Idiopathic granulomatous mastitis: a diagnostic dilemma

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Introduction

A 26-year-old Caucasian woman presented with a few weeks' history of right breast lumps and ulceration, with erythema nodosum of both legs. Radiological investigations raised the suspicion of inflammatory breast carcinoma. However, histology showed the presence of a non-caseating granulomatous lobulitis and excluded malignant features. Idiopathic granulomatous mastitis was diagnosed, after exclusion of other mimicking granulomatous conditions. This is extremely rare in Caucasian women. Prednisolone was used as the first-line treatment with no success. She was therefore started on methotrexate as a second-line treatment, which resulted in a significant clinical and radiological response.

Discussion

Idiopathic granulomatous mastitis is a rare benign inflammatory disease that usually affects the breast unilaterally. The annual incidence is 2.4/100 000 population, and it is extremely rare in Caucasians (Wolfrum et al, 2018) – published reports come mainly from the Middle East, Turkey and Asia. It has also been reported in men and in Hispanic women. The condition is linked to parity, lactation and smoking in premenopausal women. The development of erythema nodosum is a rare systemic manifestation of idiopathic granulomatous mastitis, which could be of autoimmune aetiology. Some authors suggested that the pathogenesis of erythema nodosum might be a type IV delayed hypersensitivity reaction to antigens (Hida et al, 2014; Al Manasra and Al-Hurani, 2016; Kalaycı et al, 2016; Fruchter et al, 2017; Gümüş et al, 2018).

Diagnosis is by exclusion because of the lack of pathognomonic clinical, radiological or histological features. The histological findings are usually multinucleated giant cell granulomas with large non-caseating lobulitis. Malignancy and other granulomatous

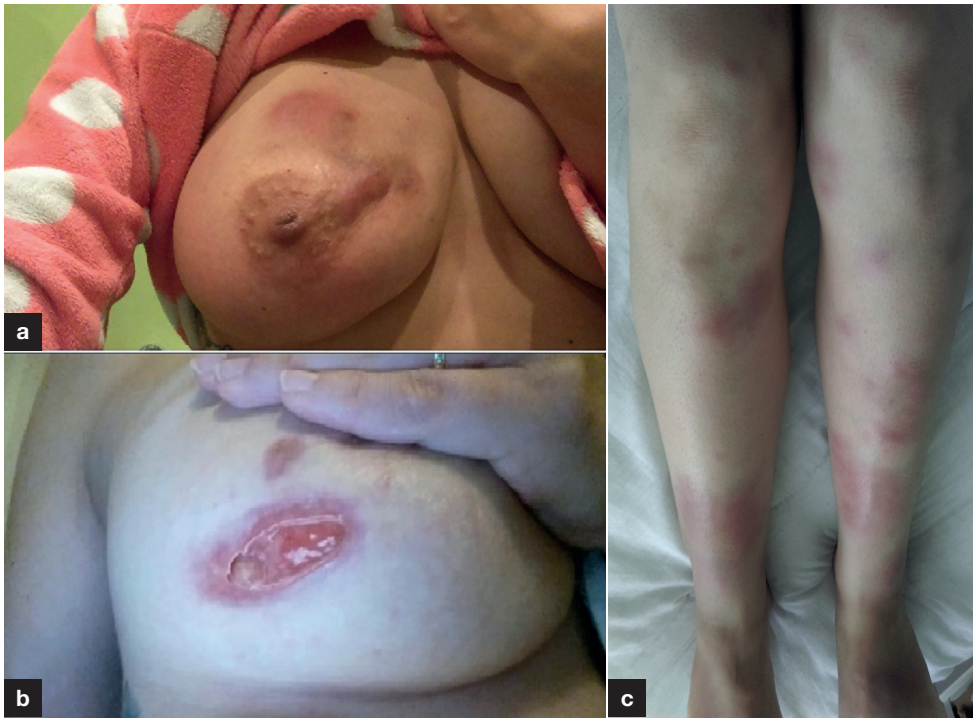

Figure 1. Pre-treatment images of the right breast demonstrating (a) swelling and patchy erythematous changes and (b) ulcerating region on the lower outer quadrant, with (c) erythema nodosum of both legs.

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conditions such as tuberculosis, sarcoidosis, connective tissue disorders and granulomatosis with polyangiitis have to be excluded.

