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Original Article

Clinicopathological Correlation of Inflammatory Benign Lesions with Emphasis on Mimickers of Breast Carcinomas in Rural Inhabitants of India

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Abstract

Background: Breast cancer is one of the commonest malignancies among Indian womwen. There are many inflammatory breast lesions which mimic malignancy and they never proceed to malignancy. It includes abscess, variants of mastitis and fat necrosis.

Methods: This study was conducted in the Department of Pathology, UPUMS, Saifai, Etawah (U.P). Fine-needle aspiration cytopathology was the diagnostic tool.

Results: The maximum numbers of patients belonged to 21 to 40 years (67.97%). The left sided palpable breast lump was frequently involved (42.59%). Lump size ≤5 *cm* was found more (68.27%). The frequent cytological diagnosis was breast abscess (57.40%) among which pyogenic was (56.49%). The tuberculosis was diagnosed in 1.81%. Idiopathic lobular mastitis was 0.90%, whereas lymphocytic mastitis and plasma cell mastitis were each 1.20 %.

The histopathology examination was appreciated in 3.6% cases. The concordance was found more in abscess 33.33%.

Conclusion: Benign breast lesions mimicking breast carcinoma should be differentiated. Fine Needle Aspiration Cytology (FNAC) is a useful diagnostic tool. It should be considered as the initial investigation for inflammatory breast lesions along with ancillary radiological investigations and possibly histopathology. There is a need for an increased awareness of these disease entities, so that prompt and correct line of management can be opted.

Keywords: Abscess, Biopsy, Fine-Needle, Breast neoplasms, Fat necrosis, Female, Humans, Mastitis, Plasma cells, Tuberculosis

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Introduction

All breast lesions are not malignant. There are many benign breast lesions which mimic carcinomas and these benign lesions never progress to cancer. It includes infectious mastitis, breast abscess, granulomatous mastitis, lymphocytic mastopathy and fat necrosis (1). They may be asymptomatic or symptomatic and present as palpable masses or nodular growth with enlarged contour, tender, edematous, reddish ulceration. Eroded nipple and nipple discharge can often be seen. Sometimes enlarged lymph nodes are also found (2). Their clinical, physical and radiological examination are also suggestive of malignancy (1,3). Identification of these pathological conditions is required to avoid unnecessary surgeries and also helpful in developing a management plan. Fine Needle Aspiration Cytology (FNAC) is one of the best diagnostic tests for the diagnosis of these inflammatory pathologies (4); whereas histopathology examination of excised growth is the gold standard test. Histopathology examination in not required in every case as most of inflammatory lesions are treated by antibiotic/ drugs and excision of pathology is not required. A few number of case reports, and research articles on a single specific inflammatory pathology have been published, but as per literature search there is scarcity of original article depicting heterogeneity of inflammatory pathologies. Thus, this study was conducted with an aim to determine inflammatory breast pathologies on cytology and to access its correlation.

Materials and Methods

This analytical research work was carried out at Uttar Pradesh University of Medical Sciences, Saifai, Etawah (U.P), from January 2008 to February 2024. A total of 331 patients were included. Inclusion criteria: female patients who attended the OPD and presenting with breast lump with or without lymph nodes involvement. These patients were also diagnosed with inflammatory breast lesions on cytology. Exclusion criteria: male patients, female patients without inflammatory lesions or changes. Both symptomatic and asymptomatic patients were included but more emphasis was laid on features of malignancy such as palpable tender mass or nodule, with reddish discoloration, nipple retraction or eroded ulceration, discharge, raised temperature and lymph nodes enlargement. Patients detailed history was taken followed by physical examination. Fine Needle Aspiration (FNA) was done using a 21-gauge needle and 10 *mL* disposable syringe. Aspirated cellular material was taken from syringe, expelled on the slides and smears were prepared. The smears were wet fixed in 95% ethanol, and stained with H&E stain; whereas airdried smears were stained with May Grunwald Giemsa stain. On aspiration, where ever there was pus, frank or blood mixed and suspicious for tuberculosis, Ziehl Nelson stain was applied to isolate *Mycobacterium tuberculosis* and confirm tuberculosis. Similarly, where ever needed and possible Periodic acid-Schiff (PAS) was also applied to exclude any fungal infection. These slides were reported by using light microscope at different magnifications.

