Case Report

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Idiopathic granulomatous mastitis with extramammary manifestations: a case report

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Introduction and Importance: Granulomatous mastitis is a rare inflammatory disorder of the breast, which can be either idiopathic or due to secondary etiology. This disease affects women of reproductive age. The exact pathophysiology underlying idiopathic granulomatous mastitis (IGM) remains unclear, but it is believed to be mediated by immunological processes. Establishing a diagnosis of this condition could be challenging due to the long list of differential diagnoses that it creates.

Case Presentation: We report a 24-year-old Syrian female presented to the clinic complaining of a 2-week history of fatigue, fever and chills, swelling, and localized pain in her left breast. Physical examination revealed erythema nodosum, episcleritis, and arthralgia in the wrists, ankles, and elbows. An excisional biopsy was done and a microscopic examination of the lesion confirmed granulomatous perilobular mastitis. Symptoms had resolved after the surgical excision and follow-up evaluation showed no signs of recurrence.

Clinical Discussion: IGM typically presents as an enlarging breast mass that can be mistaken for breast cancer or an abscess. The diagnostic approach should consider the presence of extramammary symptoms such as fever, arthralgia, and fatigue. Treatment options include corticosteroids, surgical excision, or steroid-sparing agents, but relapse rates vary.

Conclusions: Episcleritis should be considered as a potential extramammary manifestation in cases of IGM. We highlight the importance of recognizing and investigating the potential systemic involvement in patients with IGM. Accurate interpretation of pathological and radiological findings by a multidisciplinary breast team can facilitate the diagnosis and reduce unnecessary interventions.

Keywords: breast disease, episcleritis, erythema nodosum, idiopathic granulomatous mastitis, inflammatory disorders

Introduction

Granulomatous mastitis (GM) is a rare inflammatory condition of the breast of either idiopathic or secondary etiology. This disease typically affects non-White (Middle Eastern or Hispanic) women of reproductive age, with a mean age of 37 years[1]. Several factors have been identified as idiopathic granulomatous mastitis (IGM) risk factors, including reaction to chemicals such as oral contraceptive pills, infectious diseases, and autoimmune diseases in response to immunological stimuli due to milk flow in epithelial lobules[2,3]. GM is reported to be associated with polyarthritis and/or erythema nodosum (EN) as extramammary manifestations[4]. This particular presentation creates the need to exclude differential diagnoses such as sarcoidosis, granulomatosis with polyangiitis, and inflammatory bowel disease.

In this article, a young woman presented with fatigue, fever, localized swelling, and pain in her left breast with milky discharge. Further evaluation revealed episcleritis, arthralgia, and EN with elevated white blood cells (WBCs), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP). This case of GM which was associated with extramammary manifestation suggested a long list of differential diagnoses to be excluded.

HIGHLIGHTS

- Granulomatous mastitis is a rare inflammatory disorder that affects the breast in young to middle-aged women.
- Causes could be either idiopathic or secondary to drugs or infections.
- Potential extramammary manifestations of the disease include fever, arthralgia, erythema nodosum, and episcleritis.
- Characteristic findings on biopsy are perilobular mixed inflammatory infiltrate with central lipid vacuoles rimmed by neutrophils and an outer cuff of epithelioid histiocytes.
- Management may require surgery and/or corticosteroid use.
- A multidisciplinary breast team can facilitate the diagnosis and reduce unnecessary interventions.

Case report

A 24-year-old Syrian female presented to the clinic complaining of a 2-week history of swelling, erythema, fever and localized

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erythema, and pain in her left breast with milky discharge from her left nipple. The breast lesion initially appeared in the upper half of her breast and had, within 2 days, spread to her entire left breast. Her symptoms increased in intensity steadily. She reported tender, red nodules on both shins. The patient mentioned pain and redness in her right eye (Fig. 1). In addition, she had arthralgia affecting her ankles, wrists, and elbows. She also complained of pyrexia, chills, and fatigue. She was not taking oral contraceptives or any other medications. She had no history of taking immunosuppressive drugs or disorders indicating immunosuppression. The patient denied any recent breast trauma. She had two children and all her children were breast-fed. Her youngest child was 3 years old, and she had not been breast-feeding for 2 years.

