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Case Report

Breast Carcinoma Masquerading as Granulomatous Mastitis on Fine Needle Aspiration Cytology lessons to learn!

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Abstract
Chronic granulomatous mastitis is not an uncommon entity. It mimics breast carcinoma on physical, gross & microscopic examinations; both on histopathological and fine needle aspiration cytology. At other times invasive ductal carcinoma may suggest granulomatous mastitis. A case is presented here where ductal carcinoma was misinterpreted as granulomatous mastitis on fine needle aspiration cytology smears in a 48 yr old woman who presented with large painful lump in her left breast. The mass was subsequently excised and the histopathological examination revealed infiltrating ductal carcinoma. Reexamination of the cytology smears did show some atypical cells commensurate with the ductal carcinoma. We here discuss various reasons and factors responsible for over and under interpretation of cytological atypia.

Key words: Granulomatous mastitis, Breast disease, Ductal carcinoma, Cytological atypia, Fine Needle Aspiration Cytology, FNAC, False positive cytology, False negative cytology, Laboratory error.

Introduction

Chronic Granulomatous mastitis is not a rare inflammatory breast disease.[1] It may mimic breast cancer and other infections such as tuberculosis, sarcoidosis and parasitic infections.[2] Various cognitive and technical factors may cause false diagnosis of chronic granulomatous mastitis.

It's most likely cause appears to be ducts obstruction with extravasation of the fatty secretions eliciting granulomatous response. Other narrated factors include autoimmune reactions, infections and chemical reaction associated with oral contraceptive use. In response to damage to ductal epithelium, extravasation of secretions, lymphocytes and macrophages migrate to the site of injury and produce a local inflammatory response.[3,4] The management options include high dose short term steroids and a course of antibiotics with or without surgical excision. The recurrence rate is as high as 50%.[5]

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Report of a case

A 48 year woman was referred to the Azad Jammu & Kashmir (AJ&K) Medical College for FNAC assessment of her breast lump which was present for the last 6 months; but had recently become painful with sensations of needles in and around the area of the lump. She did not give history of fever but there was recent weight loss and backache. She was hepatitis C positive for which she received interferon treatment. She reported that the lump was initially small, but over the period of last few months it had grown gradually in size. She has five children. She is one year post menopause. She gives no history of breast carcinoma in her family.

On examination a hard, fixed non tender 9x9x6.5 cm lump was felt in the left breast with intact overlying skin. No signs of inflammation were seen. The nipple and areola complex were essentially normal. There were no palpable lymph nodes. An FNAC was performed using 5 cc syringes with attached 23 gauge needle, 4 passes were made and 6 slides prepared out of which 3 were stained with hemacolour and 3 were with Hematoxyline and eosin (H&E).

Microscopic Examination

The smears revealed several clusters of large plump cells containing abundant eosinophilic cytoplasm.

There were frequent macrophages containing lipid droplets. Clusters of these cells gave impression of ill defined granulomas. Slight variation of nuclei in size and shape was attributed to inflammatory atypia. (Figure 1)

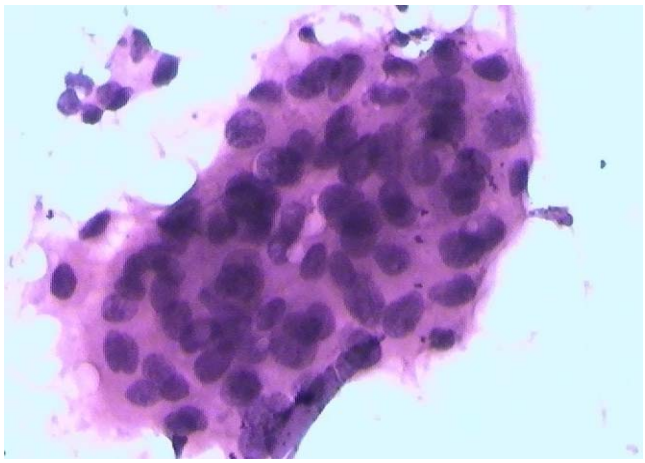

Figure 1. Syncytium of overlapped ductal cells

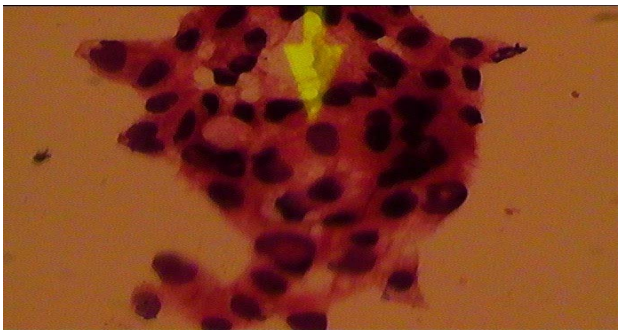

Figure 2. Syncytium of overlapped ductal cells giving an impression of granuloma (H&E X 200)