For histopathology examination, surgically excised lumpectomy or biopsy were taken followed by processing, sectioning and staining with H&E stain. Special stains like PAS and Ziehl Nelson stain where ever required were also applied to rule out differentials and confirm the pathologies. The correlation of cytology with other associated parameters and histopathology were evaluated.

Results

In the current study, 331 cases were included. The maximum number of patients belonged to 21-40 years group (n=225, 67.97%). The left sided breast lump was the most frequent (n=141, 42.59%) in comparison to others. Simultaneously, lump size was divided into two groups; lump size up to 5 *cm* was found more (n=226, 68.27%). Skin changes on breast like inflammation, tenderness and ulceration collectively were seen in 70 patients (21.14%).

Nipple changes which include discharge and erosion were observed in 21 patients (6.34%). The enlarged axillary lymph nodes were only appreciated in 5 cases (1.5%). The aspirate was divided into two types among which blood mix aspirate was commonly seen 310 of the cases (93.65%). The most frequent cytological diagnosis was breast abscess observed in 190 cases (57.40%); among abscesses pyogenic/ non specific types were seen in 187(56.49%). It was

Table 1. Age and clinical findings of patients presenting with inflammatory breast disease

Age group of patients	20 years and below	21–40 years	41-60 years	61 years and above
Total cases 331	53(16.01%)	225(67.97%)	46(13.89%)	7(2.11%)

Table 2. Age and clinical findings of patients with aspirate variants

Palpable breast lump site			Lump size		Skin changes (inflammation, tenderness, ulceration)	Nipple changes (discharge/ ,retraction)	Enlarged lymph nodes	Aspirate	
Left sided	Right sided	Bilateral	Up to 5*cm*	>5*cm*				Blood mix	Pus
141 (42.59%)	112 (33.83%)	6 (1.81%)	226 (68.27%)	105 (31.72%)	70 (21.14%)	21 (6.34%)	5 (1.5%)	310(93. 65%)	21 (3.02%)

Table 3. Cytomorphology diagnosis

Abscess	Granulomatous mastitis			Mastitis/inflammatory				Fat necrosis
Pyogenic/ non specific	Tubercular	Granulomatous mastitis secondary to infective & other causes	Idiopathic lobular granulomatosis	Non specific	Tubercular	Lymphocytic	Duct ectasia/ plasma cell mastitis	
187 (56.49%)	3 (0.90%)	30 (9.06%)	3 (0.90%)	71 (21.45%)	3 (0.90%)	4 (1.20%)	4 (1.20%)	26 (7.85%)

followed by nonspecific mastitis 71(21.45%) and nonspecific granulomatous mastitis in 30(9.06%). Tuberculosis was diagnosed in 6 cases (1.81%).

Histopathology examination was appreciated in only 12(3.61%) cases. The cytology histopathology correlation was established in these cases.

Concordance was frequently found in 6 cases (50%), 33.33% in abscess followed by 2(16.66%) in granulomatous mastitis.

Discussion

Breast cancer is the most common cancer diagnosed in women and the second most common cause of death among women worldwide. Meanwhile there are many benign breast pathologies which are clinically and radiologically appreciated as malignancy. It includes inflammatory breast lesions like infectious mastitis, breast abscess, granulomatous mastitis, lymphocytic or plasma cell mastitis and fat necrosis.

The age of the patients with inflammatory breast lesions varies from younger to older age groups. The maximum no. of patients belongs to reproductive age group *i.e*., 21-40 years (67.97%) (Table 1). In regard to region, most of the inflammatory lesions are found in the left breast. Baharoon S (5) reported that bilateral lumps are rare, occurring in less than 3% of patients. The present study, palpable bilateral inflammatory breast lesions were seen 1.81% of cases only.

The breast lump may vary in size. Ail DA *et al* (2), reported that the average size of the breast lumps in mastitis was 2×2 *cm* in tubercular mastitis while 4×3 *cm* in non-tubercular mastitis. They mentioned that in both the inflammatory breast pathologies, the size was less than 5 *cm*. Here, in this study most of the patients had breast lumps of 5 *cm* and less (Table 2).

