Idiopathic granulomatus lobular mastitis

A forgotten clinical diagnosis

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ABSTRACT

Objectives: To review clinicopathological features of all cases diagnosed as idiopathic granulomatous lobular mastitis (IGLM) in our hospital and compare them with other data from the Kingdom of Saudi Arabia.

Methods: Reports of all breast specimens received in histopathology laboratory in Qatif Central Hospital, Kingdom of Saudi Arabia over a 14 year period (1988 through to 2002) were collected and those diagnosed as IGLM were selected for analysis of both pathological material and clinical data.

Results: Eleven patients representing 1.6% of all breast specimens were diagnosed as IGLM. The mean age was 35 years (range 25-50). Both breasts were equally affected. The most frequent presenting symptom was a breast mass of 2-22 weeks duration. The most common clinical diagnosis was chronic abscess (5 patients). Relation to pregnancy, lactation or oral contraceptives pills was elicited in 4 patients. Recurrence at different time intervals occurred in 3 patients. Microscopically there was an evident granulomatous inflammation mostly in lobular distribution. Ductal inflammation with epithelial changes was noted in most cases. Staining and cultures were negative for both mycobacterium and fungal organisms.

Conclusion: Granulomatous mastitis is not unheard of and clinicians should keep it in their list of differential diagnosis of breast lumps so appropriate handling of breast specimens including microbiological studies can be pursued. Utility of fine needle aspiration biopsy as a diagnostic tool is to be considered.

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Three decades ago, idiopathic Granulomatous Lobular Mastitis (IGLM) also known as granulomatous mastitis or granulomatous lobular mastitis was first described.[1] It is a rare benign inflammatory disease of the breast that may clinically mimic breast carcinoma. It is a disease of women in the reproductive age group with a breast mass being the most common presenting symptom. The diagnosis is by exclusion of other causes of granulomatous inflammation by special stains in tissue sections and by microbiological investigation.

Methods. All reports of breast specimens received in histopathology laboratory in Qatif Central Hospital over a 14 year period, 1988 through to 2001 were reviewed. Seven hundred and fourteen specimens from 669 female patients were examined. Eleven patients were diagnosed as IGLM representing 1.6%. The medical records of those patients were reviewed, and the following data were collected: age, presenting symptoms, side involved, clinical diagnosis, relation to pregnancy, lactation or oral contraceptives and recurrence. The paraffin blocks of those specimens were sectioned and stained for hematoxylin and eosin (H&E), periodic acid-Schiff (PAS), Grogott-Gomori methanamine silver (GMS), and Zeihl-Neelsen stain (ZN). The pathology reports were reviewed for gross specimens' description.

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Table 1 - Clinical data.

No	Age (years)	Slide	Mass	Pain	Discharge	Symptoms (weeks)	Skin changes	LN	Lactation pregnancy OCP	Clinical Dx	Recurrence	Other medical conditions
1	30	L	+ LOQ	-	-	22	-	+	OCP LD 3 yr	Unknown	-	Sickle cell trait
2	35	L	+ UOQ	-	-	13	-	+	LD 2 yr	TB Fibroadenoma	-	Pulmonary tuberculosis
3	37	L	+ UOQ	-	-	9	-	+	LD 5 yr	Chronic abscess	-	Hypertensive
4	33	R	+ U	-	-	9	Nipple retraction	-	Lactating	Cancer	-	Diabetic
5	40	R	+ U	+	+	13	Redness	-	LD 2 yr	Chronic abscess	-	Hypertensive
6	25	L	+ LIQ	+	-	9	-	-	LD 1 year	Cancer	After 1 yr	
7	36	R	+ LOQ	+	-	6	Ulceration	-	Lactating	Chronic abscess	Twice 2 & 9 yrs	Sickle cell trait
8	34	R	+ LOQ	-	-	U	-	-	LD 1.5 yr	Unknown	-	
9	30	R	+ UIQ	-	-	U	-	-	Pregnant	Unknown	-	-
10	42	L	+ U	-	-	U	-	-	LD 6 yr	Chronic abscess	-	
11	27	L	+ LIQ	-	+	4	Skin redness	-	LD 3 yr	Recurrent abscess	After 2 months	

+ - presence, - absence, U - unknown, LOQ - lower outer quadrant, UOQ - upper outer quadrant, LIQ - lower inner quadrant, UIQ - upper inner quadrant, LN - lymph node, LD - last delivery, OCP - oral contraceptive pills, Dx-diagnosis

