Role of conservative therapy prior to surgery in xanthogranulomatous mastitis: a case report

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Background: Xanthogranulomatous mastitis is an extremely rare condition that is characterised by the infiltration of the breast parenchyma by foamy histiocytes. There have been only 26 reported cases amongst 10 publications. The clinical and radiological presentation of xanthogranulomatous mastitis often causes diagnostic confusion due to its similarity to breast cancer and other forms of chronic inflammatory mastitis. A histological diagnosis is often required either by core needle biopsy or excisional biopsy. Upon review of the literature, surgical excision was the most predominant mode of management.

Case Description: We present a case of xanthogranulomatous mastitis in a 40-year-old female who presented with clinical and radiological features of breast malignancy. This was a significantly large mass with a dimension of 90.7 mm by 36.4 mm, which if surgically excised, would have led to permanent cosmetic changes. Multiple core needle biopsies were completed to consider other differentials of histiocytic lesions including cystic neutrophilic granulomatous mastitis, histiocytoid lobular breast carcinoma, Rosai-Dorfman disease and Erdheim-Chester disease.

Conclusions: Clinical improvement was noted with reduction in size from prolonged antibiotic therapy suggesting an initial conservative approach in the management of xanthogranulomatous mastitis. By contributing our experience with xanthogranulomatous mastitis, we also present a review of literature on its aetiology, clinical features, and management of this pathology.

Keywords: Case report; xanthogranulomatous mastitis; chronic mastitis; breast cancer mimic

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Introduction

Xanthogranulomatous inflammation is a rare chronic inflammatory response that is predominantly detected in the gallbladder or kidneys. The involvement of the breasts is rarely reported due to a combination of low incidence, and the tendency to be clinically asymptomatic (1).

By reviewing the literature on xanthogranulomatous pyelonephritis (XGP) and cholecystitis (XGC), the aetiology of xanthogranulomatous inflammation has been suggested to be primarily obstruction and infection. Obstruction due to stones accounted for almost 85–90.7% of XGC (2,3) whilst majority of XGP cases also had obstruction due to stones or underlying infection (4). Infectious, haemorrhagic, and immunological aetiologies have also been implicated with xanthogranulomatous inflammation.

Despite successful management of xanthogranulomatous mastitis (XGM) with surgical excision with no incidences of recurrence to date (1), we describe a case of XGM with the largest documented dimension that would confer significant surgical risks. We share the details of how long-term antibiotics decreased the dimensions of the lesion suggesting a first-line role of conservative therapy prior to surgical excision in larger masses. We present the following case in accordance with the CARE reporting

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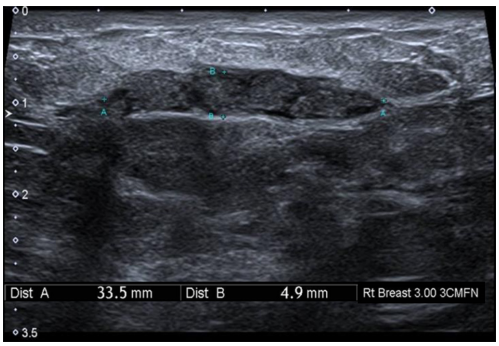

Figure 1 Ultrasound of the mass on first presentation showing scattered heterogenous focal mass measuring 34 mm × 5 mm × 26 mm reflecting dilated ducts containing debris. mm, millimetre.

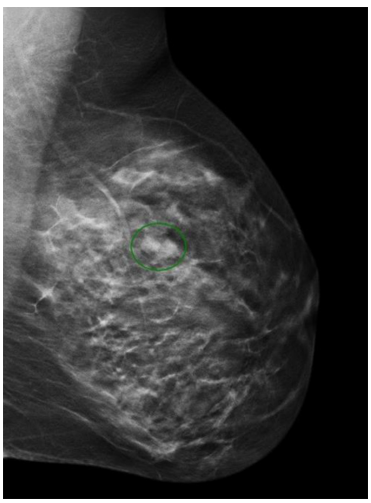

Figure 2 MLO view of the right breasts with density of BI-RADS category C. Asymmetrical density in the upper left breast but no definite mammographically suspicious lesions on the right breast. MLO, mediolateral-oblique; BI-RADS, Breast Imaging-Reporting and Data System.

checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-2022-52/rc).