The patients with inflammatory breast lesions may be symptomatic or non-symptomatic. The symptoms include breast lump which may be hard, tender, with sign of inflammation like raised temperature, redness and pain. Other than that nipple discharge and retraction can be seen. Mastitis, traumatic fat necrosis, duct ectasis, and tuberculosis are benign

inflammatory conditions which draw the nipple inward (6). Masses which are fixed to the underlying tissue and associated with nipple retraction with sinus formation, raise the suspicion of malignancy (5).

Skin changes like sign of inflammation were commonly seen because of inflammatory process. Here, in this study signs of inflammation were seen in 21.14%, whereas skin ulceration was rarely appreciated. In addition to that systemic inflammatory symptoms including fever, was occasionally seen and found in 5.3% of the cases with skin inflammation. Similarly, nipple changes were appreciated in 6.34% consisting of nipple discharge and retraction (Figure 1).

Abscesses are the localized collection of pus with in the breast parenchyma (7). It becomes necessary to exclude abscesses in older age group, as abscess may be associated with malignancy. On aspiration, most of time frank pus is aspirated which indicates abscesses. In the current study, pus was aspirated in 21 patients (3.02%).

Abscess may be due to many causes which includes lactation and non-lactational causes. Lactational causes are found in lactating women and in 1-3% of the cases it develops as abscess. The non lactational causes are injury, diabetes, nipple piercings, breast implant, smoking tuberculosis, *etc.* (8) (Figure1). In many cases, the underlying cause of breast abscess can not be identified. We also agreed with this as in every case, the underlying cause was not identified.

The reason behind that is in rural population most of illiterate women come to institute for consultation/ treatment who can not express or tell their health problems.

Microscopic features varies depending on the etiology. The abscess mainly consists of inflammatory infiltrate along with necrosis and occasionally foreign body giant cell reaction (9) (Figures 2,3).

In the current study, pyogenic/nonspecific inflammation was found as being more common (56.49%) (Table 3).

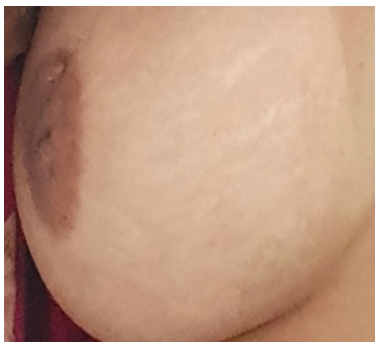

Figure 1

Figure 1. Clinical picture of breast abscess showing 1×1 *cm* breast growth with ulcer.

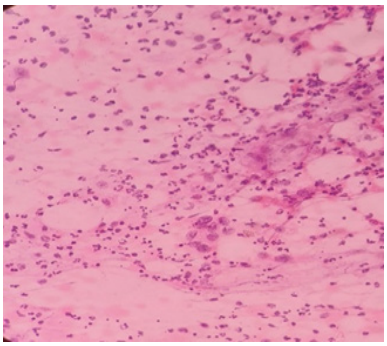

Figure 2

Figure 2. H&E stained smear of breast abscess showing acute inflammatory cells with histocytes.

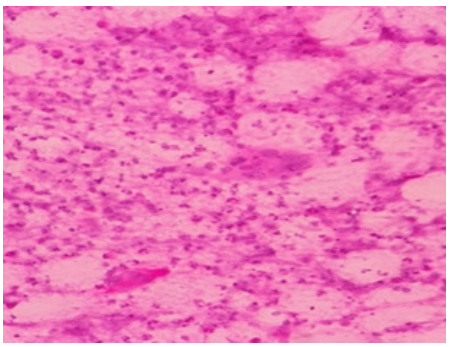

Figure 3

Figure 3. PAS stained smear of breast abscess showing acute inflammatory cells with histocytes.

