

# Atypical Breast Carcinoma- A Series of Six Cases

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## ABSTRACT

Breast cancer comprises 10.4% of all cancer among women world and it the second most common type of cancer. Increased public awareness and screening have led to earlier diagnosis at different stages. Surgical resection can be done earlier and complete cure of the disease can be achieved. As a result survival rates for breast cancer in young women have improved significantly. Six unusual type of breast carcinoma, presented to the Surgery Outpatient Department were referred to Pathology Department for further investigations. Patients age and sex, clinical characteristics of the tumour, the duration of the lesion, the size, radiological investigation, Fine Needle Aspiration Cytology (FNAC), trucut biopsy and histopathological examination were noted. Immunohistochemical examination also done in all the cases. Out of the six cases of breast carcinoma, one was the mucinous carcinoma of breast, two invasive papillary breast carcinoma, one apocrine carcinoma, one invasive Pleomorphic Lobular Carcinoma (PLC) of breast and one was fibromatosis like metaplastic carcinoma of breast. All the patients were female except, a 71-year-old male who presented with invasive papillary carcinoma. All the female patients were presented at postmenopausal age group. After careful examination of the cytology and histopathological slides the final diagnosis was made which helped the clinician for further treatment. Rare breast cancers do not differ from other types of breast cancer in their presentation. But they vary by treatment regimens and outcomes. So, proper diagnosis with imaging, FNAC, trucut biopsy and histopathological examination is a combined tool for proper diagnosis and treatment.

**Keywords:** Histopathology, Immunohistochemistry, Invasive papillary carcinoma, Trucut biopsy

## INTRODUCTION

Breast cancer comprises 10.4% of all cancer among women world and it the second most common type of cancer. Data shows in 2004, breast cancer caused near about 519,000 deaths worldwide [1].

Breast cancer is more common in women than in men, due to less amount of fibrofatty tissue. Although males tend to have poor prognosis [2]. Cancer develops if the immune system both adaptive and innate is not working properly or the number of cells produced is too much to eliminate. Breast tumour is caused by various reasons like-chemical and radiation exposure, advanced age, poor nutrition etc. [3]. Increased public awareness and improved screening have led to early diagnosis. Also, survival rates for breast cancer have improved significantly, particularly in women with early and proper diagnosis [4].

The present study describes six cases of rare types of breast carcinoma. This include mucinous carcinoma of breast, two invasive papillary breast carcinoma, one apocrine carcinoma, one invasive PLC of breast and the last one was fibromatosis like metaplastic carcinoma of breast. Present case series describes their clinical history and various approach i.e, radiological and invasive {FNAC, Trucut biopsy, mastectomy}, histopathological examination and immunohistochemical study.

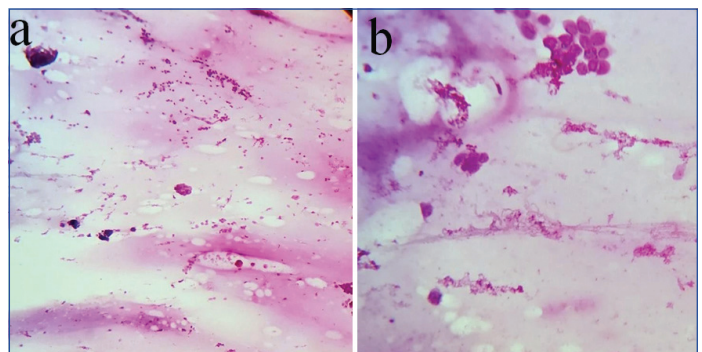
## CASE SERIES

### Case 1

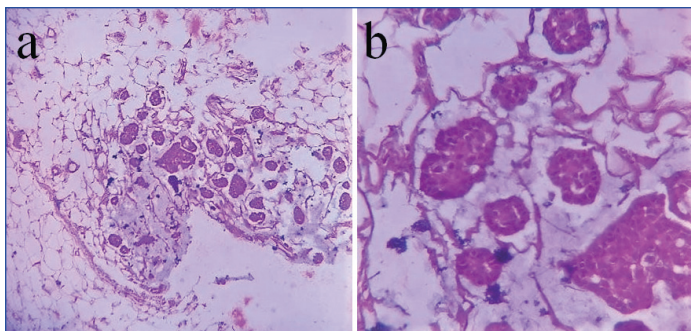
A 70-year-old female patient presented at Surgery Outpatient Department with a lump on her left breast. The lump was slow growing since last seven months and was located in the upper outer quadrant of the left breast. There was no significant past medical history or family history.