Case presentation

A 40-year-old Caucasian female presented with self-detected lumps in both breasts. She denied symptoms of pain, nipple discharge or weight loss. She had a past medical history of schizophrenia, which was treated with paliperidone, and no history of trauma, implants, or previously diagnosed cancer. On examination, a palpable right-sided lump at 12 to 3 o'clock with nipple inversion and skin tethering was detected on C-cup sized breasts. Routine blood tests showed no lipid abnormalities.

Initial investigations included bilateral ultrasound (*Figure 1*) and mammography with tomosynthesis (*Figure 2*) which showed a left sided well-circumscribed lesion consistent with a fibroadenoma. The right sided mass correlated with a scattered heterogeneous focal region measuring 34 mm × 5 mm × 26 mm from 12 to 4 o'clock at 3 cm from the nipple with dilated ducts. Due to clinical and radiological suspicion of malignancy, magnetic resonance imaging of the breasts was done, showing two large areas of extensive ductal enhancement on the right breast suggestive of high-grade ductal carcinoma in situ (*Figure 3*).

Histological examination of the right breast mass was conducted with nine core needle biopsies (CNB), shown in *Figure 4A*. There was a mixed inflammatory infiltrate of neutrophils, lymphocytes and prominent foamy macrophages. A significant cystic component was not identified. No emperipolesis and no Touton giant cells were observed. No micro-organisms were identified on Gram, Ziehl-Neelsen or Periodic Acid Schiff-Diastase stains. Immunohistochemistry for AE1/AE3 highlighted only a few background acini and was negative within the abnormal tissue. The features were consistent with an active xanthogranulomatous mastitis.

An 8-week course of 100 mg oral doxycycline twice daily was trialled. A conservative approach was sought as there was no histological evidence of a malignant mass and surgical intervention would confer significant risk. Follow up CNB 4 weeks post-antibiotic therapy showed resolution of the xanthogranulomatous inflammation, and instead showed fibrosis and mild chronic inflammation with areas of fat necrosis as seen in *Figure 4B*.

Subsequent 6-weekly follow up reviews showed clinical improvement with reduction in size on palpation to approximately 3 cm × 3 cm from the 12 to 2 o'clock region. Follow-up ultrasound also revealed reduced size of the lesion but with persistent inflammatory changes as shown in *Figure 5A,5B*. On review of the literature, this was found to be the first case of XGM that demonstrated clinical improvement with conservative measures.

Ethical statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or

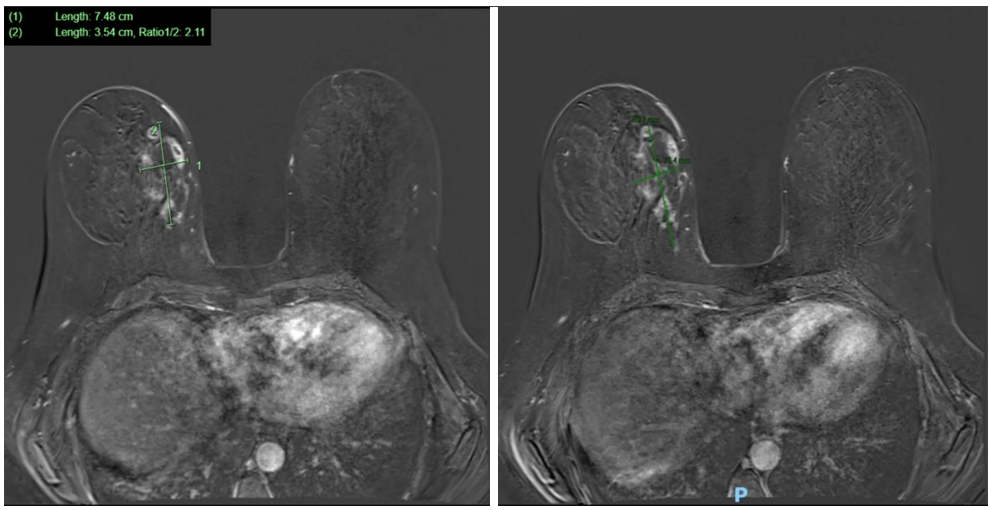

Figure 3 MRI showing extensive ductal enhancement on the right sided mass with maximal dimension of 90.7 mm × 36.4 mm spanning from 12 to 3 o'clock. MRI, magnetic resonance imaging; mm, millimetre.