Results. There were 11 patients diagnosed as IGLM accounting for 1.6%. The age ranged between 25 and 50 years with an average of 35 years. Both breasts were almost equally affected. The most common presenting symptom was a breast mass of 2-22 weeks duration (average of 9 weeks) associated with pain in 3 patients and nipple discharge in 2. In 5 patients, the mass was in the lower quadrants of the breast while it was in the upper parts in 3 and unknown in the remaining 3. The outer parts of the breast was more affected than inner parts (5 versus 3 consecutively). Skin and nipple changes were evident in 4 patients while in another 2 patients palpable ipsilateral axillary lymph nodes were reported. The most common clinical diagnosis given by surgeons was chronic abscess (5 cases) and in 2 others, breast cancer was suspected. Tuberculosis was the initial clinical impression in a single patient who had been treated for pulmonary tuberculosis 20 year ago and presented with breast mass. During follow up she developed respiratory symptoms and positive sputum for acid fast bacilli that proved to be mycobacterium tuberculosis on culture results. Relation to pregnancy, lactation or oral contraceptives pills (OCP) was elicited in 4 patients. Recurrence at different time intervals occurred in 3 patients. **Table 1** summarizes the clinical data. All patients had surgical excision of their breast lumps. A single patient (No. 11) was diagnosed on fine needle aspiration but due to strong family history of breast cancer, the patient insisted on excision of the mass, which was free of malignancy. No other therapy was used post operatively except antituberculous medication in the patient with open pulmonary tuberculosis.

Pathological findings. All patients had excision biopsies. The resected specimens were either soft fibro fatty tissues or firm in consistency with suggestion of suppuration or cavity formation. The size was variable ranging from 1.5-8 cm with a mean of 4.5 cm. Microscopically there was an evident granulomatous inflammation mostly in lobular distribution around a central empty space **(Figure 1)**. Microabcesses surrounded by epithelioid cells and multinucleated giant cells formed most of the granulomas. Both Langhans and foreign body type giant cells were present. There was no evidence of caseation necrosis in all specimens. Additionally, ductal inflammation with epithelial changes was noted in most cases. Granulation tissue reaction was only occasionally encountered (3 patients). Other associated breast findings include lactation changes (one patient), fibrocystic change (one patient), or fat necrosis (3 patients). Staining for both mycobacterium (ZN) and fungal organisms (PAS & GMS) was negative. There was no growth in all tested specimens (4 patients) including that from a patient that later developed pulmonary tuberculosis.

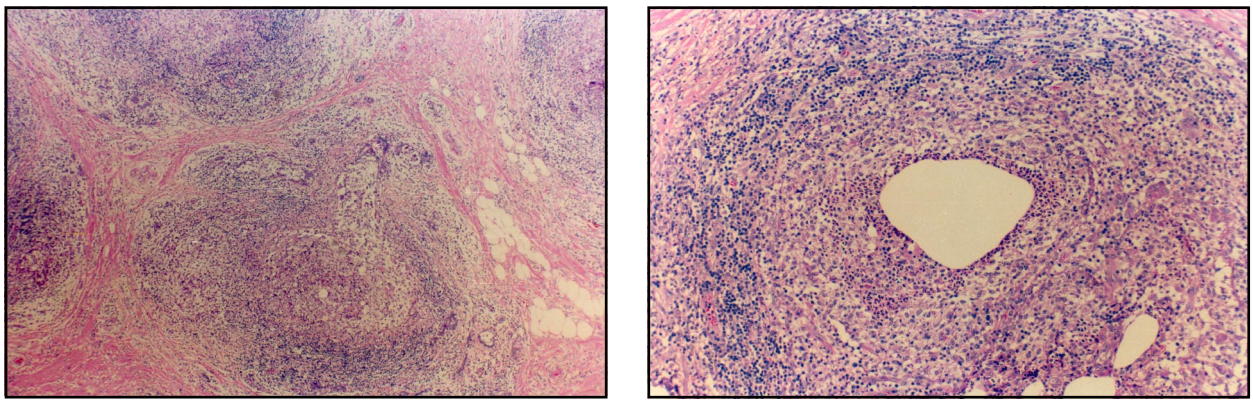

Figure 1 - **(a)** Low power view reveals multiple granulomas in lobular distribution. **(b)** High power view showing epithelioid granuloma including giant cells centered on an empty space rimmed by neutrophils (H&E x 10 x 25).