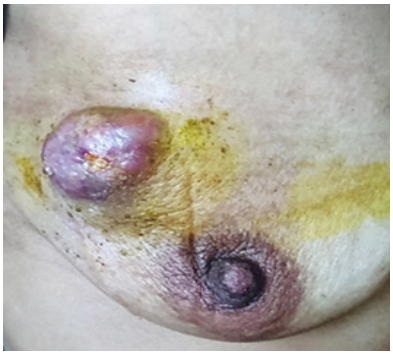

Figure 4

Figure 4. Clinical picture of tubercular abscess which shows 4×3 *cm* breast growth with ulcer.

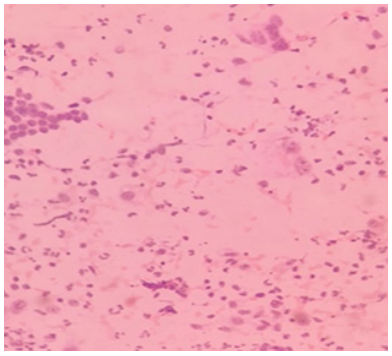

Figure 5

Figure 5. H&E stained smear of tubercular abscess showing acute inflammatory cells, histiocytes with benign ductal sheet.

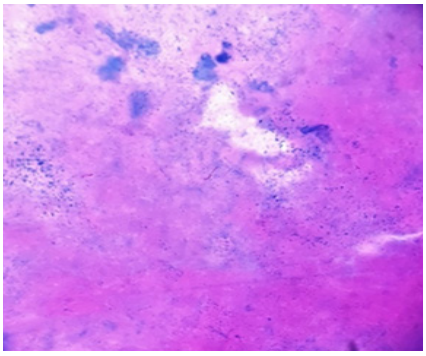

Figure 6

Figure 6. ZN stained smear of tubercular abscess showing presence of AFB confirming tubercular abscess.

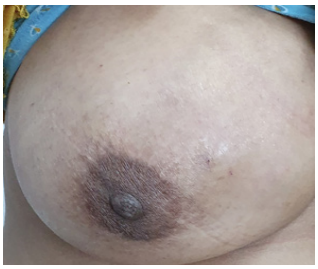

Figure 7

Figure 7. Clinical picture of granulomatous mastitis which shows 2×2 *cm* breast growth.

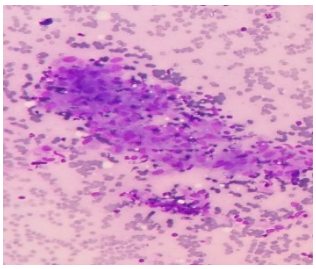

Figure 8

Figure 8. MGG stained smear of granulomatous mastitis showing epithelioid cell aggregation.

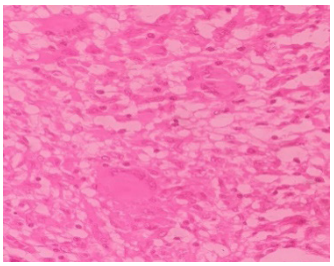

Figure 9

Figure 9. H&E stained section of granulomatous mastitis showing presence of epithelioid cells granuloma with chronic inflammatory cells infiltrate.

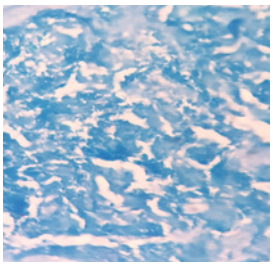

Figure 10

Figure 10. ZN stained section of granulomatous mastitis showing non contributory???

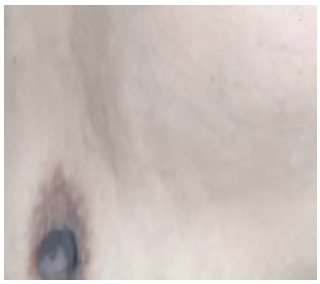

Figure 11

Figure 11. Clinical picture of idiopathic granulomatous mastitis showing 4×4 *cm* breast growth.

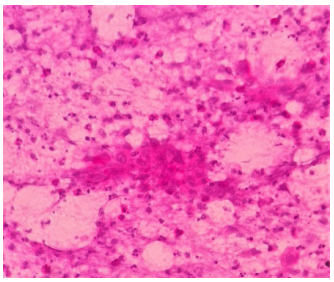

Figure 12

Figure 12. PAS stained smear of idiopathic granulomatous mastitis showing histiocytes with plenty of polymorphs.

