



## RADIOLOGICAL AND PATHOLOGICAL FINDINGS OF VARIOUS CAUSES OF UNILATERAL GIGANTOMASTIA

Suvarna Latha Penukonda<sup>1</sup>, Bhawna Dev<sup>3</sup>, JayaGanesh<sup>2</sup>, Leena<sup>4</sup>, Rujuta<sup>1</sup> and Renuka<sup>1</sup>

<sup>1,2</sup>Saveetha Medical College, Thandalam, Tamilnadu, India.

<sup>3,4</sup>Department of Diagnostic Imaging, Sri Ramachandra University, Porur, Chennai

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### ABSTRACT

**Objective:** To present the radiological and pathological findings of various causes of unilateral gigantomastia.

**Materials and methods:** Twenty-eight patients presenting clinically with unilateral diffuse breast enlargement were investigated radiologically. Twenty-six of these were females and two were males with unilateral gynecomastia. Some were treated medically and followed up while some cases were treated surgically. Histopathology was obtained in all cases.

**Discussion and conclusion:** Macromastia may be of varied etiology including benign and malignant conditions. Out of 26 cases studied eight different diagnoses were found. Those included Giant fibroadenoma (7 cases), phyllodes tumor (4 cases), Pseudoangiomatous stromal hyperplasia (2 cases), juvenile gigantomastia (2 cases), Mastitis (3 cases), Invasive carcinoma (8 cases), Multicentric carcinoma (1 case) and Unilateral male gynecomastia (2 cases). Many a times the clinical findings are inconclusive and require radiological evaluation to decide the management of the lesion. Confirmation of diagnosis was made by histopathological examination.

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### INTRODUCTION

Massive breast enlargement is called as macromastia or gigantomastia. Unilateral macromastia is a rare entity<sup>(13)</sup>. It relates to massive enlargement of the breast in non-obese women<sup>(13)</sup>.

### METHODS AND RESULTS

A total of twenty-six women with age ranging from 15 to 68 and two males of age 37 and 43 presenting clinically with enlarged breast on one side were evaluated radiologically using X-ray mammogram and Ultrasound. All these cases were subjected to FNAC or biopsy or surgery with histopathological examination. Eight different diagnoses found among these patients were presented here with sample images of each diagnosis.

#### Case 1- Juvenile macromastia

A 15-year-old girl with history of right breast enlargement for many years, noticed a rapid and painless enlargement of the right breast for 1-½ months. Physical examination revealed a markedly enlarged right breast (Figure 1a), measuring approximately 25 cm in the cranio-caudal dimension.

On physical examination, the entire breast was occupied by the mass and is firm in consistency. The breast was non-tender. The overlying skin was stretched and tense. There was no axillary lymphadenopathy noticeable on examination.

X ray chest showed (Figure 1b) grossly enlarged right breast shadow.

Ultrasound of the breast showed (Figure 1c) a diffuse hypertrophy of the fatty and fibroglandular tissue with moderately vascular on Doppler interrogation.

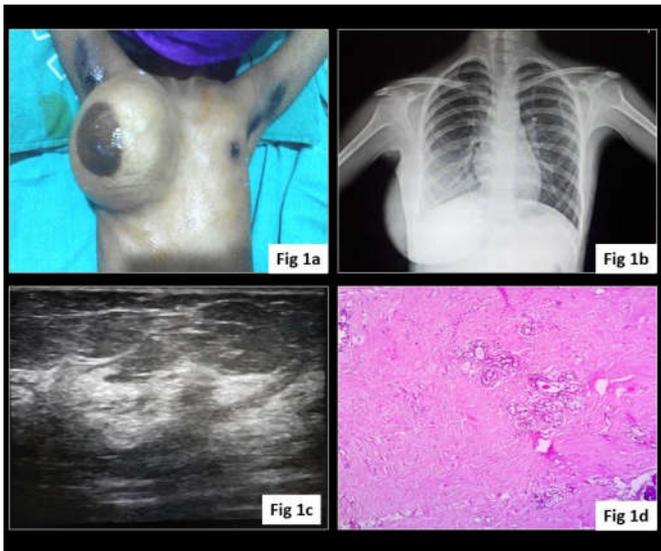
Right axillary lymph nodes were noted with preservation of the normal fatty hilum.