On examination the tumour was 3x3 cm in diameter, with irregular borders, without pain and overlying ulceration and was not fixed to the underlying structure or chest wall. No axillary or supraclavicular lymph node was palpable. In bilateral breast ultrasound, both

breasts had heterogeneous echotexture. In the left breast, a mass of 3x2 cm in size was present, located in 2 O' clock position at 6.5 cm from the nipple, with irregular borders and heterogeneous internal echoes, non parallel orientation, non circumscribed with spiculated edge. The FNAC smear showed loose cluster of atypical cells with high Nuclear-to-Cytoplasmic (N:C) ratio. The background of the smear was mucinous. The cytomorphology showed mucinous carcinoma of the breast [Table/Fig-1]. Core needle biopsy was done for the confirmation of the case. The section showed cluster or sheets of neoplastic cells suspended in abundant extracellular pool of mucin, partitioned by delicate fibrous septa. The clusters varied in size and shape. The histological feature were suggestive of mucinous carcinoma of breast [Table/Fig-2]. Estrogen Receptor (ER), Progesterone Receptor (PR) and Human Epidermal growth factor Receptor-2 (HER2/neu) status was done which showed ER, PR positivity and HER2/neu negativity. Result of the HER2/neu was confirmed by FISH technique. The surgery was performed. Staging of the tumour was T2N0M0. Hormone based letrozole therapy was given for 5 years. Follow-up was done clinically after every three months and patient was doing well.



**[Table/Fig-1]:** Mucinous carcinoma of breast. a) FNAC shows loose cluster of atypical cells. The background of the smear is mucinous (May-Grünwald-Giemsa stain (MGG),40X); b) FNAC shows cluster of atypical cells with high N:C ratio (MGG,100X).

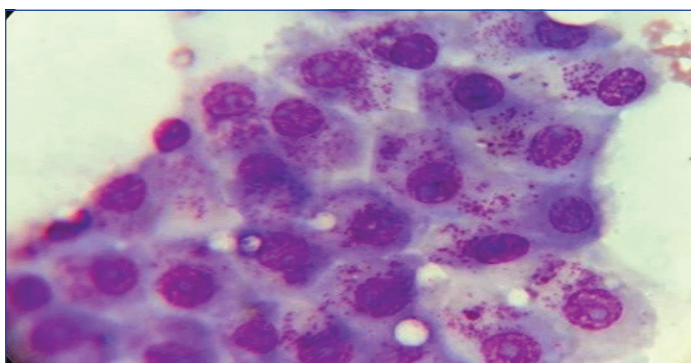


**[Table/Fig-2]:** a) Cluster or sheets of neoplastic cells suspended in abundant extracellular pool of mucin, partitioned by delicate fibrous septa (H&E, 100X); (b) Clusters or sheets of neoplastic cells under high magnification (H&E, 400X).

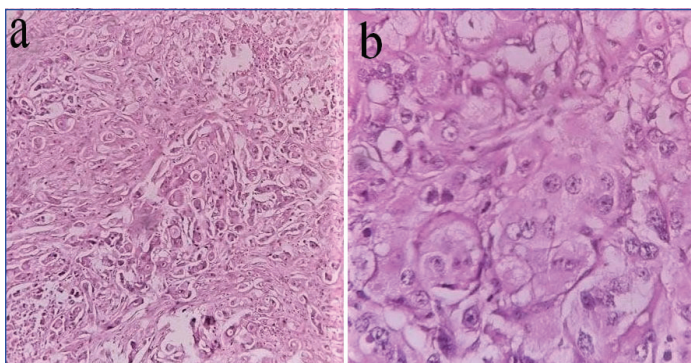
## Case 2

A 50-year-old female presented to the Surgery Outpatient Department with a mass in the right breast for seven months. It was small initially and was gradually increasing in nature. There was no history of nipple retraction and discharge. The patient had no rise in body temperature and no abnormality detected on general physical examination.

