



Granulomatous Mastitis: A Cytological Dilemma

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Abstract

Granulomatous mastitis (GM) is a rare, chronic inflammatory breast disease of unknown etiology that can mimic malignancy on clinical examination. The cytological features of GM, though consists of epithelioid cells, giant cells and inflammatory cells is not specific and can mimic many other conditions. A thorough work up is essential, as GM is usually a diagnosis of exclusion. We report cytological findings of a case of GM in a 50 yr old female which mimicked carcinoma clinically.

Keywords: Granulomatous mastitis; Cytology**Abbreviation:** GM: Granulomatous Mastitis; FNAC: Fine Needle Aspiration Cytology**Key Messages:** A diagnosis of GM should also be considered when high numbers of single epithelioid histiocytes are seen in smears in the absence of granulomas.

Introduction

Granulomatous mastitis (GM) is a rare chronic inflammatory breast disease of unknown etiology with a tendency for persistence or recurrence [1]. GM is commonly found in young parous females [2]. They present as breast lumps within 5 years of childbirth [2]. The clinical presentation is similar to that of carcinoma breast. In addition, the radiological features can also mimic carcinoma and hence is worrisome [3]. Several etiologies have been postulated including an immune reaction to extravasated milk secretion, trauma, infection, use of oral contraceptive pills and prolactinemia [4-8]. GM is a benign process and it is important to recognise it to avoid invasive surgery and its complications such as skin ulceration and sinus formation.

Fine needle aspiration cytology is a simple, cost effective and non invasive technique. It is routinely used in the diagnosis of various breast lesions. However, the cytological features of GM are not specific and overlap with other etiologies [9]. A confident diagnosis can be made only after exclusion of other conditions like Tuberculosis, sarcoidosis, fungal infection and Wegener's granulomatosis. Most reports of GM have been described in young women of childbearing age [4-8]. We report cytological findings of GM in an elderly patient which simulated carcinoma clinically.

Case History

A 50 yr old female presented with a lump in the left breast since 3 months. On clinical examination, a firm to hard lump measuring 4 × 3cm was present in the upper medial quadrant of left breast. No axillary nodes were palpable. Hematological examination did not reveal any significant findings. ESR was 15 mm/hr. Chest X ray was normal. A clinical diagnosis of carcinoma breast was made. FNAC was done with a 22G needle and a 10 ml syringe. Smears were stained with H&E, Papanicolaou and Geimsa stain.

Observation and Analysis

Smears were moderately cellular and consisted of numerous inflammatory cells made up of lymphocytes, histiocytes, plasma cells along with few binucleate plasma cells (Figure1). Arborising

networks of capillary channels were also seen. (Figure 2B) Few ductal epithelial cells showing regenerative atypia were seen in small clusters. Ziel Neelson (ZN) stain for acid fast bacilli was negative. Multiple aspirations from different sites showed similar features. A cytological diagnosis of chronic mastitis was suggested.

Histopathological examination revealed aggregates of epithelioid histiocytes, ill defined epithelioid granulomas, multinucleate giant cells, inflammatory infiltrate consisting of lymphocytes and plasma cells along with granulation tissue fragments (Figure 3). ZN stain for acid fast bacilli was negative. PAS stain was negative for fungal organisms. Gram's stain did not show presence of any bacteria. Culture for mycobacterial tuberculosis yielded no growth. Hence a diagnosis of granulomatous mastitis was considered.

The cytological smears were reviewed again and showed a focal cluster of epithelioid histiocytes (Figure 2A). Also seen were numerous single epithelioid histiocytes with distinct reniform nuclei (Figure 1). These epithelioid histiocytes were mistaken initially for histiocytes of

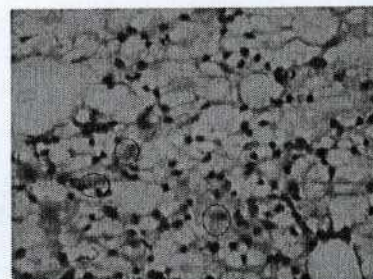


Figure 1: Cytological smear showing dense inflammatory cell infiltrate with many single epithelioid histiocytes (circled) with reniform to oval nuclei and moderate amount of cytoplasm. (Pap x 400).

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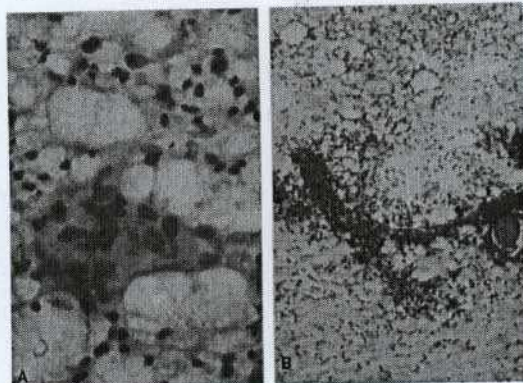


Figure 2: A. Cytological smear showing an aggregate of epithelioid histiocytes (arrow) within a mixed inflammatory background (Pap x 400). B. Smear showing arborising network of capillary fragments (double arrow) (Pap x 400).