A differential diagnosis of juvenile macromastia, giant fibroadenoma and PASH [pseudo angiomatous stromal hyperplasia] was offered. In view of recent rapid growth, phyllodes was also suspected.

In view of the rapid massive enlargement, reduction mammoplasty was performed and the specimen was sent for histopathological examination.

Histopathology showed normal breast tissue (Figure 1d) confirming the diagnosis of "Juvenile macromastia".

\*Corresponding author: Suvarna Latha Penukonda  
Saveetha Medical College, Thandalam, Tamilnadu, India.

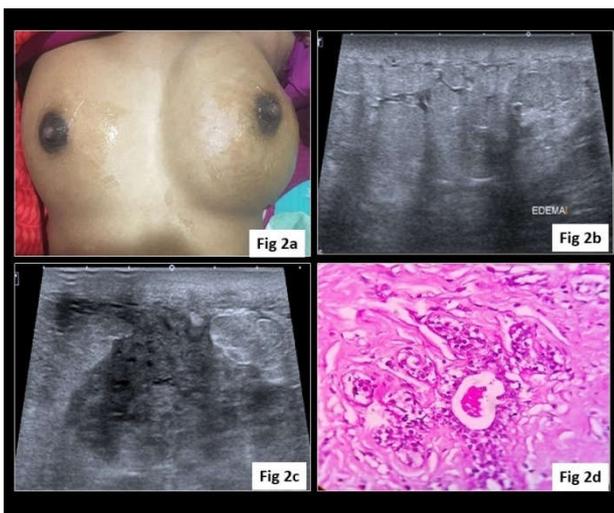


**Figure 1**

**1a-** Massive enlargement of the right breast with relative aplasia of the left in a teenage girl  
**1b-** Chest x- ray shows enlarged dense right breast shadow  
**1c.**Ultrasound of the breast shows diffusely hypertrophied breast tissue  
**1d.** Histopathology, Low power view showed normal breast tissue with lobules of acinar proliferation

**Case 2- Lactational Mastitis**

A 28-year-old lactating woman presented with painful enlargement of the left breast for 2 days. On examination breast is enlarged with the overlying skin stretched out. [Fig 2a] A few prominent veins are seen over the breast. The breast is tender worse in the upper inner quadrant. High frequency ultrasound of the left breast was performed. It showed features of normal lactating breast with diffuse hyperplasia of the glandular tissue. Diffuse hyperechoic appearance of tissues indicates tissue edema. [Fig 2b] There is a small focal anechoic area in the lower inner quadrant. Patient complained of maximum tenderness in this area. [Fig 2d] On color Doppler there was diffusely increased vascularity noted in the breast especially around the hypoechoic area. [Fig 2c]



**Figure 2**

**2a.**Diffuse painful enlargement of the left breast  
**2b.** Thickening of skin and breast tissue with diffuse hyperechoic appearance due to edema  
**2c.** A small area of fluid collection corresponding to maximum site of tenderness consistent with abscess formation  
**2d.** Histology showed diffuse periductal inflammation indicating mastitis

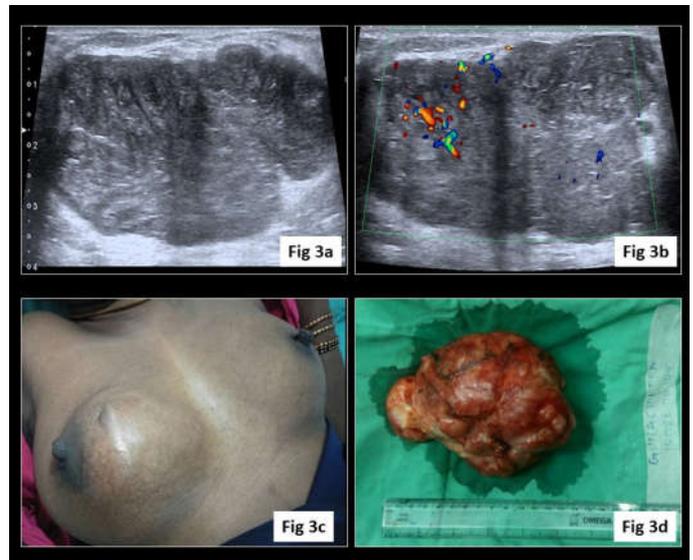
In view of the given history, clinical findings and the Ultrasound and Doppler appearance the diagnosis of ‘acute puerperal mastitis’ was made with a small abscess in the upper inner quadrant. Biopsy confirmed features of mastitis (Figure 2e). Patient was treated medically. Follow-up Ultrasound after the subsidence of symptoms showed normal appearance.