Physical examination revealed 3×3 cm mobile, firm to hard mass in the superior and outer quadrant of the right breast. The FNAC showed moderately cellular smear, loosely cohesive clusters of large, polygonal cells with abundant, basophilic and granular cytoplasm. Cell showed centrally placed nucleus, which is vesicular, moderately pleomorphic and with prominent nucleoli. The cells in clusters showed irregular nuclear border with nuclear overlapping. All the cells were of apocrine type. Background showed necrosis [Table/Fig-3]. Later core needle biopsy was done for further confirmation. The section showed a tumour mass composed of cells arranged in nests and sheets. They were round to oval polygonal shaped cells, with granular eosinophilic cytoplasm. Also had prominent nucleoli [Table/Fig-4]. The cells showed few mitotic figures. The histological features suggested the diagnosis of apocrine carcinoma [Table/Fig-3]. Immunohistochemistry was done by Peroxidase,



**[Table/Fig-3]:** Apocrine carcinoma of breast. The FNAC shows large, polygonal cells with abundant, basophilic and granular cytoplasm and the nucleus was centrally placed, vesicular, moderately pleomorphic and showed prominent nucleoli with irregular nuclear borders (MGG, 400X).



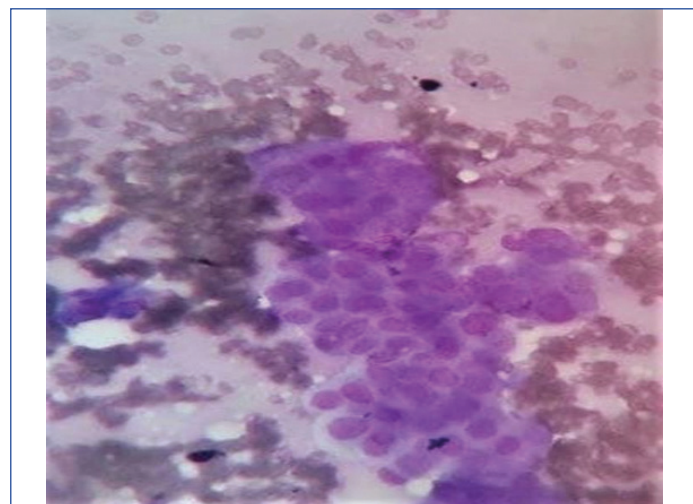
**[Table/Fig-4]:** Apocrine carcinoma breast. a) Loosely cohesive clusters of large, polygonal cells with abundant, basophilic and granular cytoplasm (H&E, 100X); b) Nucleus of the tumour cells centrally placed, vesicular, moderately pleomorphic and showed prominent nucleoli with irregular nuclear borders (H&E, 400X).

Anti-Peroxidase (PAP) technique which showed oestrogen and progesterone receptor negative, HER2/neu receptor equivocal. The FISH done and HER2/neu positivity was confirmed. Surgery was done and tumour stage was T3N0M0. Chemotherapy was given followed by radiotherapy to the chest wall and patient was under trastuzumab medication for 12 months. Follow-up was done every three month and patient was doing well.

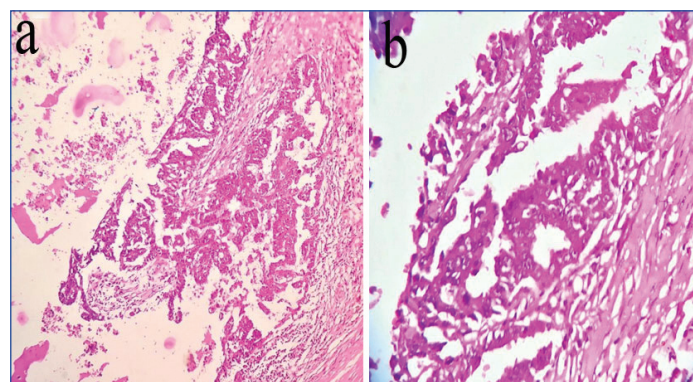
## Case 3

A 60-year-old female came to Surgery Outpatient Department with complaints of lump in the right breast for the past one year, gradually increasing in size. There was no history of associated pain, nipple discharge, or significant family history.