On physical examination, the patient was febrile (body temperature was 38.3°C), and we noted a firm mass of 8 × 5 cm in the patient's upper medial portion of her left breast with erythema and mild retraction of the nipple.

Painful red nodules were found over both shins (Fig. 2), which was consistent with EN. Both ankle, wrist, and elbow joints were painful and warm, which demonstrated arthritis. No lymphadenopathy was observed. Ophthalmologic evaluation revealed redness of the right eye with mild pain and discomfort which was consistent with episcleritis. Visual acuity was 20/20. The remainder of her physical examination was normal.

These clinical features of fever, chills, and fatigue, along with physical findings of EN, arthritis, and episcleritis, suggested a differential diagnosis that necessitated several tests to rule out many systemic conditions. Laboratory blood test results demonstrated increased WBC count (Table 1) and elevated CRP and ESR (Table 2). Blood culture revealed no bacterial growth. No organisms were seen on Gram, periodic acid-Schiff, and Ziehl–Neelsen stainings. Acid-fast bacillus detection was negative, and culture results showed no bacterial growth after 72 h of incubation.

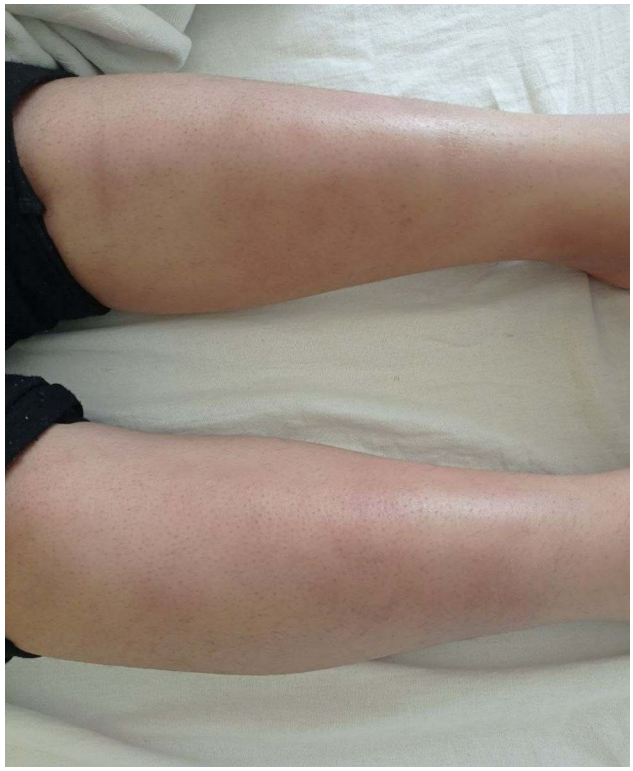

Figure 2. The figure demonstrates erythema nodosum on the anterior surface of the legs.

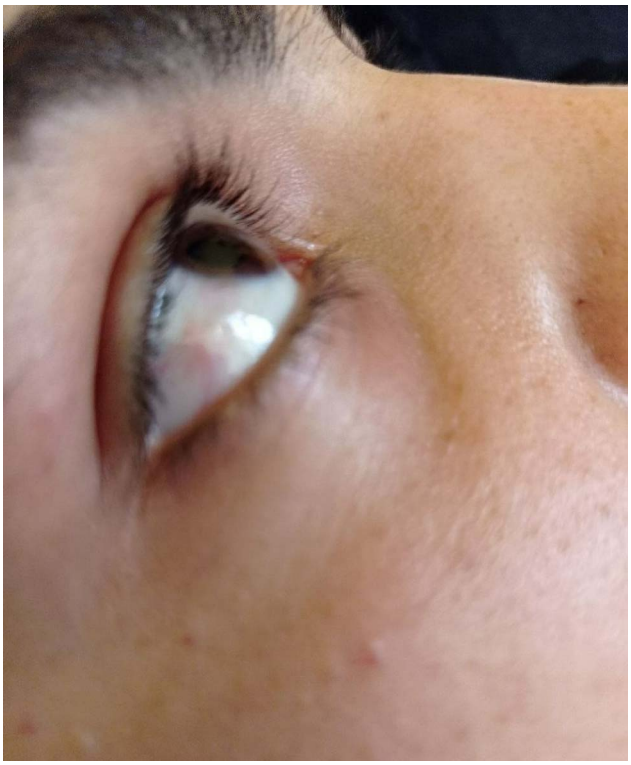

Figure 1. The figure demonstrates a unilateral redness in the right eye that indicates episcleritis.

