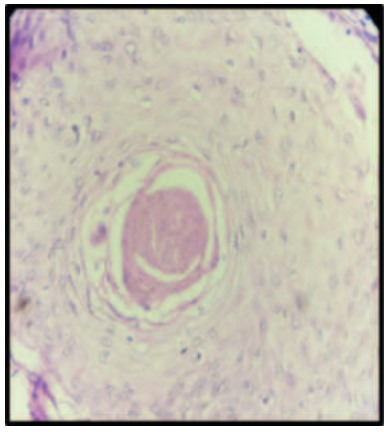

**Figure 14:10x Image Showing Tumour Cells Arranged In Lobules Sheets And Nests And Cribriform Pattern With Areas Of Necrosis**

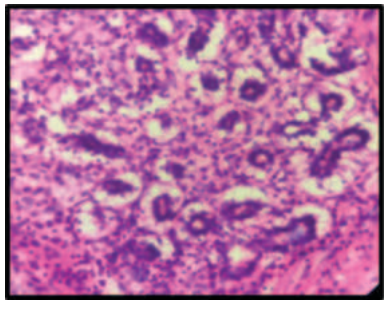

**Figure 15:40x Of Keratin Pearl Surrounded By Tumour Cells**

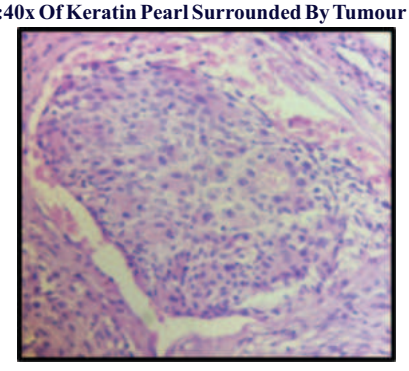

**Figure 16:40x Round To Polygonal Tumour Cells With Hyperchromatic Nucleus Arranged In Nests**

Histologically tumour showed prominent keratinization and an infiltrative growth pattern (figure 14,15,16)

**DISCUSSION**

PASH was first described in 1986, an uncommon benign breast condition ranging from an incidental microscopic finding to a palpable mass.it is associated with benign and malignant breast lesions in up to 23% of cases. It is thought to be hormonally responsive typically seen in premenopausal and perimenopausal women. PASH can be classified as simple and fascicular or proliferative type characterized by a proliferation of fibrous stroma, with fibroblasts and myofibroblasts, and a network of slit-like empty clefts within acellular hyalinized stroma. Imaging findings are not specific, and establishing imaging-pathologic concordance is necessary Typical PASH lesions are progesterone, estrogen, and androgen receptor, CD34, and vimentin positive and are negative for endothelial markers (CD31 and factor VIII) and cytokeratin .PASH can be mistaken for low-grade angiosarcoma, which has vascular channels containing erythrocytes. The term pseudoangiomatous highlights the difference between the pseudovascular spaces of PASH (which do not contain red blood cells) and the true vascular spaces of angiosarcoma.Angiosarcoma has malignant features such as atypical endothelial cells, mitoses, or pleomorphism.Treatment is usually surgical excision, although "watch and wait" strategy can be applied if PASH diagnosis is made on core biopsy and if the lump is less than 2 cm in size. [2]

Breast angiosarcoma is classified into primary, arising de novo, or

secondary, developing as consequence of chronic lymphoedema or breast irradiation after breast conserving surgery.Primary breast angiosarcomas represent less than 0.04% of total breast malignancies.generally develop during the third and the fourth decades of life (median age 35) Presents with rapidly growing painless and palpable mass (≥4 cm) .Non-specific radiological findings. FNAC and core biopsy are generally not helpful in the diagnosis as they give high false-negatives.Macroscopically, the tumor size varies between 1 and 20cm (average of 5cm) and is poorly defined, spongy when cut and hemorrhagic. [5]

Histologically, tumor proliferation is composed of irregular anastomotic vascular cavities, lined with one or more layers of endothelial cells. Low-grade (Grade I) angiosarcoma - complex anastomosing vascular channels with minimal nuclear atypia and no endothelial multilayering, can be mistaken for a hemangioma .Intermediate-grade (II) - increased cellularity with more prominent endothelial atypia and formation of papillary structures .High-grade (III) angiosarcomas are composed of solidly spindled areas with poorly defined vessels and prominent nuclear atypia, necrosis, and blood lakes.