**Case 3 Giant Fibroadenoma**

A 50-year-old female presented with a large mass in the right breast. [Figure 3a]. The mass was of 9 months’ duration.

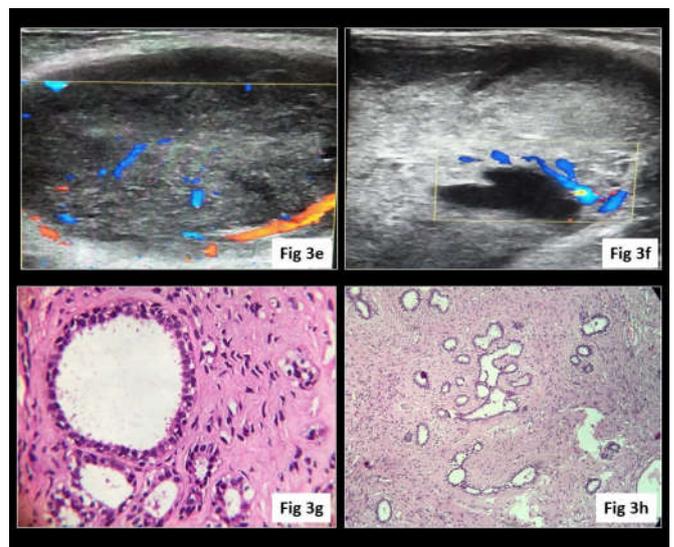
Ultrasound examination showed [Figure 3b] a large lobulated hypoechoic moderately vascular mass occupying large part of the breast, predominantly occupying the inner quadrants.

Excision of the mass was performed subsequently. Macroscopy of the specimen showed a single globular soft tissue measuring 11.0 x 10.0 x 9.0 cm. [Figure 3c] Histopathology findings confirmed [Figure 3d] “Giant fibroadenoma”



**Figure 3**

**3a, 3b:**Ultrasound- A lobulated hypoechoic mass with moderate vascularity  
**3c:**Chronic right breast mass  
**3d:**Surgical specimen



**3e, 3f:**Another case of giant fibroadenoma: A large solid mass with a cystic space

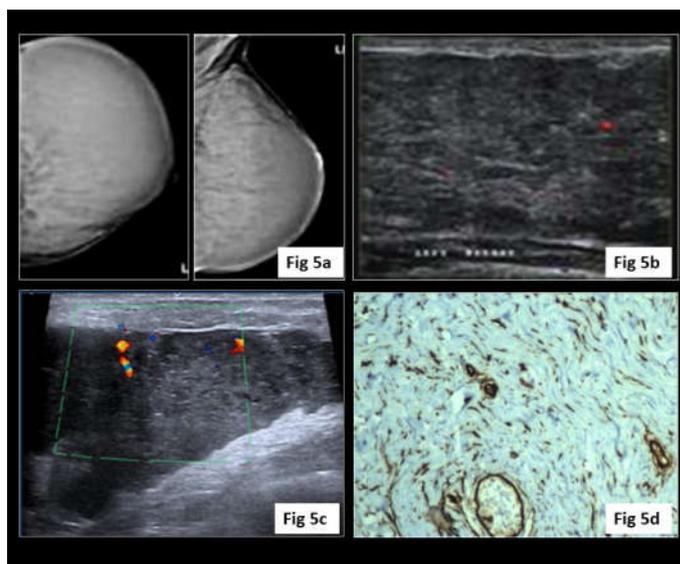
**3g, 3h:**Microscopy show numerous compressed ductal structures lined by luminal and myo-epithelial cells surrounded by fibromyxoid stroma in a pericanalicular and intra-canalicular distribution. A few areas show adenosis and hyalinization. There is no evidence of atypia. These findings were consistent with giant fibroadenoma

**Case 4- Phyllodes tumor**

A 35-year-old female presented with a rapidly enlarging large mass in the left breast. Mammogram (Figure 4a) shows a huge multi-lobulated mass involving the entire left breast. There is no evidence of skin puckering or nipple retraction.