The pregnancy test was negative. Chest radiography was unremarkable. High-resolution computerized tomography of the chest did not show any hilar or mediastinal densities, and angiotensin-converting enzyme was normal (Table 2), which made sarcoidosis unlikely. Tuberculin skin testing was negative. Culture for *Corynebacterium* was done to rule out cystic neutrophilic GM. HIV testing was negative. Hepatitis B and C serological titers were negative. An anti-streptolysin O test was done with normal results (Table 2), which ruled out streptococcus infection. Anti-nuclear antibody (ANA) was negative. Perinuclear anti-neutrophil cytoplasmic antibodies (p-ANCA) and anti-neutrophil cytoplasmic autoantibody (c-ANCA) were negative, which excluded vasculitis (Table 2).

Breast ultrasonography findings were initially suggestive of an abscess (Fig. 3) so vancomycin was administered on an empiric basis. However, no clinical improvement had been achieved with antibiotics.

Eventually, an excisional biopsy of the mass was done. Microscopic examination of the biopsy showed a perilobular mixed inflammatory infiltrate with central lipid vacuoles rimmed by neutrophils and an outer cuff of epithelioid histiocytes. No proliferative disease was noted. No vasculitis was noted. A diagnosis of granulomatous perilobular mastitis was established.

Table 1

Routine laboratory panel.

Laboratory test	Results	Reference range
WBCs	14.7	4.5–11.0 × 10^3/μl
Hemoglobin	8.2	12–14 g/dl
Platelets	312	150–400 × 10^3/μl
Sodium	140	135–148 mmol/l
Potassium	3.72	3.5–5.0 mmol/l
Urea	26	10–50 mg/dl
Creatinine	0.52	0.6–1.13 mg/dl
Glucose	103	70–100 mg/dl
AST	12	0–32 U/l
ALT	8	0–31 U/l
ALP	78	35–104 U/l

ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate aminotransferase; WBCs, white blood cells.

After the surgical excision of the mass, follow-up evaluation showed improvement in the breast, cutaneous, joints, and constitutional symptoms. No signs of recurrence were observed on long-term follow-up visits. The patient was initially prescribed prednisolone eye drops to relieve eye symptoms with spontaneous resolution of episcleritis weeks after the surgical excision.

Discussion

IGM was initially reported as a rare benign chronic inflammatory illness of the breast by Kessler and Wolloch in 1972. It is defined by the presence of noncaseating granulomas that are restricted to the breast lobules[5]. Although its precise pathophysiology is uncertain, it is believed to be immunologically mediated. Young, healthy parous women are usually affected by IGM, which is frequently linked to pregnancy and breastfeeding. IGM frequently progresses in a chronic, relapsing manner without a recognized standard of care[5].

It should be differentiated from other causes of chronic inflammatory breast diseases such as tuberculosis, Wegener's granulomatosis, sarcoidosis, fungal infection, duct ectasias, carcinoma, and fat necrosis, where again granulomas may be the presenting feature under the microscope[6].

The nature of extramammary manifestations of IGM, including inflammatory arthritis, arthralgias, and EN, is suggestive of an underlying immune process[7]. Episcleritis was concomitantly present in our case, distinguishing it from other IGM cases reported previously.

Table 2

Special laboratory tests.

Laboratory test	Results	Reference range
CRP	13.8	< 0.5 mg/dl
ESR	95	0–20 mm/h
ANA	Negative	
p-ANCA (anti-MPO)	Negative	
c-ANCA (anti-PR3)	Negative	
ASLO	43	(up to 200)
Angiotensin-converting enzyme (U/l)	34.7	(8–52)

ANA, anti-nuclear antibody; ASLO, anti-streptolysin O; c-ANCA, anti-neutrophil cytoplasmic autoantibody; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; MPO, myeloperoxidase; p-ANCA, perinuclear anti-neutrophil cytoplasmic antibodies; PR3, proteinase 3.