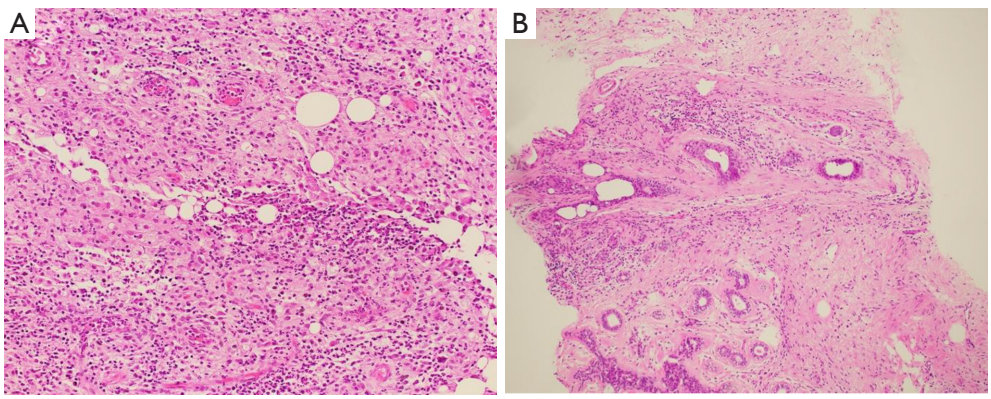

Figure 4 H&E stain of a core needle biopsy of the right breast before and after antibiotic treatment. (A) CNB showing XGM with no cystic component with ×100 magnification; (B) CNB 4 weeks post antibiotics showing mild chronic inflammation with no identifiable granulomata under ×40 magnification. H&E, haematoxylin and eosin; CNB, core needle biopsy; XGM, xanthogranulomatous mastitis.

national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

The aim of this report was to present an alternative treatment method for patients with XGM whilst providing a review of literature on this rare condition. Only 26 cases of XGM have been reported (*Table 1*) showing an epidemiological prevalence in younger Asian females with a mean age of 45 years. The pathology involves an inflammatory process characterised by the infiltration of foamy macrophages which is more commonly reported in the form of xanthogranulomatous pyelonephritis and xanthogranulomatous cholecystitis (1).

The trigger for XGM is not completely known although some papers have suggested a traumatic aetiology in the form of implant rupture or prolonged cutaneous scratching (5-7). By reviewing the literature on XGC and XGP, infectious and obstructive aetiologies to this inflammation have also been suggested (3,8). When reviewing previous