On systemic examination, no illness was detected. Routine blood and urine tests were within normal limits. On local examination a large, firm to hard, nodular, palpable mass measuring 9×8 cm involving central and outer quadrants noted. No nipple retraction or discharge was observed. No palpable axillary lymph node was found. Gross examination of the excised specimen showed a well-circumscribed, greyish mass measuring 8×7 cm with areas of cystic degeneration and necrosis. Fine needle aspiration smears were highly cellular and showed features of atypical ductal hyperplasia [Table/Fig-5]. Core needle biopsy was done which showed a highly cellular tumour comprised of pleomorphic ductal epithelial cells arranged predominantly in papillary pattern with fine fibrovascular core invading into stroma. The papillae were lined by tumour cells with high N:C ratio and hyperchromatic nuclei along with areas of haemorrhage and necrosis. Proliferation of these tumour cells were also seen within the cystic spaces. Ductal carcinoma in-situ component was noted at places. Gross examination of the excised specimen showed a well-circumscribed, greyish mass measuring 8×7 cm with areas of cystic degeneration and necrosis. The overall features were suggestive of invasive papillary carcinoma [Table/Fig-6].



**[Table/Fig-5]:** FNAC shows atypical cell cluster with high N:C ratio (MGG, 400X).



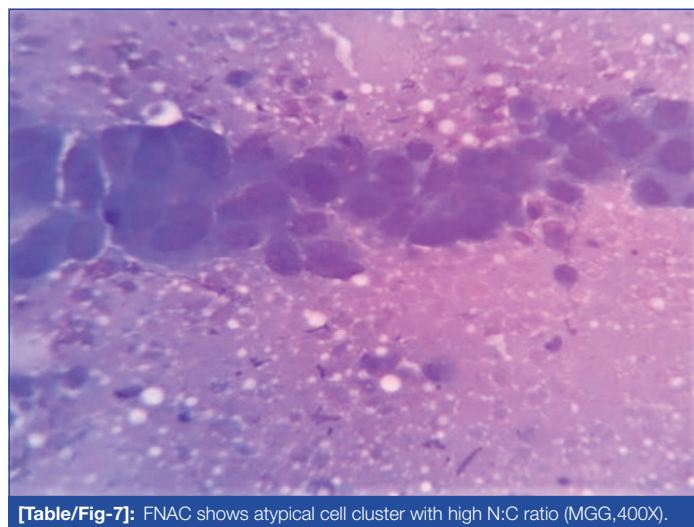
**[Table/Fig-6]:** Invasive Papillary carcinoma breast. a) Papillary arrangement of neoplastic cells and invasion (H&E, 100); b) Papillary arrangement of neoplastic cells (H&E, 400).

The tumour was ER, PR and HER2/neu strongly positive. Further FISH study was done to confirm the result of HER2/neu positivity. Clinical stage of the patient was T3N0M0. Neoadjuvant chemotherapy was given followed by surgery. After surgery adjuvant chemotherapy was given followed by radiotherapy. Patient was on trastuzumab for 12 months and letrozole for 5 years. Follow-up was done clinically every 3 monthly and patient was doing well.

#### Case 4

A 71-year-old male presented with the swelling in the left breast for last 6 months at the Surgery Outpatient Department. The patient was apparently well six months ago when he noticed a small swelling in his left breast which was insidious in onset and gradually progressive in nature. No significant past or family history was noted.

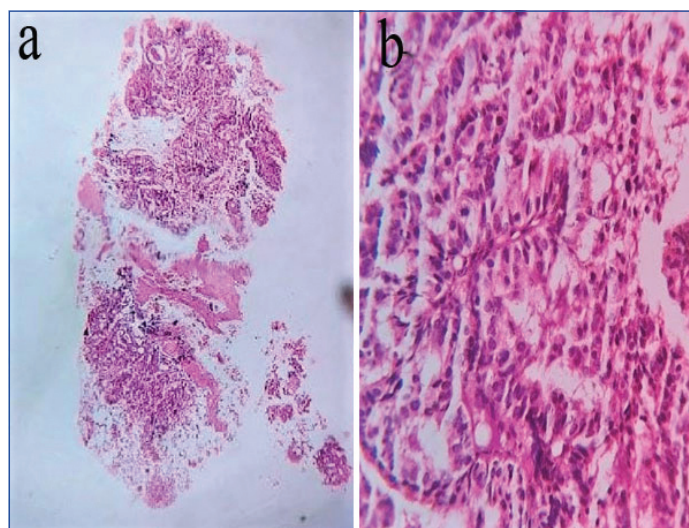
On physical examination a firm to hard swelling was palpated on the central quadrant of the left breast measuring approximately 2×2 cm, not associated with any pain, skin changes or nipple discharge. There was no significant swelling in axillae. The opposite breast was absolutely normal looking without any palpable mass. The Ultrasound (USG) of bilateral breast and axillae was done. The left breast showed a 24×26 mm predominantly cystic space occupying lesion with thick hypoechoic internal septations and solid internal components taking internal vascularity of arterial pattern. There was no abnormality noted in the retromammary and axillary lymph node. The USG guided FNAC showed cell rich aspirate with plenty of loosely cohesive clusters as well as dispersed atypical ductal epithelial cells with high N:C ratio and vacuolated cytoplasm. Nucleus was having open chromatin and inconspicuous nucleoli. No bare oval nuclei were identified. Overall cytological features suggestive of Invasive papillary carcinoma of breast [Table/Fig-7].