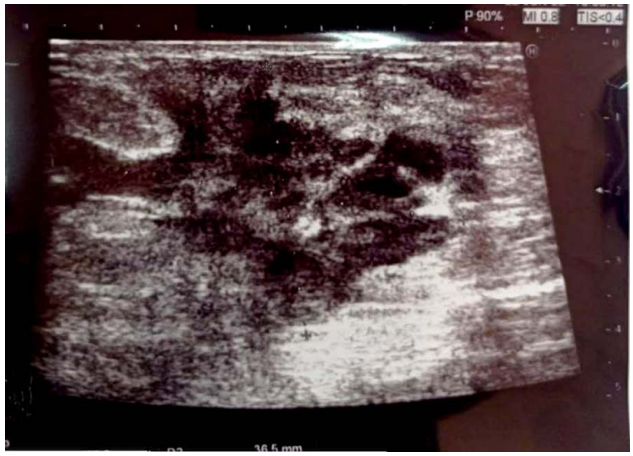

Figure 3. Ultrasound of the patient's left breast revealed a large, hypoechoic area with clear borders measuring ~38 × 57 69 mm with areas of internal vascularity.

Episcleritis is an inflammation of the episclera, which is a thin layer of tissue between the conjunctiva and sclera. It can affect one or both eyes. The majority of episcleritis cases are idiopathic, but up to 36% of patients have an associated systemic disease that could be responsible for the development of the condition. Some of these systemic diseases are rheumatoid arthritis, Crohn's disease, ulcerative colitis, psoriatic arthritis, systemic lupus erythematosus, reactive arthritis, relapsing polychondritis, ankylosing spondylitis, polyarteritis nodosa, Behcet's disease, Cogan syndrome, and granulomatosis with polyangiitis (which was formerly known as Wegener granulomatosis)[8].

IGM can be self-limited and resolve spontaneously in some patients. However, most patients require treatments such as corticosteroids or surgical excision. Its treatment remains controversial. Due to the severity and extent of the disease in some patients, surgical excision to achieve a healthy margin is not possible without severe breast deformity; therefore, surgical treatment can be limited to patients with limited involvement, those with corticosteroid side effects, or those resistant to other treatments. IGM can also mimic breast abscesses since the physical exam and radiological findings are similar[4].

Antibiotics have no role in the management of true cases of IGM[9]. The use of corticosteroids was first proposed by Dehetrogh *et al.*[10]. Several case series have reported the successful use of corticosteroids in the treatment of IGM[11].

Steroids should be started at a dose of 1 mg/kg per day and tapered slowly according to clinical response[12]. It may be necessary to continue high doses of steroids until the lesions completely resolve. Responses usually occur within weeks of the treatment, but some patients may need to be treated for several months[13].

Approximately half of the cases relapse after stopping or decreasing the dose of steroids. The use of steroid-sparing agents such as methotrexate or azathioprine provides options that may facilitate the tapering of steroids[14].

IGM can be treated by surgical excision of the mass, but some studies have suggested that the recurrence rate with surgical treatment is higher than that with steroid treatment[15]. Recurrence rates after surgical excision are reported to be ~5–50%[16].

Conclusions

What sets this case apart from others previously reported in the medical literature is the concomitant presence of episcleritis, in addition to the classic extramammary manifestations of IGM, such as EN and inflammatory arthritis. This combination of clinical features highlights the importance of recognizing and investigating the potential systemic involvement in patients with IGM. The management of IGM cases needs to be tailored according to the clinical presentation. Precise pathologic and radiologic data interpretation by a multidisciplinary breast team will facilitate the diagnosis and minimize unnecessary interventions.

Ethical approval

Not required.

Consent

Written informed consent was obtained from the patient. A copy of the written consent is available for review by the Editor in-Chief of this journal on request.

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Author contribution

S.A., S.H., and G.H.: involved in patient care and management, data collection, and wrote the main manuscript; M.S. and H.S.: participated in preparing the manuscript and prepared figures and tables; M.A.: participated in preparing the manuscript, revised, and submitted the final manuscript. All authors read and approved the final manuscript.

Conflicts of interest disclosure

There are no conflicts of interest.

Research registration unique identifying number (UIN)

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Data availability statement

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