Ultrasound of the left breast (Figure 4b) shows multilobulated lesion with large cystic spaces and solid components with internal vascularity. Left axillary lymph node is enlarged and appears suspicious (Figure 4c).

Histopathological examination (Figure 4d) showed increased stromal cellularity with very low mitosis suggestive of border line phyllodes tumor.

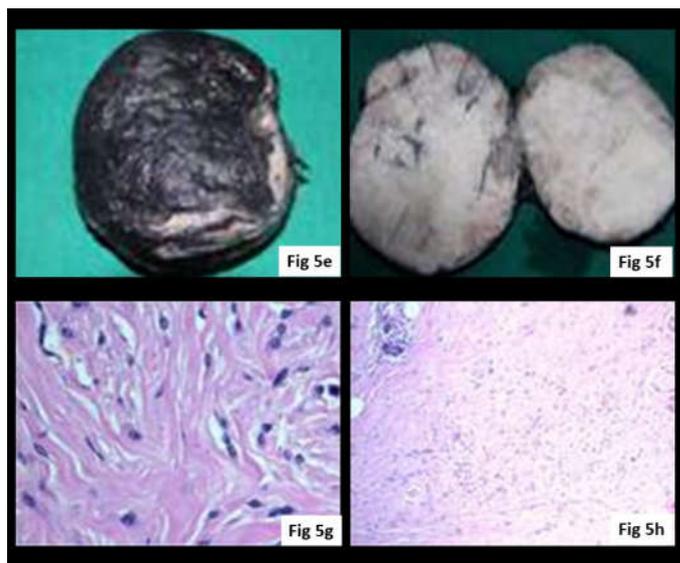


**Figure 5**

**5a:**Digital mammogram done in two views showed enlarged left breast with diffusely increased homogenous density.

**5b& c:** Ultrasound scan of the left breast shows diffuse non-specific increase in parenchymal thickness and parenchymal heterogeneity with loss of normal fatty and fibroglandular appearance. Thin vascular like channels were seen which do not show any color flow.

**Figure 5d:** Immunohistochemistry - CD 34 stain decorating the spindle cells. x 10



**5 e&f:**Excised specimen of left breast shows grey white mass with vascular congestion on the surface. Cut surface of the specimen which shows firm, homogenous grey white surface

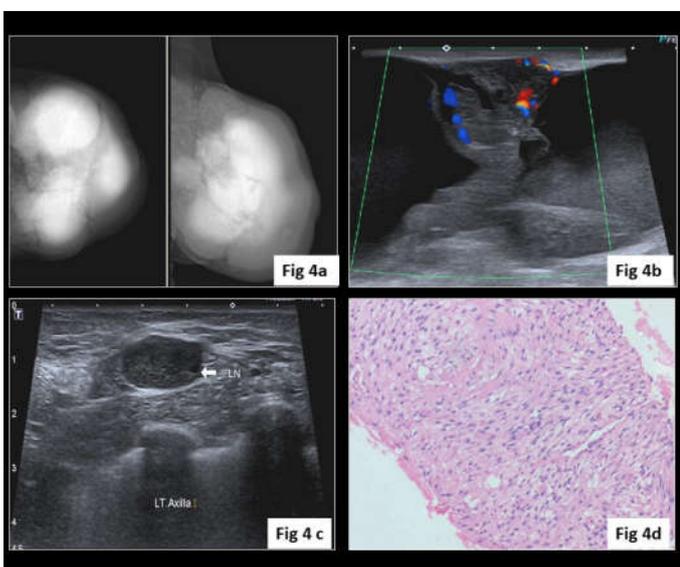
**5 g&h** HPE- Bland spindle cells appear to be lining the slit like spaces with interspersed collagen. High power (x 40) view showing slit like spaces, spindle cells and collagen. No atypia or mitosis

**Case 6: Invasive ductal carcinoma**

A 65-year-old female presented with enlarging left breast over a period of 6 months with a lump felt on the medial side.