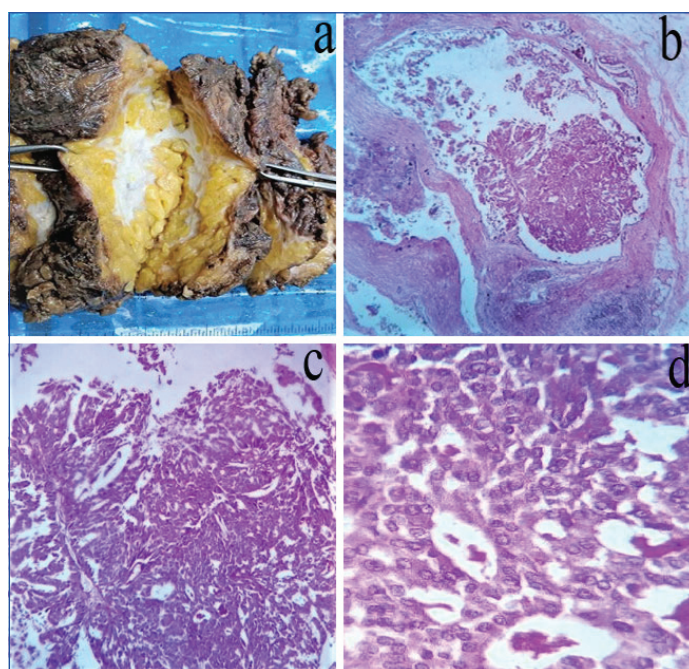
[Table/Fig-7]: FNAC shows atypical cell cluster with high N:C ratio (MGG,400X).

Trucut biopsy from the left breast showed ductular and glandular tissue of breast. Focal area showed papillary pattern of arrangement of neoplastic cells. Mild to moderate nuclear atypia present. Myoepithelial cell layer preserved at focal places. Plenty of inflammatory infiltrate noted. The overall features were suggestive of malignancy [Table/Fig-8]. Then modified radical mastectomy was done. Grossly, the specimen of left breast measuring 12×10×3 cm with overlying elliptical skin measuring 9.5×5×0.1 cm was excised. On cut section a fibrotic area noted measuring 1.5 cm in maximum diameter situated 2 cm away from deep resection plane. The microscopic section showed a tumour mass composed of papillary structure lined by atypical cells with scanty cytoplasm. Invasion was noted into adjacent stromal tissue. Scattered areas of calcification were also seen. The overall features were suggestive of invasive papillary carcinoma (Modified Bloom Richardson Grade III) [Table/Fig-9] [1]. Immunohistochemistry was done by peroxidase-ant peroxidase technique ER, PR shows negative and HER2/neu

receptor shows positive results [Table/Fig-10]. Further FISH study was done to confirm the result of HER2/neu positivity. Surgery was done in the patient and tumour stage was T3N1M0. Taxane based chemotherapy followed by radiotherapy was given. Follow-up was done clinically every three months and patient was doing well.



[Table/Fig-8]: Papillary carcinoma of breast. a) Papillary arrangement of neoplastic cells (H&E,400X); b) Neoplastic cells invading underlying tissue (H&E,400X).