Case Report

A 26-year-old Caucasian woman first presented to the breast clinic with a painful and swollen right breast, and tender nodules on both legs of 6–8 weeks' duration. She had been prescribed two courses of oral antibiotics in primary care in the last 3 weeks before her presentation to the breast clinic, which had no therapeutic effect.

The patient had no significant past medical or drug history and was a non-smoker. She had no relevant family history. She had two children; both had been breast-fed for a few weeks. The youngest child was around 18 months old when her symptoms started.

Clinically, her right breast was swollen and disfigured, with erythema of the overlying skin. Multiple hard and tender lumps of variable sizes were palpable in both the upper and lower inner quadrants, and there was ulceration at the outer lower quadrant. Examination of the left breast and both axillae was unremarkable. The only notable systemic sign was a clinically diagnosed erythema nodosum of both legs (Figure 1).

Magnetic resonance imaging with Dotarem contrast showed numerous enhancing cavitating and irregular solid foci, with areas of skin enhancement and thickening (Figure 2a). An ultrasound scan of the symptomatic breast showed extensive and complex hypoechoic changes spanning the central and inner parts of the breast (Figure 2b). Both ultrasound and magnetic resonance imaging confirmed the presence of a small fluid element associated with the thickened surrounding skin, raising a suspicion of inflammatory cancer. However, the lesion's core biopsy showed features of acute on chronic inflammation, non-caseating granulomas and foreign-body type multi-nucleated giant cells (Figure 2c). The breast tissue was stained with periodic acid–Schiff and Ziehl-Neelsen stains, excluding living fungal or mycobacterial infections respectively. Pustular fluid aspirated from the breast lesion had a high white cell count, with negative standard microbiology cultures and Gram stains. Prolonged anaerobic culture and mycobacteria microscopy were negative for acid-fast bacilli.

Because of the complex clinical, radiological and histological nature of the breast lesion, the case was closely managed at multidisciplinary level by the breast and rheumatology teams. Granulomatous conditions such as tuberculosis, sarcoidosis and vasculitis were excluded through a vast number of investigations, including chest X-ray, tuberculosis testing, immunological and vasculitis screening (eg anti-nuclear antibody screen, ACE, QuantiFERON-TB gold test, anti-neutrophil cytoplasmic antibody and anti-streptolysin-O (ASO) titre). All of these tests were negative, so the diagnosis of exclusion was idiopathic granulomatous mastitis. As per local policy, Grocott stain, Giemsa stain or C3 and C4 tests were not performed.

The patient was started on a 4-week course of oral prednisolone (20 mg daily), with no improvement. Treatment was switched to methotrexate (10 mg once a week) for 6 months. This resulted in a significant clinical improvement of the breast and the leg lesions. Thirty months after her initial presentation, the clinical and radiological signs had almost completely resolved (Figure 3). She was subsequently discharged from follow up.

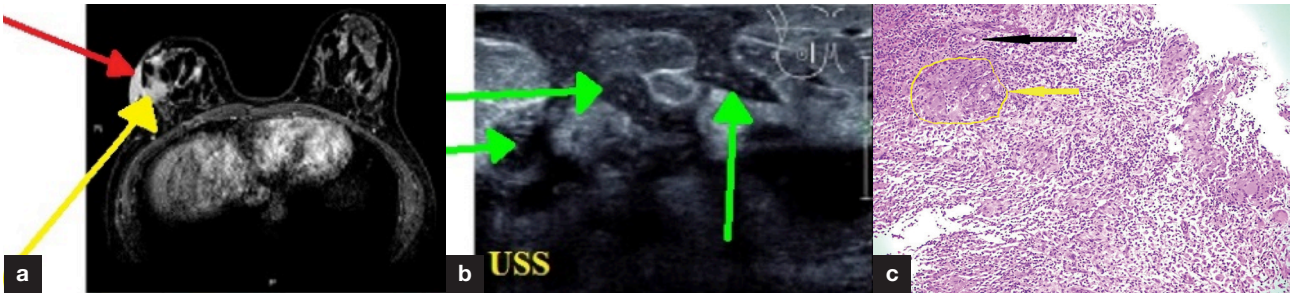

Figure 2. a. Magnetic resonance imaging with Dotarem contrast (T2 sequence) showing enhancing irregular mass in right breast (yellow arrow) with thickened and enhancing skin (red arrow). b. Ultrasound of the right breast demonstrating extensive hypoechoic changes (green arrows). c. Histology slide (magnification ×200, haematoxylin and eosin staining) showing non-caseating granuloma (yellow arrow) with multinucleate giant cells (black arrow).