Occasionally, reactive ductal cells are appreciated which occur due to inflammation and often mimic malignancy. In such cases, FNAC should be advised after antibiotic treatment to exclude possibilities of malignancy.

Breast tuberculosis accounts for <1% of all breast lesions (10). It often mimics breast carcinoma. Lack of awareness of manifestations and simulating benign or malignant lesions of disease are contributory to its overlooking and misdiagnosis. First description of mammary tuberculosis was given by Sir Astley Cooper in 1829 and called it as scrofulous swelling of bosom (11). Tuberculous involvement of breast may occur *via* lymphatic, hematogenous, or contiguous seeding and rarely by direct inoculation of bacilli *via* the abraded nipple. The lymphatic route is the most likely route of breast involvement which occurs by retrograde extension from the axillary lymph node. No well defined clinical features suggestive of breast tuberculosis are mentioned. The most common symptom is hard lump in breast followed by ulcer, purulent discharge, enlarged regional lymph nodes and uncommon presentations includes peau de orange, skin erythema, induration, nipple retraction (1). Similar clinical findings were observed in the current study (Figure 4). The breast tuberculosis microscopically may present as abscess and epithelioid cells or rarely granuloma with other inflammatory cells (Figure 5). Identification of mycobacterium is required to confirm the pathology and exclude differentials (2) (Figure 6). The tubercular mastitis is identified by presence of caseating granuloma with Langhan's giant cells on cytology and histopathology with confirmation by identification of AFB bacilli. In current study on cytology examination, tubercular abscess and tubercular mastitis were diagnosed in 0.90% of the cases each, confirmed by identification of the bacilli.

For the suspicious cases of underlying tubercular pathology, where caseating granuloma with Langhan's giant cells are identified and microbial identification of micro-organism is not possible on ZN staining (Figures 7-10), other methods of isolation including RT-PCR is recommended to confirm the diagnosis.

Granulomatous mastitis is non neoplastic, uncommon breast disease which clinically and radiologically mimics malignancy. It is of two types: granulomatous due to secondary causes or idiopathic granulomatous mastitis. Secondary causes include tuberculosis, sarcoidosis, fungal, cat scratch disease and Wegener's granulomatosis (12). Therefore, in the current study in 9.06% of the cases granulomatous mastitis was

reported (Figures 7-9).

Idiopathic granulomatous lobular mastitis is chronic, destructive non-necrotizing granulomatous inflammation of lobules. It was first described by Kessler and Wolloch in 1972 (3). The etiology is mostly idiopathic but needs to be distinguished from specific granulomatous pathologies. A variety of factors including microbial agents, hormonal effects and immunological disorders play important role in etiology. It occurs in women of premenopausal age. On clinical and imaging analysis, granulomatous lobular mastitis is often suggestive of malignancy (13,14). Microscopically, granulomatous lobular mastitis is characterized by non-necrotizing granulomas consisting of epithelioid histiocytes, Langhans giant cells, a lymphoplasmacytic inflammation and necrosis is usually absent. These features were also appreciated in this research work (Figures 11,12).

Mastitis is the focal or diffuse inflammation of the parenchyma of breast. It may be infectious or non-infectious. Infectious organism includes mycobacterium, *Bartonella henselae*, Actinomyces, fungi including aspergillosis, which may develop in association with implants. Noninfectious causes include endogenous and exogenous noncellular materials like secretions, milk, keratin, hair and exogenous metal, animal hair (15).

It can present as swollen, red, tender breast with or without axillary lymph nodes enlargement. The other systemic symptoms which may occur are fever, chills, fatigue and body ache. It is usually unilateral and may mimic inflammatory breast carcinoma. On cytology examination, it reveals inflammatory cell infiltrate mainly comprising of polymorph, lymphocytes, histiocytes and often foreign body giant cell reaction which rule out malignancy.