Discussion. Kessler and Wolloch[1] reported 5 young women with breast masses clinically diagnosed as breast cancer but on histological examination of resected specimens, granulomatous inflammation centered on the breast lobules was evident. It was unrelated to infection, trauma or foreign body. An immunologically related reaction was a proposed pathogenetic mechanism in view of its histology resemblance to granulomatous orchitis and thyroiditis, however, DeHertogh[2] did not substantiate this theory. More cases were subsequently reported[3] with the emphasis on histological distinction from other commoner chronic mastitides group. The last mentioned group of granulomatous breast conditions includes a long list of infectious agents such as mycobacterium tuberculosis,[4] brucellosis, blastomycosis, actinomycosis, filariasis,[5] cysticercosis, histoplasmosis[6] and sparganum.[7] The distribution of granulomas is diffuse and unlimited to the lobules in infection related granulomatous mastitis, will be accompanied by caseation necrosis in tuberculosis, and the microorganisms whether fungal or mycobacterial will be demonstrated by special stains. Other inflammatory diseases such as sarcoidosis,[8] Wagener's granulomatosis and giant cell arteritis[9] can rarely involve the breast and should be excluded by appropriate serological and radiological investigations if clinically suspected.

Breast mass is a universal presenting symptom, which can be occasionally painful. Lymphadenopathy if present as in three of our patients may lead to erroneous clinical diagnosis of breast carcinoma especially if skin or nipple changes are evident. There was no clinical suspicion of IGLM prior to the histopathological evaluation of the resected breast mass, which is a common occurrence. None of our patients proved to be infection related in both tissue sections and culture materials even in the only proved case of pulmonary tuberculosis. The latter patient was not on antituberculous drugs at the time breast culture material was obtained although one could still argue that breast lesion could still be related to tuberculosis despite negative culture results. All our patients were parous women and relation to lactation; pregnancy or OCP was elicited in 4 of them.

Although the exact pathogenesis is unknown, various theories have been proposed. The most popular theory is thought to be an immunologic response to milk products. The fact that all reported cases occurred in parous women of reproductive age group made some authors term this entity as postpartum lobular granulomatous mastitis.[10] Other investigators have claimed that IGLM is in reality a form of duct ectasia affecting the terminal duct lobular units.[11] The second common theory is autoimmune reaction as occurred in histological similar condition such as granulomatous orchitis and granulomatous thyroiditis in which autoimmune mechanism plays a major role. Occasional presence of extra-mammary manifestation such as erythema nodosum,[9] oligoarthritis and episcleritis[12] are additional factors supporting this mechanism. Response to steroid[2] strengthens this theory despite the fact that no immunodysfunction have been elicited in such cases. Recurrence even after surgical excision is well known[13] as was encountered in 3 patients (27%) of our series. The true prevalence of IGLM in KSA is difficult to determine since all published cases, like ours, are hospital based. However, data from different regions of KSA reported a prevalence of 1.2-2.3%[14-18] similar to our figure of 1.6%. The mean age of their patients was 28.8-40.9 years. Our group of patients have a mean of 35 years which reflects the fact that all patients are in the reproductive age group. Kfoury[14] reported right side predominance with a ratio of 3:1, which was not observed in our study. Clinical confusion with

malignancy was also noticed in other studies from KSA.[14,16] The use of fine needle aspiration biopsy (FNA) in diagnosis of various breast lesions is well established and widely accepted. Cytological features have been previously described[19,20] and diagnosis of granulomatous inflammation can be successfully made. Such cases can subsequently be treated without unnecessary surgery. In one patient from our series, diagnosis was correctly made by FNA. Special stains and appropriate microbiological investigations are necessary to exclude infectious etiology. Fine needle aspiration diagnosis can alleviate unnecessary anxiety and doubts regarding the nature of the lesion especially when carcinoma is suspected. Additionally the therapeutic options will be expanded to include steroids,[9,21] which proved to be effective in such cases especially if we keep in mind the possible postoperative surgical complications.[5,22]

In conclusion, granulomatous mastitis, in our experience, is not unheard of. Clinicians should keep it in their list of differential diagnosis of breast lumps particularly in young pregnant or lactating women. It would be helpful to handle all breast specimens unfixed to the pathologists and for the latter to preserve samples for possible microbiological studies that should include bacteriological, mycological and mycobacterial cultures. The diagnosis is based upon the finding of granulomatous inflammation centered mainly around the lobules with negative results for mycological and mycobacterial organisms. Utility of fine needle aspiration biopsy as a diagnostic tool is to be considered particularly if conservative therapy, such as aspiration and drainage or steroids, is advocated.

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