

Fine Needle Aspiration Cytology of Inflammatory Breast Lesions

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Abstract

Objective: To study the characteristics of inflammatory breast aspirate by Fine Needle Aspiration, performed by pathologist.

Methods: Inflammatory breast aspirates reported at two hospitals in Taif area (King Abdul Aziz Specialist Hospital and Al Hada Armed Forces Hospital, Taif, Kingdom of Saudi Arabia (KSA) from January 2000 till September 2007 were reviewed. The cytopathology reports, slides, clinical information, microbiology culture results, Tuberculosis; Polymerase Chain Reaction (TB; PCR) and histology were reviewed. The aspirates were identified as inflammatory based on presence of inflammatory cells and / or granulomas with occasional benign ductal epithelial cells. Cases of inflammatory carcinoma or duct ectasia were excluded.

Results: Forty-nine cases of inflammatory breast aspirates were included in the study. The aspirates were categorized into: Acute mastitis / Abscess 13 (26.5%), Granulomatous Mastitis 15 (30.6%), Fat Necrosis / Organized Haematoma 8 (16.4%) and Inflammation, not otherwise specified (NOS) 13 (26.5%), based on morphologic criteria combined with clinical impression. The Granulomatous Mastitis cases were subcategorized into Idiopathic and Infection related which included Brucellosis, Tuberculosis, and fungal mastitis.

Conclusion: FNA of inflammatory breast lesions is a useful tool if performed by a pathologist and combined with further workup including microbiologic culture correlation. It helps in management and treatment of the patient and avoiding unnecessary surgery (JPMA 59:167; 2009).

Introduction

Fine needle aspiration (FNA) of the breast has gained significant credibility in the diagnosis of breast diseases especially malignancy.¹ It is a widely used technique for the initial diagnosis of mammary lesions. The inflammatory breast aspirate should be managed and handled to get as much information as possible, especially if surgical intervention will not be considered. FNA performed by pathologist gives the advantage of assessment of the quick smear with further decision to submit material for microbiological cultures or special studies.² The inflammatory breast aspirate shows low cellularity with the epithelial cells arranged in clusters and small groups with the presence of myoepithelial cells. Cytological atypia and nuclear changes are minimal.^{1,2}

Materials and Methods

The inflammatory breast aspirates reported at two hospitals in Taif (King Abdul Aziz Specialist Hospital and Al Hada Armed Forces Hospital, Taif, K.S.A) were reviewed in the period from January 2000 until September 2007. The cytopathology reports, slides, clinical information, microbiological culture results, (TB, PCR) and available subsequent histology were analyzed. The aspirates were identified as inflammatory based on the presence of inflammatory cells and/or granulomas with occasional

benign ductal epithelial cells. Cases of inflammatory carcinoma or duct ectasia were excluded. The aspirates were categorized into four main categories: acute mastitis/abscess, granulomatous mastitis (GM), fat necrosis/organized haematoma, and inflammation, not otherwise specified (NOS). Based on cytomorphologic criteria combined with clinical impression and microbiological cultures, the granulomatous mastitis cases were subcategorized into idiopathic and infection related. All culture negative GM were categorized as idiopathic lobular GM (ILGM). The infection related granulomatous mastitis was further classified into TB, Brucellosis, and fungal based on culture results and TB PCR when available.

Results

Forty-nine cases of inflammatory breast aspirates were included in the study after the exclusion criteria. All the patients were females, no FNA for inflammatory lesions of the males were found. Thirteen (26.5%) cases qualified for acute mastitis/abscess, 15 (30.6%) cases as GM, 8 (16.4%) as fat necrosis/organized haematoma and 13 (26.5%) cases were called inflammation (NOS). The cytomorphological features for acute mastitis and abscess included the presence of neutrophils, macrophages, cytophagocytosis, and cell debris in the background with occasional epithelial cells forming tight clusters with mild cytologic atypia (Fig-1). The microbiological cultures for

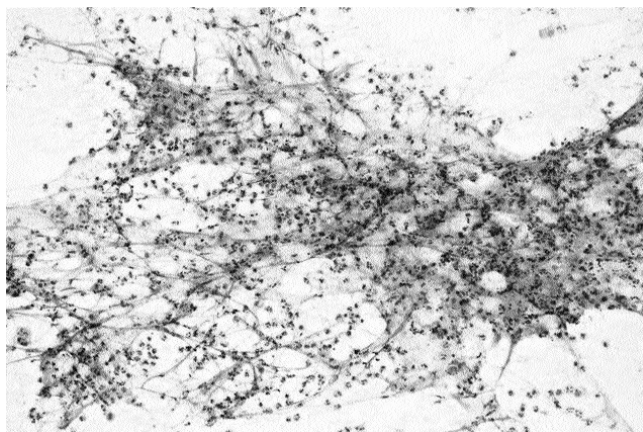


Figure 1: Smear preparation of acute mastitis showing numerous neutrophils, few histiocytes and necrotic debris (Papanicolaou 100X).

all the 13 cases were negative. Upon clinical review, all those patients were already on antibiotics for a period ranging from 5-11 days prior to FNA. Eight (61.5%) cases had subsequent drainage, 5(62.5%) of which showed acute mastitis and 3 (37.5%) showed abscess on subsequent histopathological evaluation.