IHC markers : Endothelial expression markers CD31, CD34, von Willebrand factor (vWF), Ulex europaeus agglutinin 1 (UEA-1), Friend integration 1 leukemia (Fli-1), endothelin-1, vascular endothelial growth factor (VEGFR), and specific erythroblast gene associated (ERG) transformations. Prognosis is poor due to the very aggressive course, local recurrences and distant metastasis.Simple mastectomy is recommended although breast conserving surgery can be optioned in selected cases. Regional axillary clearance is not necessary because they tend to metastasize hematogenously.[6]

Adenomyoepitheliomas are rare breast tumors that are characterized by their double composition of both epithelial and myoepithelial cells. Most of them are benign in nature and have a good prognosis. sometimes they may show malignant transformation - originating from the epithelial component/ myoepithelial component or from both of them. can appear at different ages ranging from 16 to 86 years, with a median age of 56. Presents as a single palpable well circumscribed firm mass (mean 1–2 cm) . Mammography shows round, oval or lobulate high density masses with sharp borders. A bigger size and irregular borders can be potential signs of malignancy. Benign adenomyoepithelioma has been classified as tubular , lobulated or spindle cell variants based on their growth patterns. These lesions can be diagnostically challenging because of their heterogeneity.[8]

Malignant adenomyoepithelioma or adenomyoepithelial carcinoma of the breast is a rare tumor, for which only a limited number of reports have been published. Large range for age of presentation, with palpable abnormality being the most common presenting symptom. Ultrasonagraphy shows an oval or irregular hypoechoic mass with circumscribed or microlobulated margins. Malignant features include irregular invasive margins with surrounding stromal reaction, cellular atypia and pleomorphism, necrosis, and a high mitotic count throughout the tumor. Overgrowth of myoepithelial cells, high cellularity, and satellite foci - features of malignancy[10]. Treated with wide excision with negative margins. To date, there is insufficient evidence for standardized therapy regimens following excision, and adjuvant therapy should be considered on a case-by-case basis.[9]

Immunochemistry - positive for smooth muscle actin +, p63+, cytokeratin 14+, cytokeratin 5+ (myoepithelial contingent), and AE 1/3 (epithelial contingent).

### IHC Markers

1) The myoepithelial part is shown by the positivity of cytokeratin 5/6 antibodies, calponin, p63, smooth muscle actin, smooth muscle myosin, caldesmone, cd10 and S100 protein;
2) The epithelial part shows a positive staining for low molecular weight keratin, cytokeratin antibodies and AE1/AE3

Given the unclear and unpredictable propensity for malignant transformation and the risk of local recurrence, conservative excision with negative margins currently seems to be the appropriate surgical treatment. Apocrine carcinoma of the breast is a rare cancer and its incidence is reported between 0.3–4% of all female breast cancer. seen in women between 6th and 7th decade. usually present with palpable mass, tend to be unilateral but are frequently multifocal/multicentric .Microscopically, apocrine carcinomas (ACs) demonstrate the same architectural growth pattern as invasive ductal carcinomas of no special type, differing only in their cytological appearance.Japaze et al. proposed a strict criteria to diagnose apocrine lesions; this included 75% cells containing apocrine features and the cells to be large in size containing eosinophilic cytoplasm with sharply defined borders, nucleus to cytoplasm ratio of 1:2 and containing large nucleoli. [13]

The tumor expresses mainly androgen receptor (AR), while ER and PR are absent. over-expression of HER2 is frequently seen. Hormone therapy targeted against AR may be applicable.It expresses GCDFP-15 (76–100%) which is a 15,000 Dalton monomer glycoprotein and is considered a specific tissue marker of apocrine epithelium. (Gross cystic disease fluid protein 15)

## CONCLUSION

Rare breast lesions represent distinct entities with different clinical behaviour and response to treatment. The management of rare cases represents a real challenge in daily clinical practice.Systematic evaluation of patient with detailed histopathology by the pathologist will aid in accurate diagnosis and further management

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