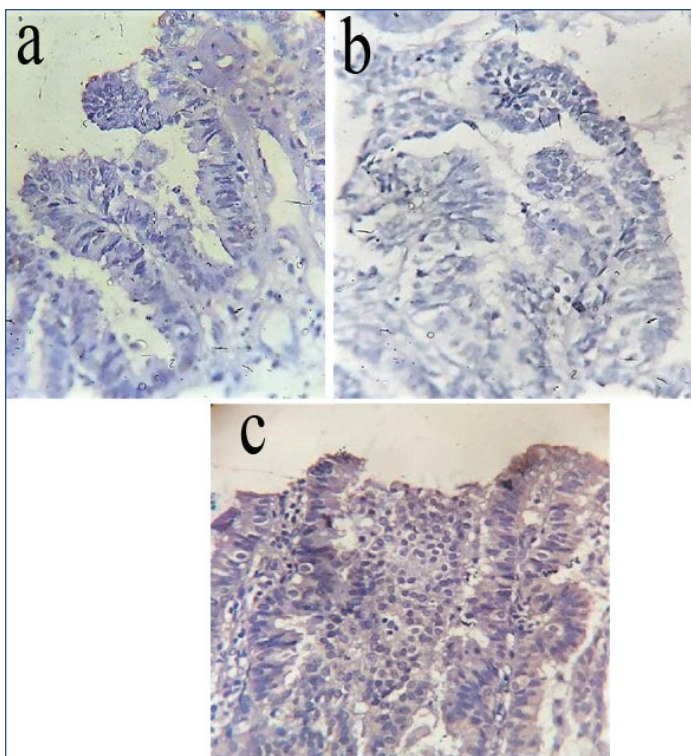


[Table/Fig-9]: a) Gross specimen of left breast showing fibrotic areas. b) Tumour mass composed of papillary structure invading underlying tissue (H&E,40X); c) Papillary structure lined by atypical cells with scanty cytoplasm (H&E,100X). d) Papillary arrangement of neoplastic cells (H&E,400X).

#### Case 5

A 42-year-old female presented with complaint of progressively increasing mass in left breast for last six months. She does not report any pain or skin changes. She has not experienced fever, weight loss, headache, nausea, vomiting, dizziness, or bone pain.

A well-defined palpable mass was noted in the upper outer quadrant of the left breast. No additional abnormalities were appreciated in both breasts. An ultrasound breast revealed a hypoechoic mass with irregular margins measuring 20×13×7 cm. She underwent left modified radical mastectomy. On gross examination left sided breast measured 22×14×8 cm. Overlying elliptical skin measured 15×11×1 cm. On cut open a whitish growth was identified measuring 7×6 cm which was 1 cm away from deep resection margin which involved the nipple areola complex and skin [Table/Fig-11]. On microscopic examination the section showed a tumour

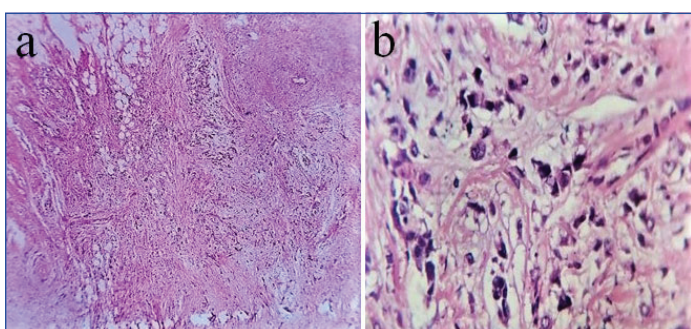


**[Table/Fig-10]:** a and b) Negativity immunoreactivity for ER and PR (IHC,400X), c) Positive immunoreactivity for HER2/neu (IHC,400X).