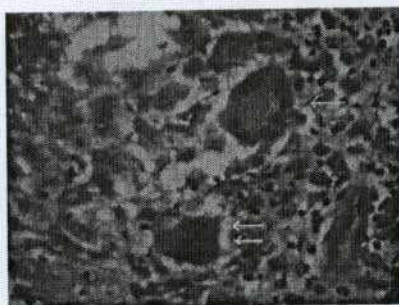


Figure 3: Histopathology showing non caseating epithelioid granulomas along with Langhans type giant cells (arrow) and foreign body type giant cells (double arrow) (H & E x 400).

a chronic infiltrate. Hence a cytological diagnosis of granulomatous mastitis was possible on review.

Discussion

GM is an uncommon breast lesion that was first described by Kessler and Wolloch in 1972 [10]. It is seen in women of child bearing age and usually present within 5 yrs of childbirth [2]. However it has been reported in patients as young as 11 years and as old as 80 years [11,12]. The most common clinical presentation is a unilateral firm discrete breast lump, often associated with inflammation of overlying skin [2]. It can be seen in any quadrant of the breast except in subareolar region [13]. It can also show nipple retraction or peau de orange appearance, thus simulating carcinoma [14].

The histological features are characterized by non caseating granulomas within the breast parenchyma and lobulitis with or without neutrophilic microabscess [15]. The cytological features are characterized by aggregates of epithelioid histiocytes, multinucleate giant cells lymphocytes, plasma cells and a variable number of neutrophils [1]. Presence of single epithelioid histiocytes having a reniform to plump nuclei and a moderate to abundant pale pink cytoplasm has also been reported by many authors [4,9,16].

Though, most studies have shown the presence of neutrophils as the predominant inflammatory infiltrate, these were significantly absent in the present case. The presence of numerous lymphocytes and

plasma cells, along with binucleate plasma cells, significant arborising vascular network along with absence of multinucleate giant cells, led us to give an initial diagnosis of chronic mastitis. However, a review of the slide showed a focal cluster of epithelioid histiocytes along with single epithelioid histiocytes with a distinct reniform or oval nuclei, which was missed on initial examination. Tse GM et al. found epithelioid granulomas only in half of their case series thus, suggesting that they are not pathognomic for GM [9]. They opined that presence of these single epithelioid histiocytes in the absence of well defined granulomas should alert the pathologist to the possibility of a granulomatous inflammation [9]. Most studies have also described presence of granulation tissue fragments in GM [9,16].

Accurate cytological diagnosis still remains a challenge, because the features overlap with other etiologies like tuberculosis (TB), fungal infections, fat necrosis, sarcoidosis etc. The single most important differential diagnosis is with tuberculosis especially in endemic countries like India [17]. Treating TB with steroids would aggravate the infection, whereas giving unnecessary anti tubercular drugs may cause numerous side effects. The absence of caseous necrosis and a predominantly neutrophilic infiltrate in the background favour a diagnosis of GM [9]. Langhans giant cells, epithelioid cells and caseation are features of TB. However, acid fast stains and culture is also essential in confirming diagnosis of TB.

Demonstration of fungi by special stains like PAS and culture is necessary to diagnose fungal mastitis. In fat necrosis, the presence of abundant foamy cells is a classic feature, whereas in GM foamy cells are seen only occasionally. In addition, epithelial cells which are seen in GM are not seen in fat necrosis [16]. In sarcoidosis, smears show abundant lymphocytes with neutrophils or necrosis along with epithelioid granulomas [16]. As the cytological features are not specific, GM is usually a diagnosis of exclusion. The definite diagnosis depends on clinical correlation, histopathological picture and a negative microbiological investigation.

The cause of idiopathic GM remains unclear. Autoimmune disease, infection, trauma have been implicated by some authors [2]. Several theories about the mechanisms of idiopathic GM have been proposed. Miller et al. [18] suggested that squamous metaplasia in the ducts can initiate the process as a response to keratin. Murthy [7] reasoned that oral contraceptive pills increase the amount of secretion in the ducts and cause the inflammatory response. Others suggested that increased prolactin levels or localised immune response to extravasated milk secretion can cause mastitis [5,8]. An association with local infection by *Corynebacterium Kroppenstedtii* has recently been suggested [5].

In conclusion, the cytological diagnosis of GM is difficult because there are no specific features. A high index of suspicion and awareness of this entity by the cytopathologist is needed, to make a diagnosis and to prevent unnecessary mastectomies. A diagnosis of GM should also be considered when numerous epithelioid histiocytes are seen in smears, even in the absence of granulomas [9]. A definite diagnosis depends on histopathological examination and negative microbiological investigations.

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