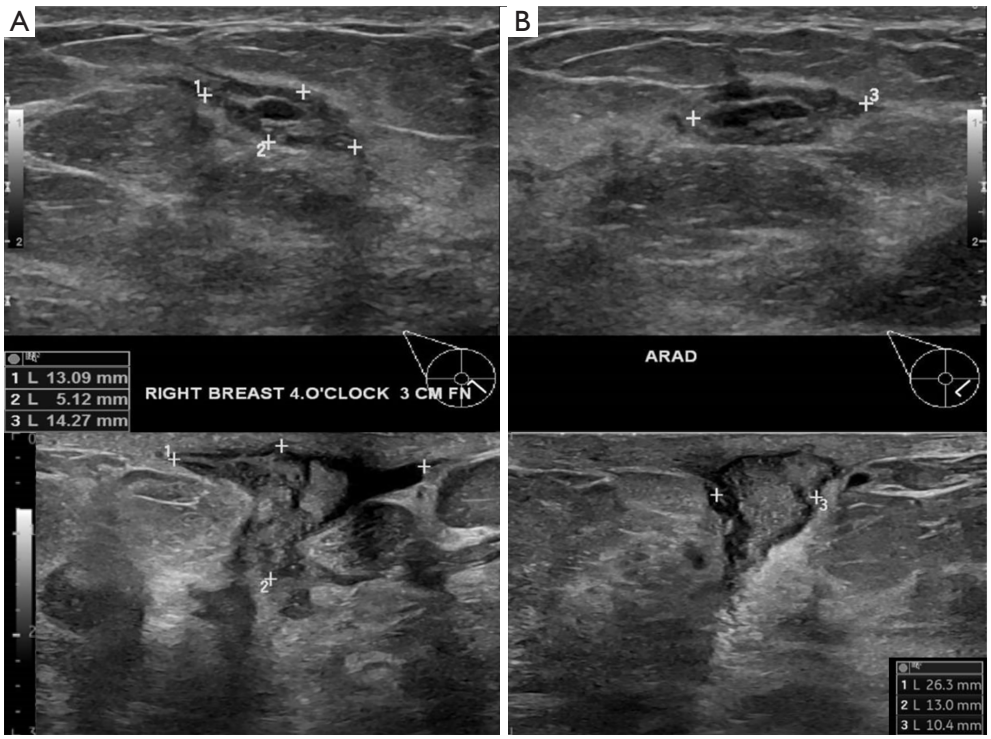

Figure 5 Series of follow-up US of the right breasts. (A) Ultrasound of the mass after 6 weeks of antibiotics demonstrating altered echogenicity of the breast parenchyma in the areas corresponding to the MRI; (B) ultrasound 2 weeks post cessation of antibiotic therapy showing persistent diffuse inflammatory changes. US; ultrasonography; MRI, magnetic resonance imaging.

XGM cases, a potential obstructive cause was found in three cases with co-existent malignant masses, however, this was not implicated in the remaining cases. Despite being characterised by foamy histiocytes, all cases have demonstrated no association to lipid abnormalities whilst stains for bacterial, fungal, and mycobacterial organisms were negative.

The major concern of XGM is its diagnostic challenge to differentiate it from breast malignancy both clinically and radiologically. Most cases of XGM (17/26) were asymptomatic with incidental findings on routine screening whilst a minority of cases presented with pain (4/26) or a palpable lump (5/26). Radiologically there is a tendency for XGM masses to mimic malignancy as in this case warranting a pathological diagnosis either by core or excisional biopsy.

The entity of cystic neutrophilic granulomatous mastitis (CNGM) should be considered as a differential diagnosis for this case. This entity is characterised by rounded clear spaces/vacuoles which are rimmed by neutrophils and epithelioid histiocytes. As a diagnostic feature, Gram positive bacilli should be seen within these spaces, or Corynebacterium species should be grown on culture. In retrospect a culture should have been performed to consider differentials like CNGM, however, due to the good response to antibiotics and classic histological features of XGM its results would have had minor clinical implications. Fat necrosis can show foamy histiocytes due to phagocytosis of necrotic adipocytes, but in this condition, adipose tissue is the predominant component, generally with prominent adipocyte necrosis and haemosiderin deposition, and a neutrophilic infiltrate is not a typical feature. Later stage lesions show variable fibrosis and calcification.

More sinister neoplastic conditions also need consideration. Histiocytoid lobular breast carcinoma has an abundant finely vacuolated cytoplasm that can mimic foamy macrophages, but would be positive for cytokeratins such as AE1/AE3. Histiocytic neoplasms such as Rosai-Dorfman disease (RDD) and Erdheim-Chester disease (ECD) are exceedingly rare in the breast. RDD features large eosinophilic histiocytes showing emperipolesis whereas ECD features foamy histiocytes with Touton giant cells with a sparse lymphoplasmacytic inflammatory infiltrate.

Table 1 Case publications

Study	Year	Case	Nationality	Age (years)	Presenting complaint	Location	Malignancy	Size (cm)	Mode of detection	Treatment
Kapoor *et al.*	2021	1	–	18	Pain	Right	None	2×1.1×1.8	US	–
		2	–	53	Asymptomatic	Left	None	0.8	US	–
Bamanikar *et al.*	2018	3	India	42	Pain	Left	None	3	MMG	Surgical
Leong *et al.*	2018	4	Singapore	41	Pain	Left	None	–	–	–
de Oliveira *et al.*	2017	5	Brazil	47	Pain, pruritus	Bilateral	None	R: 6.8×4.1, L: 4.2×3.0	US	Surgical
Dinets *et al.*	2016	6	Ukraine	30	Asymptomatic	Left	None	4×5	–	Surgical
Jyoti *et al.*	2013	7	India	19	Palpable mass	Unknown	None	–	–	Surgical
Hussain *et al.*	2012	8	UK	56	Palpable mass	Left	None	10	Px	Surgical
Koo and Jung	2009	9	Korea	42	Asymptomatic	Left	None	0.5	–	Surgical
		10	Korea	67	Asymptomatic	Right	None	1.3	–	Surgical
		11	Korea	44	Asymptomatic	Left	IDC	1.2	–	Surgical
		12	Korea	26	Palpable mass	Right	None	4.8	–	Surgical
		13	Korea	36	Asymptomatic	Left	None	1.8	–	Surgical
		14	Korea	36	Asymptomatic	Right	IDC	1.5	–	Surgical
		15	Korea	55	Asymptomatic	Left	None	0.5	–	Surgical
		16	Korea	37	Asymptomatic	Left	None	0.8	–	Surgical
		17	Korea	70	Palpable mass	Bilateral	None	3	–	Surgical
		18	Korea	53	Asymptomatic	Left	None	2	–	Surgical
		19	Korea	48	Asymptomatic	Right	DCIS	1.5	–	Surgical
		20	Korea	37	Asymptomatic	Right	None	1.5	–	Surgical
		21	Korea	47	Asymptomatic	Left	None	1.2	–	Surgical
		22	Korea	46	Asymptomatic	Left	None	1	–	Surgical
		23	Korea	44	Asymptomatic	Left	None	1.5	–	Surgical
		24	Korea	46	Asymptomatic	Right	None	1.2	–	Surgical
Hwang *et al.*	2007	25	Korea	60	Asymptomatic	Bilateral	None	R: 3, L: 3	MMG	Surgical
Shin *et al.*	2005	26	USA	74	Palpable mass	Right	None	2.2	–	Surgical