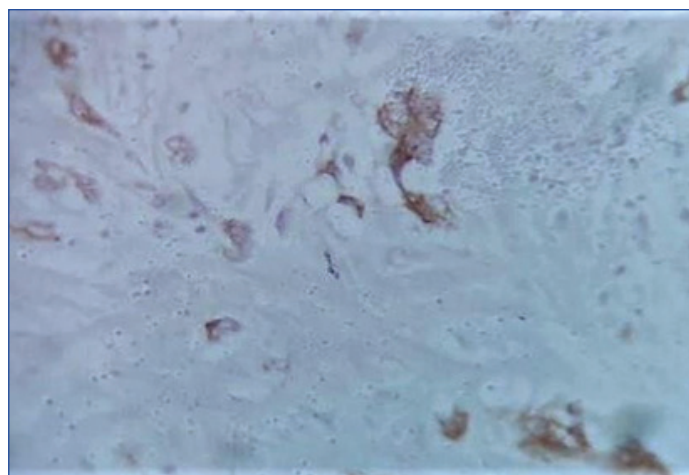


**[Table/Fig-11]:** Gross specimen of left breast showing whitish mass.

mass composed of neoplastic cells arranged in single cord like fashion diffusely infiltrating into stroma. Individual cells showed scanty cytoplasm, high nuclear pleomorphism, prominent nucleoli. Tumour giant cell identified. The overall features were suggestive of invasive pleomorphic lobular carcinoma of breast (PTNM-T4N1Mx). Modified Bloom Richardson grade-III [Table/Fig-12] [5]. Tumour cells present up to subepithelial tissue of nipple. Epidermotropism not identified. Lymphovascular invasion present. Immunohistochemistry was done by peroxidase- anti peroxidase technique. The ER, PR receptor status was negative and HER2/neu was positive. Further FISH study was done to confirm the result of HER2/neu positivity [Table/Fig-13].



**[Table/Fig-12]:** a) Tumour mass composed of neoplastic cells arranged in single cord like fascicle diffusely infiltrating into stroma (H&E,100X); b) Individual cells with scanty cytoplasm, high nuclear pleomorphism, prominent nucleoli (H&E,400X).



**[Table/Fig-13]:** Positive immunoreactivity for HER2/Neu (IHC,400X).

Surgery was done and the patient stage was T3N0M0. Taxane based chemotherapy was given followed by radiotherapy. Follow-up was done clinically every three months and patient was doing well.

### Case 6

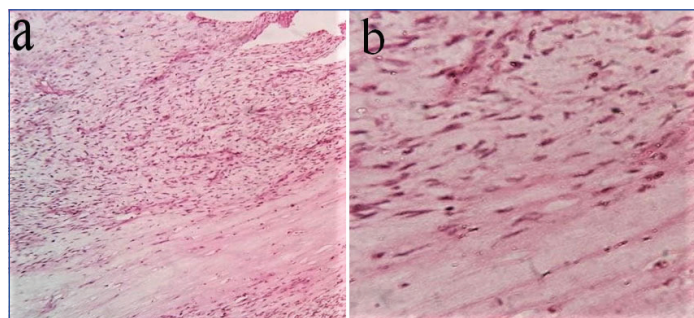
A 57-year-old female patient attended Surgery Outpatient Department with a history of mass in left breast for 1.5 year. She was apparently well 1.5 years ago. She does not report any pain. She has not experienced fever, weight loss, headache, nausea, vomiting, dizziness, or bone pain.

On gross examination, whole breast measured 12×8×5 cm and demonstrated an everted nipple. Ultrasonography described it as a large heterogeneously echogenic mass 4.5×3 cm involving all quadrants of the breast with posterior acoustic shadowing with increased vascularity and dilated ducts extending from mass to nipple Breast Imaging-Reporting and Data System (BI-RADS). On gross examination specimen showed a mass measuring about 6 cm in greatest dimension with a cystic cavity near the mass. Haemorrhagic fluid and necrotic debris noted in the cavity. Mass was 1cm away from the skin margin [Table/Fig-14]. The microscopic images from the growth proper showed a tumour mass with monomorphic appearance composed of spindle shaped cells. The cells were arranged in a vague whorl pattern and fascicles also. Mild to moderate pleomorphism was noted. Some matrix producing areas were also noted. All margin including deeper margin were free of tumour. The overall features were suggestive of fibromatosis like metaplastic breast carcinoma. Further Immunohistochemistry was done by peroxidase-anti peroxidase technique which showed triple negativity. Further FISH study was done to confirm the result of HER2/neu negativity [Table/Fig-15]. Clinical stage of the patient was T4N1M0. Neoadjuvant chemotherapy was given followed by



**[Table/Fig-14]:** Gross specimen of left breast showing a solid cystic mass.

surgery. After surgery adjuvant chemotherapy was given followed by radiotherapy. Patient was on trastuzumab for 12 months and letrozole for 6 months. Follow-up was done clinically every three months and patient was doing well.



**[Table/Fig-15]:** a) Monomorphic spindle shaped cells in fascicles (H&E,100X); b) Arrangement of spindle shaped cells with moderate degree of pleomorphism (H&E,400X).