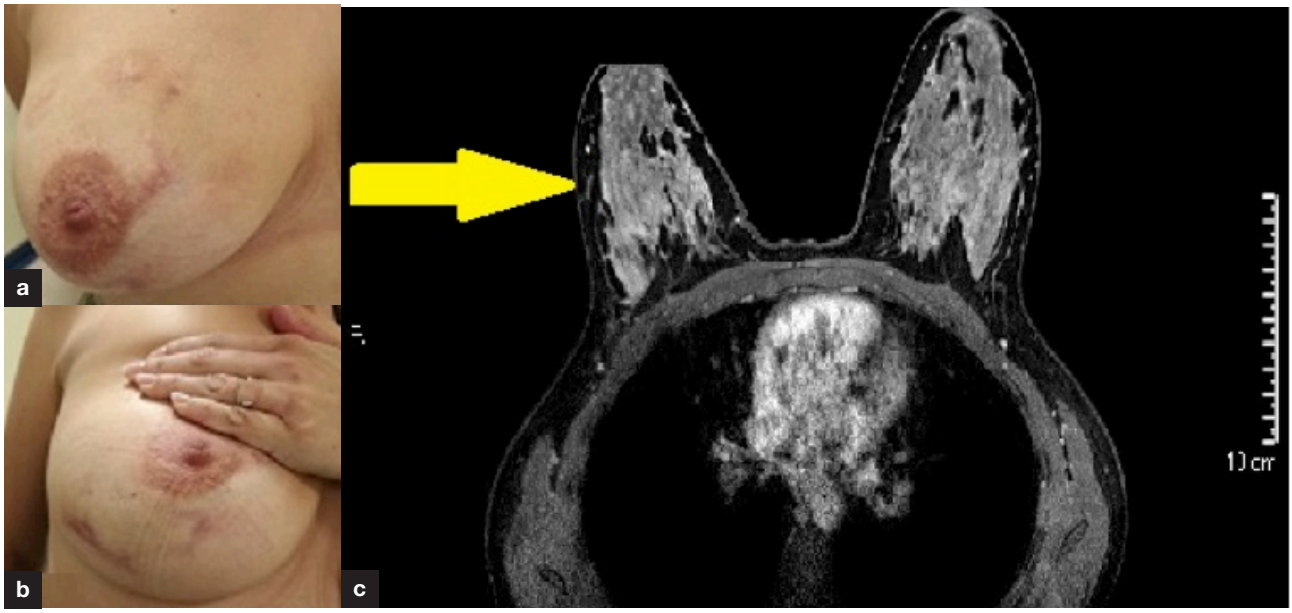

Figure 3. a and b. Post treatment clinical and (c) radiological normal right breast on magnetic resonance imaging – T2 sequence (yellow arrow).

A short course of low dose prednisolone is the usual first-line treatment, with reported success rates of around 50% (Freeman et al, 2017). Immunosuppressants like methotrexate are recommended as a second-line treatment (Wolfrum et al, 2018). A study compared oral corticosteroids and methotrexate for the primary management of idiopathic granulomatous mastitis and reported a higher recurrence rate in the steroid-only group compared to methotrexate alone or combined therapy (Akbulut et al, 2011). Surgery (simple mastectomy or lumpectomy), with additional corticosteroid therapy, is preserved for complex cases who fail medical therapy (Calis and Karabeyoglu, 2017).

Conclusions

This case report highlights a very unusual presentation of idiopathic granulomatous mastitis in a Caucasian woman who was a non-smoker. Idiopathic granulomatous mastitis is a diagnosis of exclusion after ruling out malignancy and other granulomatous conditions. The management plan should always include triple assessment (ie clinical, radiological and pathological assessments) at a multidisciplinary level.

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Learning points

- Idiopathic granulomatous mastitis is extremely rare in Caucasians.
- There are no pathognomonic clinical, radiological or histological findings of idiopathic granulomatous mastitis. Diagnosis is usually via exclusion of malignancy and other mimicking granulomatous conditions.
- A short course of oral prednisolone is the usual first-line treatment, with early escalation to immunosuppressants if there is an inadequate response. Surgery is limited to complex cases that do not respond to medical treatment.
- Management should always involve triple assessment at a multidisciplinary team level.

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