Bilateral mammogram showed a large mass in the lower inner quadrant of the left breast with diffuse thickening of the ligaments of cooper. Thickening and edema of the skin and subcutaneous tissue in the peri-areolar region. [Figure 6a]

Ultrasound scan of both breasts was performed. A large hypoechoic mass with lobulated out line is seen in the left breast occupying the inner quadrants. A few specks of micro-



**Figure 4**

**4a:**A huge multilobulated mass involving the entire left breast  
**4b:**Ultrasound showed a huge lobulated mass with solid and cystic areas. Moderate vascularity seen in the solid areas.  
**4c:**Left axillary lymph node is enlarged and hypoechoic with cortical thickening and loss of fatty hilum.  
**4d:**Increased stromal cellularity with absence of ducts and very low mitosis(H&Ex100)

**Case 5: Diffuse Pseudo Angiomatous Stromal Hyperplasia (PASH)**

A 36-year-old female presented with gradual painless enlargement of the left breast over the period of 1 year. No abnormal nipple discharge. On clinical examination, the left breast was diffusely enlarged and shows dilated veins on the skin. On palpation, the breast was soft rubbery consistency with no tenderness and no discrete palpable lump.<sup>(9)</sup>

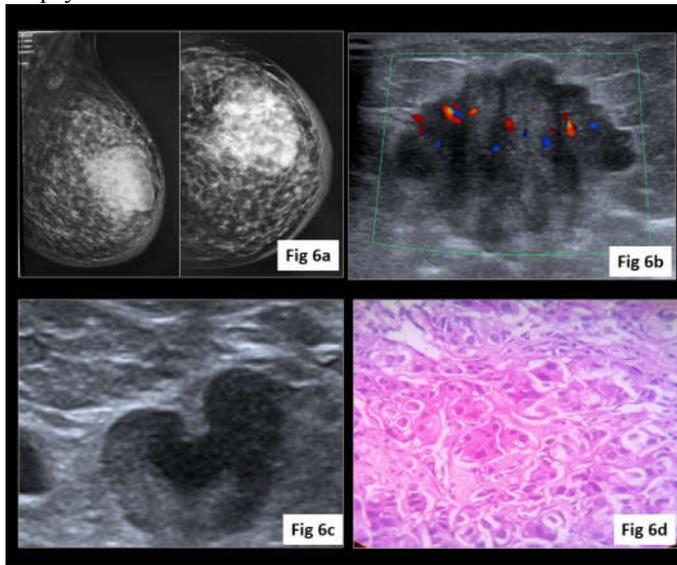
Digital mammogram of both breasts performed in two standard mediolateral oblique and craniocaudal views followed by ultrasound examination of both breasts<sup>(9)</sup>. [Figure 6a & b].

Subsequently patient was operated and histopathology obtained. [Figure 6c & 6d].

Patient followed up for one year. No recurrence observed.

calcification are seen within the mass. Diffusely increased vascularity noted within the mass. Enlarged axillary lymph nodes are seen with grossly thickened cortex and loss of fatty hilum. [Figure 6b]

Biopsy confirmed invasive ductal carcinoma.