## DISCUSSION

Breast cancer refers to the erratic growth and proliferation of cells that originate in the breast tissue [5]. Breast is composed of two types of tissues i.e., glandular tissues and stromal tissues. Glandular tissues composed of the milk-producing glands (lobules) and the ducts (the milk passages) and stromal tissues include fatty and fibrous connective tissues of the breast [6]. There are several types of tumours that may develop within different areas of the breast.

The above case series described six cases of rare breast carcinoma. This included mucinous carcinoma of breast, one apocrine carcinoma, two invasive papillary breast carcinoma, one invasive Pleomorphic Lobular Carcinoma (PLC) of breast and the last one is metaplastic carcinoma of breast with their clinical history and various approach both radiological and invasive (FNAC, trucut biopsy, mastectomy) histopathological examination and immunohistochemical study. These patients were presented first at Surgery Outpatient Department and then referred to the Radiology and Pathology Department for further investigation. All the patients were female except one who was a 71-year-old male presented with invasive papillary carcinoma. All the female patients were presented at postmenopausal age group.

Primary mucinous carcinoma of breast should have mucinous component of atleast 90%. Mixed mucinous carcinoma contains a mixture of mucinous and non mucinous components and the prognosis better in pure mucinous carcinoma [7]. In the present case series it was a PMC.

Apocrine metaplasia characterised by fine granular eosinophilic cytoplasm with apical budding of cytoplasm. Gayatri G et al., reported an incidence of apocrine carcinoma near about 0.4% and Durham JR et al., reported 62% [4,8].

Criteria for the diagnosis of apocrine carcinoma are as follows:

- 1) Apocrine features consisting of 75% of cells;
- 2) Large cells with eosinophilic granular cytoplasm;
- 3) Nucleus to cytoplasmic ratio more;
- 4) Nucleus large, round to oval and vesicular may be pleomorphic;
- 5) Sharply defined borders.

Minor and non mandatory criteria include prominent nucleoli in >50% of fields and apical cytoplasmic snouts into luminal spaces. Our case fulfilled all the five criteria [8].

In present series, there were two cases of invasive papillary carcinoma one of which presented in female and the other was in a male patient. The term papillary lesions of the breast encompass a morphologically heterogeneous group of lesions and pose difficulty in differentiating benign from malignant lesions [9]. Malignant papillary neoplasms of breast include a number of lesions such as Ductal Carcinoma In-Situ (DCIS) arising in intraductal papilloma, papillary

DCIS, encapsulated papillary carcinoma, solid papillary carcinoma, and invasive papillary carcinoma [9].

The aetiology of male breast cancer remains poorly understood, but an imbalance in the oestrogen-testosterone ratio is definitely implicated [10]. Histologically, papillary carcinoma is divided into intraductal and intracystic; subdivided into invasive and non invasive [11]. Most important histological criterion for invasion is extension of tumour into breast parenchyma. The prognosis of papillary carcinoma depends on the presence or absence of invasion. Non invasive papillary carcinoma can be regarded as a form of intraductal carcinoma and complete resection cures such patient. Even in patients with nodal metastasis, the prognosis of invasive papillary carcinoma has been reported to be favourable. In the present case series, no testicular/liver disease was noted. The tumour infiltration into the breast parenchyma/fat was present [11].

Dixon JM et al., in 1982, first described PLC as a variant of invasive lobular carcinoma which was characterised by a diffuse pattern but without its typical cytologic features. Its more aggressive nature than classical infiltrative lobular carcinoma due to its higher-grade cytologic features, higher incidence of distant metastasis, presence of lymph vascular invasion, and a more advanced stage at presentation [12].

Metaplastic carcinoma of the breast is currently classified in six subtypes, namely:

- i) Low-grade Aden squamous carcinoma;
- ii) Fibromatosis-like metaplastic carcinoma;
- iii) Spindle-cell carcinoma;
- iv) Squamous cell carcinoma;
- v) Metaplastic carcinoma with heterologous mesenchymal differentiation, and
- vi) Mixed metaplastic carcinoma.

The prognosis of patients with MBC depends on its grading and staging and also varies with the subtypes [13]. In present case series also no lymph node involvement was noted, no epithelial component only stromal component was seen.

## CONCLUSION(S)

Careful history, clinical examination, radiology, FNAC, trucut biopsy, gross and histopathological examination done in present case series, helped to definitive diagnosis of various breast carcinomas which will guide the clinician to plan for definite treatment regime for the particular patient. This case series will help the clinician to be aware of these rare variants and of its possible outcome.

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