Lymphocytic mastitis also called as diabetic mastopathy is unusual finding in early onset and long-standing type 1 diabetes or other auto immune diseases. It is uncommon and accounts for less than 1% benign breast disease. Hyperglycemia leads to stromal matrix expansion and accumulation of glycosylation end products and B cell inflammatory response (16). Firm, palpable, non-tender mass or diffuse nodularity are the modes of presentation. It is usually seen in premenopausal women with average age 45 years. Lymphocytic mastitis clinically and radiologically mimics carcinoma. Cytology examination exhibits ductal cells, lymphocytes and epithelioid fibroblast in fragments of dense connective tissue. In this study, 1.20% of the cases were of lymphocytic mastitis on cytology, whereas on histopathology one case was reported as lymphocytic mastitis which was diagnosed as abscess on cytology.

Fat necrosis is the inflammatory reaction of adipose tissue. It occurs due of injury which may be due to various causes such as ruptured cysts or ducts, autoimmune diseases such as lupus mastitis and polyarteritis nodosa, anticoagulation, blunt trauma, pressure, prior biopsy, surgery, or radiation therapy (17). The mean patient age is around 50 years.

Clinically, fat necrosis may be asymptomatic or may present as a palpable peri areolar mass with or without skin bruising, tenderness, or retraction. The radiology examination also reveals malignancy. On cytology examination, it depicts foamy histiocytes and foreign body-type giant cells reaction surrounded by adipocytes and lipid vacuoles (18). Histopathology examination also has similar findings. In the current study, on cytology 7.85% of the cases had fat necrosis. On histopathology a single case was reported as fat necrosis which was reported as abscess on cytology.

Mammary duct ectasia is an inflammatory condition which is characterized by dilatation of the central ducts with associated fibrosis and chronic inflammation. It is also called as plasma cell mastitis. It occurs in 4th to 7th decade of life. It is mostly noted in multiparous women with history of nursing. Duct ectasia may present as unilateral or bilateral non-bloody nipple discharge, nipple retraction, or a palpable mass that is typically subareolar and sometimes associated with pain. The clinical symptoms may include unilateral or bilateral thick nipple discharge of varying color due to intraluminal inspissated secretions and a painless irregular subareolar mass with or without skin retraction. Duct ectasia may closely mimic carcinoma, especially when a hard lump form around nipple, may distort the nipple and simultaneously the milk ducts and lymph nodes are enlarged (19).

The etiology of the condition remains unknown but it appears to begin with periductal inflammation followed by destruction of the elastic tissue to cause ectasia and periductal fibrosis. The lymphatic fluids stagnate in the breast, and the stagnate fluid acts as

foreign material. The cytology examination reveals thick cheesy secretion composed of amorphous material, cellular debris, abundance of plasma cells with other inflammatory cells, and cluster or sheets of ductal cells, whereas histopathology examination exhibits dilated ducts with either necrotic or atrophic lining of flattened epithelium and lumen containing granular, amorphous, pink debris and foam cells. Periductal and interstitial chronic inflammation, chiefly consists of plasma cells, lymphocytes, histiocytes with multinucleate histiocytic giant cells. These findings were concordant with other researches. Histopathology examination was done in only 12 cases because it was not required in every case of inflammatory/infective breast pathology, as most of them were treated with drugs or antibiotic therapy. However, in a very few cases FNAC was required specially when inflammatory growth did not subside with antibiotic treatment *e.g.* in some specific inflammatory pathologies like tuberculosis, idiopathic granulomatous mastitis and mammary duct ectasia where histopathology is required to confirm the pathology. In present study ,the concordance with histopathology was found in 6(50%) cases 4(33.33%) abscess and rest 2(16.66%) in granulation mastitis.

Conclusion

Breast carcinoma is the commonest malignancy among women in India. But every breast mass is not a malignancy, although it may mimic malignancy. Cytology examination of every mass should be carried out for the diagnosis; so as to provide proper management and avoiding unnecessary surgeries. We also promote a definitive diagnosis at FNAC level, to ensure early and effective treatment and minimize unnecessary radical surgery. More studies with the same aim should be carried out on a large scale to better evaluate the mimickers. Breast health awareness program should be implemented at different levels.

Acknowledgement

The current institute number of university is ECR/1830/Inst/UP/2023. However, the ethical clearance no. 230/2018 for research on breast pathology was approved by previous committee.

Conflict of Interest

There was no conflict of interest in this manuscript.

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