**Figure 6**

- 6a:**Left mammogram: CC, MLO - mass in the Upper outer quadrant of the left breast. Thickening and edema in the peri-areolar region. Dense trabecular pattern in the central breast
- 6b:**Ultrasound shows multiple large irregular hypoechoic mass with lobulated margins
- 6c:** An enlarged lymph node is seen in the axilla with grossly thickened cortex and loss of fatty hilum
- 6d:**HPE shows ductal epithelial cells with hyperchromatic nuclei in cords and nests- Positive for malignancy

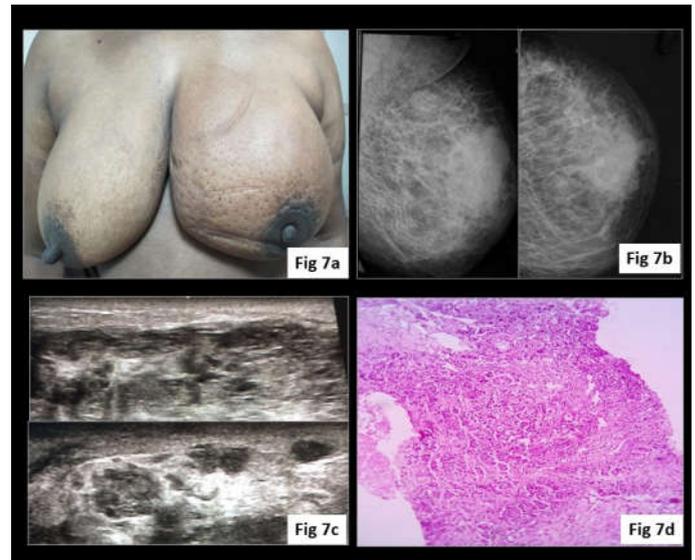
#### Case 7- Multi-centric breast cancer

A 58-year-old female presented with grossly enlarged left breast. She gives history of enlarging breast lump over the past 4 months. She also has a positive family history of breast cancer.

On examination left breast is grossly enlarged with the overlying skin showing Peau d'orange appearance. [Figure 7a]. On palpation, lobulated mass is felt which was firm to hard in consistency.

Bilateral mammogram showed dense fibro-glandular breasts. [Figure 7b]. A large retroareolar hyperdense mass is seen in the left breast with lobulated margins. There are few more nodular opacities with incompletely defined margins. Multiple enlarged left axillary nodes were seen with loss of fatty hilum. Ultrasound examination of both breasts was performed. It confirms presence of large malignant looking mass in the left breast with multiple satellite nodules of varying sizes scattered in the breast. [Figure 7c].

This appearance is consistent with "Multicentric breast cancer".



**Figure 7**

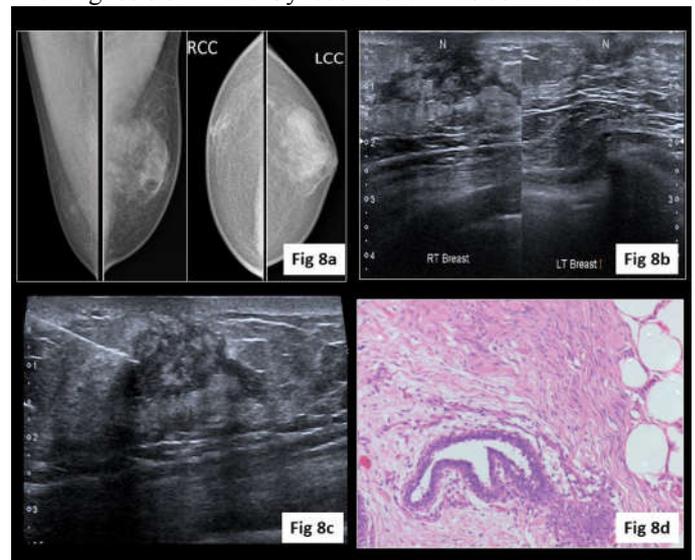
- 7a:**Grossly enlarged left breast with Peau d'orange appearance of the skin and partial nipple retraction
- 7b:**Left CC & MLO mammogram. Large retroareolar mass in the left breast with diffuse thickening of the ligaments of cooper. Multiple nodules are seen with partially defined margins
- 7c:**Ultrasound shows – A large irregular mass in the left breast at 12'o clock position. Multiple hypoechoic nodules ranging from 0.5 to 2.5 cm are seen in all quadrants
- 7d:**HPE shows Hyperchromatic nuclei in cords and nests consistent with malignancy

#### Case 8 - Male Gynecomastia

A 43-year-old male presents with gradual painless enlargement of the left breast. Mammography was performed. It shows diffuse hypertrophy of the fibro glandular tissue in the left breast predominantly in the retro-areolar region [Figure 8a].