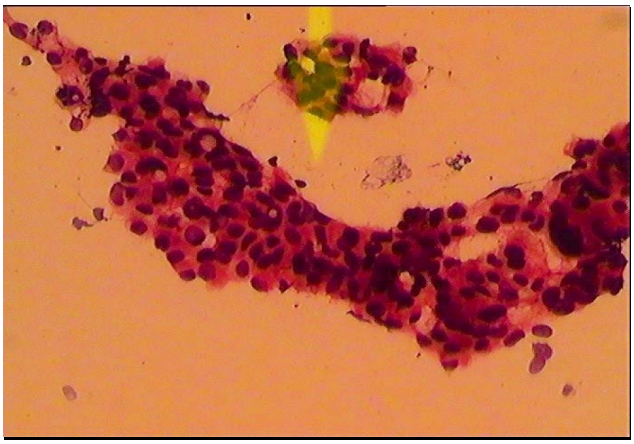

Figure 3. Clusters of cells with lipid droplets mimicking vague granuloma (H&E X 400)

Based on these findings diagnosis of granulomatous mastitis was made. Due to rather large size of the lump and no improvement on conservative management the mass was excised.

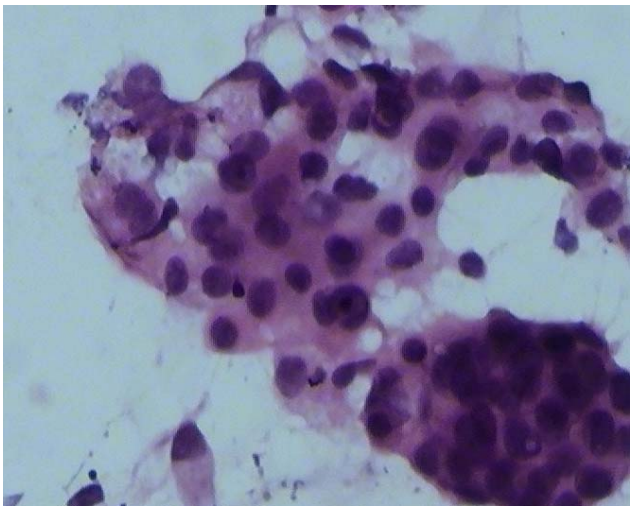

Figure 4. Sheets of cells surrounded by lipid droplets of variables sizes suggesting possible granulomatous mastitis (H&E X 100).

The mastectomy specimen revealed grade III infiltrating ductal carcinoma with infiltration into adipose tissue and lymphatic spread. It was staged as T3 N2a tumor.

Microscopically the tumor cells formed neoplastic ducts which intermingled with individual adipocytes. Lipid vacuoles were surrounded by neoplastic cells and ducts. (Figure 6).

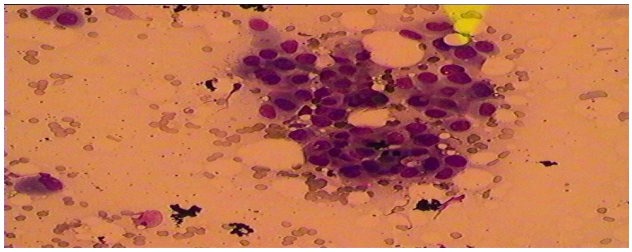

Figure 5. Infiltrating ductal carcinoma. Many lipid vacuoles are surrounded by malignant cells forming ducts. (H&E X100)

The FNAC slides were reviewed and definite atypia was noted in some cells. (Figure 6). The neoplastic ductal cells were infiltrating fat tissue which were mistaken as engulfed lipid droplets

The reasons for false negative diagnosis in this case were throughly evaluated. The main important

reasons for under-diagnosis in this case were as follows;

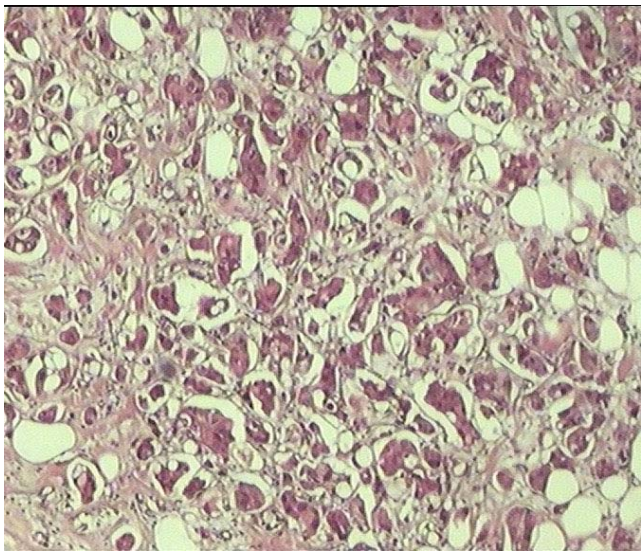

Figure 6. The neoplastic cells infiltrating adipose tissue. The lipid droplets were misinterpreted as engulfed fat. (FNAC, Hemacolor X 100)

Frequent variable sized lipid droplets intermingled with ductal cells led to the possibility of granulomatous mastitis

Once this impression was firmly adopted, the presence of atypia in some cells and usual nuclear shape variations seen in the macrophages was assumed to be due to inflammation

The fear of false positive diagnosis perhaps also contributed to become over conscious

As the presumed diagnosis was benign, need for reevaluation was not felt necessary.