Cases of GM were categorized based on the presence of cellular aspirate having numerous lymphocytes and plasma cells with granulomas formed of epithelioid histiocytes (Fig-2a & 2b) and multinucleated giant cells.

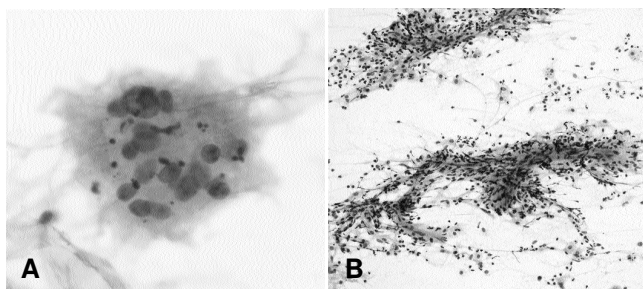


Figure 2: A- Smear preparation of granulomatous mastitis showing collections of epithelioid histiocytes and lymphocytes (Papanicolaou, 100X). B- Note a multinucleated giant cell. (H & E 100 X).

Few reactive ductal epithelial cells with enlarged nuclei and bare nuclei were seen as well. The microbiological cultures of all the 15 cases were available. Six-out of 15 (40%) cases had positive culture for *Brucella melitensis*, two (13.3%) cases were positive for TB which was further confirmed by PCR. The fungal cultures were negative in all the cases.

Seven out of 15 (46.7%) cases were classified as IGM. Four (57.1%) cases of IGM required surgery of residual mass after steroid therapy and showed Granulomatous Inflammation on histopathological examination. All the 15 cases received specific therapy and on follow-up showed a reduction of the

mass size.

The cytomorphological features of eight cases of fat necrosis / organized haematoma showed presence of foamy or haemosiderin-containing macrophages, inflammatory cells, multinucleated cells with or without cholesterol crystals and a necrotic background.

Thirteen cases were categorized as inflammation, NOS had necrotic background and few inflammatory cells in the form of neutrophils, lymphocytes and plasma cells, however, lacking specific features to fit them in the above categories. All aspirates were submitted for microbiological culture and 2 (15.3%) were diagnosed as breast brucellosis both on cytology and culture studies. The remaining 11 (84.7%) cases were negative for all cultures including routine bacterial, TB, and fungal growth.

Discussion

FNA is considered a useful tool in the diagnosis of breast masses and lesions. It differentiates malignant from benign cases and is useful in directing management and treatment of these patients. The inflammatory breast aspirate has been reviewed occasionally in literature.^{3,4} Submitting cultures from FNA material is an essential part of the diagnostic work up for the inflammatory breast aspirate. The presence of negative culture does not exclude infection; however, positive culture can direct therapy.^{2,3} In our study, the most beneficial use of microbiological cultures was in the aspirate containing granulomatous inflammation.

The significance of FNA of inflammatory lesions of the breast is described by Das et al⁵ in their review of 128 diagnosed inflammatory breast lesions. FNA cytology was found to be useful in the diagnosis of inflammatory breast lesions and their classification into acute mastitis/ breast abscess, tuberculosis mastitis, chronic non-specific mastitis and miscellaneous conditions.

Cases of acute mastitis/abscess are rarely submitted for fine needle aspiration as diagnosis is made usually on clinical basis. Breast cancer and breast infections may co-exist² therefore; either acute mastitis or breast abscess could be considered for FNA biopsy. Acute mastitis can also raise the clinical suspicion of inflammatory carcinoma. In our 13 cases, FNA was performed for a residual mass after full course of antibiotics or drainage. The usual organisms for acute mastitis are *Styphylococcus aureus*, *Styphylococcus epidermidis*, anaerobic streptococcus or *Bacteroides* species and mixed anaerobic infections. The microbiological cultures for all the cases were negative in our study.

FNA is a well established method for diagnosis of breast lesions in males also, however, little attention has been focused on inflammatory lesions in males. Silverman et al⁶ and Lopez et al⁷ have reported one and two cases of sub-areolar

abscess respectively, diagnosed on FNA in male breast. Recognition of this troublesome and rare condition on FNA cytology from the breasts in males will prevent recurrences since sub-areolar abscess is not cured by excisional biopsy.