These findings were confirmed on high frequency ultrasound. [Figure 8b] Subsequently biopsy was performed which showed Periductal edema and cellular stroma with epithelial hyperplasia [Figure 8 c & d]. No evidence of atypical mitosis to suggest malignancy.

The diagnosis of "Male Gynecomastia" was confirmed.



**Figure 8**

- 8a:**Bilateral mammogram in CC, MLO views show diffuse hypertrophy of the fibro glandular tissue in the left breast predominantly in the retro-areolar region. No mass is identified
- 8b:** Ultrasound shows hypertrophied left breast stroma

8c: Ultrasound guided biopsy of the left breast

8d: Periductal edema and cellular stroma with epithelial hyperplasia

### DISCUSSION

Invasive carcinoma of the breast is of two types. Most common is invasive ductal carcinoma (80%)<sup>(1)</sup>. Lobular carcinoma is the second most common type of breast cancer<sup>(1,2)</sup>. Invasive lobular carcinoma generally affects patients older age group. Clinically it is difficult to diagnose as it forms a mass with rubbery consistency which cannot be palpated clinically. It is usually larger in size. Multicentricity, multifocality and bilaterality are more common as compared to invasive ductal carcinoma. On mammogram invasive lobular carcinomas are isodense to fibroglandular tissues of the breast. On ultrasound these masses are hypoechoic, irregular with spiculated margins, echogenic halo and posterior acoustic shadowing<sup>(2)</sup>. Desmoplastic reaction is less common as compared to invasive ductal carcinoma<sup>(1,2)</sup>

If there are two or more malignant foci in one segment of the breast it is called as 'Multifocal' while presence of two or more malignant foci in different quadrants of the breast is called 'Multicentric'.<sup>(1,2,4)</sup> Diagnosis of multiple foci is very important in surgical planning. Bilateral mammography and bilateral breast ultrasound can identify clinically non-palpable multifocal, multicentric (MFMC) and bilateral cancer foci. Ultrasound was proved to detect MFMC with greater specificity, sensitivity and positive predictive value as compared to mammogram especially in dense breasts<sup>(3,4)</sup>

Fibroadenoma is the most common benign neoplasm occurring in female less than 30 years<sup>(5, 19)</sup>. It arises from the ductal lobular unit of the breast tissue. Fibroadenomas of more than 5 cm size are called as giant fibroadenomas<sup>(5)</sup>. These are firm painless masses, and can present as unilateral gigantomastia<sup>(17)</sup> often with poorly defined margins and consistency from the normal breast tissue. They show increase in size and frequency due to hormonal effect during puberty, pregnancy, oral contraceptives and cyclical hormonal changes.<sup>(17)</sup> Histologically it shows proliferation of glandular and fibrous tissue. Giant fibroadenomas are less likely to undergo malignant degeneration (<0.1%)<sup>(17)</sup>. There has been a case report of multiple giant fibroadenomas in a patient on Cyclosporine therapy<sup>(5)</sup>.

Phyllodes tumors constitute 0.3-1% of breast tumors.<sup>(17,18,23,24)</sup> The peak age incidence is between 2<sup>nd</sup> -5<sup>th</sup> decade and increases towards older age group. Phylloids tumors are of three types: Benign, borderline and malignant<sup>(23,24)</sup>. Sonographically phyllodes tumors were well-defined, lobulated tumors with smooth margins and heterogeneous internal echo pattern. Lobulated shape, heterogeneous internal echo pattern and absence of micro-calcification were significant independent sonographic features to distinguish phyllodes tumors from fibroadenomas<sup>(18)</sup>. Presence of cleft like and cystic spaces is a feature of phyllodes. Sonography cannot distinguish between malignant, borderline and benign phyllodes tumors. If sonographic features suggest phyllodes tumors, excisional biopsy should be performed to establish an accurate diagnosis<sup>(17,18)</sup>.