Previous encounter to several cases of granulomatous mastitis over sensitized the observer to the possibility of the granulomatous mastitis

As the slides were being seen on multihued with active discussion and simultaneous photography taking place perhaps mind did not remain focused.

DISCUSSION:

Fine needle aspiration cytology (FNAC) is a safe,cost effective and virtually noninvasive procedure which is now routinely used to diagnose various neoplastic and non neoplastic diseases. Not only palpable but also deeply located lesions can be easily targeted with help of imaging modalities. It has a high degree of sensitivity, specificity and accuracy. Its fast and almost painless procedure with very little complications. It has eliminated a great number of invasive procedures along with their expense, discomfort and complications.[5,6]. However FNAC has its own limitations and pitfalls. As generally on FNAC smears tissue architecture is not observed the pathologist has to pay much more attention to the cellular details. Magnification of 1000 magnitude is quite useful in closely observing the finest cytological details. We routinely use this magnification on almost all cytological smears and sometimes tissue pathology. Needless to say that FNAC requires a lot of training, experience and meticulous focused detailed microscopic observations and clinical correlation. Frequent revisiting the cases and holding unknown conferences are quite helpful in refining one's cytological observation.

Detailed clinical history and physical findings are extremely important Accurate positioning of needle in the lesion and standard technique are essential. The interpretation is based on individual cells, small groups of cells and stromal reactions around these cell groups. Seldom we get sufficiently large fragments giving detailed tissue architecture.

No less important are cognitive factors such as fatigue, haste, lack of focus and biases based on previous experience. Its important to see all the smears slides in a standard protocol, not missing any area or the corner. Smears must be interpreted in light of clinical scenario and gross characteristics of the lump. [7]

The FNAC errors may be classified as given in table 1follows (Table 1); If a provisional diagnosis is made, ones' mind still should be open to other possibilities as well because in a way our mind may create the diagnosis. A single feature of any cytology smear sometimes when over emphasized can lead to the human mind neglecting other characteristics of the lesion. Degenerative changes would render the smear to be difficult to interpret. Benign breast lesions are usually easy to diagnose when their characteristic cytologic patterns are obvious. Hypocellularity, degenerated apocrine cells, necrosis, and epithelial hyperplasia are some of the factors that may be encountered in evaluating a difficult smear, mimicking atypical or malignant lesions. Exceptions occur in cystic and fibrotic lesions that are inevitably hypocellular. Although false positive diagnosis are seen more often, the false negative diagnosis may occur because of aforementioned reasons. The false-negative cases in breast FNAC, although few, are commonly due to poor sampling technique, poor tumor localization, and the presence of a well-differentiated histology of the tumor.

Table 1. Factors leading to errors in cytology diagnosis.

Sampling errors	Physical Characteristics of the lesion.	Cognitive Factors:
Rapid screening or not seeing all slides thoroughly	Necrosis	Not being focused due to talking or other disturbances
Wrong Placement of the needle	Inflammatory cells infiltrate	Lack of Confidence
Lack of Experience	Fibrosis	Bias (Over-impressed by one feature)
Through and through puncture of the lesion	Dilution by secretions and blood	Mental Fatigue
Too much aspiration diluting the sample	Low cellularity e.g. Sarcomas with high vascularity	Haste

In conclusion operators' experience and confidence in correlating with the clinical and radiologic findings, the cellularity of smears, and the aspiration technique are always helpful.

Fatigue, attention deviation, haste, not seeing all slides in their entirety and being over impressed by one or two features may also result in false negative diagnosis. Presence of numerous inflammatory cells does not exclude malignancy as malignancy is often associated with necrosis and inflammatory cells response. Diligent search may reveal an occasional malignant cells. Careful attention must be paid to the nuclear features. Thus in the interpretation of breast FNAC, all these factors should be considered before a benign diagnosis is rendered.

Slow, medium pace systematic examination of all slides with full attention is required. Diagnosis must not be made in haste. Diagnosis should be synthesized at the end of seeing all the smears in correlation with clinical findings and physical characteristics of the lesion. If needed, reexamine selected slides. Good, effective screening policy and multi tier system of examination and second opinion may also be considered.

Many of these factors to some extent also apply to histopathology and other laboratory tests but cytology is far more sensitive. Based on these factors rates of false negative and false positive vary from series to series from less than 1% to over 10%. FNAC is a useful technique and its combination with radiology gives numerous benefits. However to reap these benefits we need sound training in all areas including cognitive, methodology and clinal correlation. It's a team work and close liaison and discussion with team members may prevent errors. Continuous reading, practice and learning from one's mistakes is key to the improvement. This case is shared with the readers for this objective in mind.

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Contribution of the authors:

Prof. Anwar Ul Haque conceived the idea, organized the work and studied the slides.

Dr. Abdaal Munir helped in literature search and manuscript preparation

Dr. Hajra Farooq helped in organizing the material and in microscopy sessions