US, ultrasound; MMG, mammography; Px, physical examination; R, right; L, left; IDC, invasive ductal carcinoma; DCIS, ductal carcinoma in situ.

Other forms of chronic inflammatory mastitis such as granulomatous mastitis (GM) often causes diagnostic confusion to XGM amongst clinicians. GM is a chronic inflammatory mastitis characterized by the infiltration of the breast parenchyma by epithelioid histiocytes, multinucleated giant cells and polymorphonuclear leukocytes forming micro-abscesses. It is pathologically distinct to XGM with less predominance of foamy macrophages and tends to occur in young parous females with recent history of childbirth or breastfeeding (9). It is more prevalent within the Middle Eastern, Asian and Hispanic descents. With more documented cases in the literature than XGM, the etiology of GM has been attributed to hormonal factors like pregnancy and breastfeeding and infectious causes. Recently

an autoimmune etiology to GM has been becoming more popular due to its good response to steroids and immunosuppressive treatment, T-lymphocyte dominance in immunohistochemical studies and extramammary involvement such as erythema nodosum (10).

The use of antibiotics has been a popular approach during the earlier understanding of GM due to its association with the *Corynebacterium* species. Antibiotics that had lipophilic and bactericidal properties such as clindamycin were recommended to target these species that survived in lipid-filled vacuoles. Beta lactam was shown to have poor penetration of lipid and hence was not recommended in the treatment of GM (11). As the knowledge of GM is advancing with more publications, the autoimmune etiology of this condition is being favoured. Consequently, the role of antibiotic therapy has been controversial with some studies reporting little to no improvement with antibiotics (12) whilst other papers suggest high rates of complete resolution (13). Akcan *et al.* summarised that the role of antibiotic therapy is minimal unless there is an etiological or clinical indication such as by positive microbiological cultures, or co-existing abscesses, fistulas or chronic suppuration (14). The histological differentiation of chronic mastitis is therefore essential as the initial approach to the treatment of GM rarely involves the use of antibiotics.

Whilst more publications in the literature have been guiding clinicians in the management of GM, the treatment for XGM has not been well established with all previous cases been predominantly managed with surgical excision (1,5-8,15-18). Excisional biopsy may be diagnostic and therapeutic for small lesions, however, some surgeons may prefer a complete excision due to the suspicion of malignancy. The clinical improvement with antibiotics in this case suggest a conservative initial approach in the treatment of XGM. This was appropriate due to the size of the lesion and the absence of malignancy confirmed through multiple CNB. More data with successful response to antibiotics would be needed to validate a first line conservative approach minimising the risks of operation. The impact on physiological function such as lactating, cosmetic issues especially in younger females, along with infectious and anaesthetic risks that accompanies any operations are factors to consider in surgical management.

Cases with co-existent malignancy, patient preference for surgical removal, or small lesion suitable for an excisional biopsy may opt for an initial surgical approach. Larger XGM lesions with higher surgical risks may be approached conservatively with frequent monitoring for response with consideration of surgical excision if this fails.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-2022-52/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-2022-52/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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