Granulomatous mastitis is a rare chronic inflammatory breast lesion that mimics carcinoma clinically and radiologically. The causes of granulomatous mastitis includes tuberculosis, fungus (*Aspergillus*, *Blastomyces*, *Coccidioides*, *Histoplasma*, etc), *Actinomyces*, cat-scratch disease, foreign bodies (including sutures and silicone injections or leaking breast implants), subareolar abscess, duct ectasia and idiopathic causes. The diagnosis of Idiopathic lobular granulomatous mastitis (ILGM) remains a diagnosis of exclusion and should be entertained when all other known causes of granulomatous inflammation have been excluded. This entity was first described by Kessler and Wolloch⁸ in 1972. GM is a rare disease primarily affecting young women, most often during pregnancy and/or lactation. The cytological diagnosis of GM is difficult because the features overlap with other aetiologies, including tuberculosis. Tse et al⁹ have described absence of necrosis and a predominant neutrophilic infiltrate in the background, epithelioid histiocytes even in the absence of granulomas, as features of diagnostic significance in cases of granulomatous lobular mastitis. The diagnostic features and treatment alternatives of this disease are still unclear however several clinical and pathologic features have been reported in the literature.

In our series ILGM was diagnosed by excluding infectious etiologies. These patients showed good response to steroid therapy. ILGM show more of well-formed granulomas admixed with multinucleated giant cells and very few neutrophils in the background. We also found the presence of neutrophils in an abscess-like fashion in the background, more in favour of infectious etiology rather than IGM. We recommend submission of microbiological culture material whenever the quick smear at time of FNA shows an inflammatory background to include routine bacterial, fungal and TB cultures.

The breast is considered to be a rare site of extrapulmonary mycobacterial infection, comprising 0.1% of all tuberculosis cases.¹⁰ FNA establishes the diagnosis in most cases. Khanna¹¹ reported a success rate of 100% in his series while Khakker et al reported a success rate of 73%. Thompson KS et al¹⁰ described a case of unilateral tuberculous mastitis in a 58-year old white male. We had only two culture and PCR proven cases of tuberculous mastitis. The FNA biopsy diagnosis rests on finding granulomas or multinucleated giant cells, with or without demonstrable Acid fast organisms. Tuberculous mastitis can be associated with acute inflammation, particularly early in the course of disease; therefore part of the aspirate should be cultured for TB if

infection is suspected.

Brucellosis is hyperendemic in Saudi Arabia. Breast brucellosis is unusual in humans as a first presentation. However in all the six GM cases, the patient presented with breast mass while the two Inflammation NOS cases, presented as acute mastitis. Later on retrospective inquiry with the patients, history of raw milk ingestion and off and on fever was found. All the six cases were proven Brucellosis by microbiological cultures. The aspirates of GM secondary to brucellosis were found to have more neutrophils in the background admixed with poorly formed granulomas and occasional multinucleated giant cells. Gasser et al¹² reported the isolation of *Brucella melitensis* from a suspected breast tumour of a woman who also had uveitis. Three weeks after surgical drainage, and antimicrobial therapy a new abscess developed in the other breast whose culture yielded *Brucella*.

Fungal infection of the breast was not found in our series due to rarity of primary breast mycosis and may be also due to the small sample size.

Fat necrosis is often found in the subcutaneous tissue of the breast, rather than the breast per se. usually, but not invariably there is history of trauma to the breast. Clinically, it mimics carcinoma. Fat necrosis and cancer can occur together; therefore presence of fat necrosis in a biopsy specimen does not completely exclude the possibility of malignancy.² Fat necrosis should begin to resolve in a short time; thus a brief period (<1 month) of watchful waiting after FNA may resolve any question of malignancy. The cases that were categorized as fat necrosis in our study showed spontaneous remission, which goes with the cytological features. Cytology showed large foamy macrophages, including multinucleated giant cells. Acute inflammation may be seen in early course of disease but later chronic inflammation, granulation tissue and fibrosis may occur. Epithelial cells are few but may be atypical in appearance with nuclear pleomorphism, hyperchromasia, prominent nucleoli, and mitotic figures.

It was still difficult for some of the cases to be categorized in a specific entity and it is preferred to leave the diagnosis open for such aspirates and to be categorized as inflammatory NOS with recommendation of follow up of microbiological cultures and correlation with clinical findings.

Conclusion

FNA of inflammatory breast lesions is a useful tool in directing management and treatment of the patients and avoiding unnecessary surgeries especially if performed by a pathologist and combined with further studies including microbiological cultures. Breast brucellosis should be considered in the differential diagnosis of GM in our area. Idiopathic GM should be recognized on FNA as it is a specific

clinicopathological entity that can have medical treatment avoiding unnecessary surgery.

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