Histologically phyllodes tumor shows typical leaflike pattern and atypia with evidence of marginal infiltration.<sup>(18,19)</sup> Lactational mastitis occurs during puerperium due to injury to the nipple, the source being the nose and mouth of the infant.

Common organisms include Staphylococcus Aureus followed by streptococcus.

Staphylococcal infection is more focal and forms an early abscess. Streptococcal infection is more diffuse and form a localized abscess at a later stage. Ultrasound is the imaging modality of choice especially for diagnosis and guided drainage of abscesses. In those patients who do not improve with antibiotic therapy, neoplasm should be suspected and rapidly excluded by core biopsy.<sup>(20)</sup>

Granulomatous mastitis is another kind of mastitis which occurs in young women. It is caused by Corynebacterium and is a diagnosis of exclusion.

Pseudo angiomatous stromal hyperplasia of the breast is a benign condition<sup>(7,8,9)</sup>. It shows proliferation of stromal tissue of the breast<sup>(8)</sup>. Histologically it shows interlacing slit like vascular spaces lined by spindle cells. Imaging findings of PASH are nonspecific and mimic those of fibroadenoma, phylloides and angiosarcoma. Ultrasound usually shows a well-defined oval shaped hypoechoic mass<sup>(8)</sup>. Ultrasound features as well as histological appearance makes low grade angiosarcoma an important differential diagnosis of PASH, although angiosarcoma is more infiltrative. Immunohistochemistry plays an important role in differentiating PASH from angiosarcoma<sup>(8)</sup>. PASH shows positive immunoreactivity to CD34 while angiosarcoma is positive for CD31 and Factor VIII- related antigen<sup>(7,8)</sup>. Very rarely PASH can be diffuse causing macromastia<sup>(9)</sup>

Juvenile gigantomastia is multifactorial. This is due to hormonal imbalance and increased sensitivity of the breast tissue to estrogen<sup>(6)</sup>. This condition is usually bilateral. Rarely it can occur unilaterally<sup>(6,10)</sup>. A few cases of familial breast hypertrophy associated with Cowden's syndrome<sup>(6)</sup>. Reduction mammoplasty is the treatment of choice. Clinically due to gross enlargement of the breast the patients might present with neck pain shoulder or back pain in addition to associated emotional stress<sup>(6,10)</sup>

Gygantomastia in pregnancy is described as gestational macromastia or gestational macromastia. This is of unclear etiology and is usually bilateral. However unilateral gestational macromastia can occur<sup>(11)</sup>. It may be due to excess hormones or increased sensitivity of the target organ to hormones. This condition may be associated with pain, tenderness, mastitis and abscess formation<sup>(11)</sup>. These breasts show proliferation of stromal and glandular tissue, interstitial edema and lymphocytic infiltration<sup>(11)</sup>.

Male gynecomastia is caused by proliferation of ductal and stromal tissue<sup>(16)</sup>. It may be unilateral or bilateral. When bilateral usually asymmetric. There are three types of gynecomastia.<sup>(15,16)</sup>

Nodular or florid type is an early stage and can be reversible with appropriate treatment. On mammography, it shows fan shaped subareolar stromal proliferation. Histologically it shows dilated ducts with epithelial proliferation, periductal inflammation and surrounding edema. Dendritic type shows stromal fibrosis and ductal dilatation. These changes are irreversible<sup>(16)</sup>

Diffuse gynecomastia develops in those receiving estrogen therapy. Mammogram shows heterogeneous breast mimicking that of the female breast. Ultrasound of the diffuse

gynecomastia could look suspicious for malignancy although definite mass is not seen<sup>(16)</sup>. Biopsy of the breast tissue confirms the diagnosis.

Breast hamartoma a rare benign mass with fat, fibrous and glandular tissues. A giant hamartoma in a 19-year-old pregnant woman was published by Kuhn-Beck *et al*<sup>(12)</sup>.

A rare case of unilateral macromastia due to lymphangiomatosis in a postpartum female was published by Hynes SO *et al*<sup>(13)</sup>.

Touraine *et al* described possibility of gynecomastia in patients with autoimmune diseases like Myesthenia gravis, SLE, thyroiditis, chronic arthritis etc<sup>(14)</sup>.

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