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ORIGINAL ARTICLE

Granulomatous Mastitis With Erythema Nodosum: A Case Report

Eritema Nodosumlu Granülomatöz Mastit: Bir Olgu Sunumu

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ABSTRACT

Aim: Granulomatous mastitis is a benign inflammatory condition of the breast, typically of idiopathic origin. This case report aims to evaluate the diagnosis and management of granulomatous mastitis with erythema nodosum (GMEN), a rare manifestation, and to offer insight for clinicians encountering comparable cases.
Case: A 34-year-old woman presented with right breast swelling and chest pain persisting for two months. Physical examination demonstrated two palpable masses were detected in the lower outer quadrant of the right breast, along with increased temperature and tenderness. Moreover, several erythema nodosum lesions were noted on both lower extremities. Breast ultrasound demonstrated heterogeneity in the fatty tissue of the outer half of the right breast, with a significant increase in the ductal diameter (6.1 millimeters at its widest point) and dense content within the lumens, suggesting mastitis. On the seventh day of treatment with ciprofloxacin and teicoplanin, the masses in the breast fistulized to the skin, initially discharging tissue fluid, followed by ulceration. A Tru-cut breast biopsy was conducted on the affected area, revealing mixed inflammatory infiltrates consisting of neutrophils, lymphocytes, histiocytes, granulomatous formations, and giant cells, leading to a diagnosis of idiopathic granulomatous mastitis. After thorough evaluation for differential diagnoses, the patient was initiated on methylprednisolone and methotrexate. Following six months of treatment, the patient showed clinical improvement. Three months later, because of recurrence, the patient was followed up at an external center, where treatment with azathioprine and methylprednisolone was continued.
Conclusions: Idiopathic granulomatous mastitis is a diagnosis of exclusion, and thorough evaluation for other potential causes, particularly malignancy, is crucial. It is also possible to prevent unnecessary antibiotic use with suspicion of infectious mastitis by keeping it in mind in differential diagnoses. Early diagnosis is essential because of the requirement for prolonged treatment with immunosuppressive agents.

Keywords: Case report, erythema nodosum, granulomatous mastitis

ÖZ

Amaç: Granülomatöz mastit memenin iyi huylu inflamatuar lezyonlarından olup sıklıkla idiopatiktir. Bu vaka sunumunda nadir görülen eritema nodosumlu granülomatöz mastit (GMEN) tanısı ve tedavi sürecini gözden geçirerek benzer durumlarla karşılaşan klinisyenlere yardımcı olmayı amaçladık.
Olgu: 34 yaşında kadın hasta 2 aydır olan sağ memede şişlik ve göğüs ağrısı ile başvurdu. Fizik muayenede sağ meme alt dış kadranda ısı artışı ve hassasiyetin eşlik ettiği 2 adet ele gelen kitle palpe edildi. Her iki alt ekstremitede birkaç adet eritema nodosum mevcuttu. Meme ultrasonunda sağ meme dış yarısında yağlı dokuda heterojenite ve aynı seviyede duktuslarda belirgin çap artışı (en geniş yerinde 6.1 milimetre) olup lümen içi yoğun içerikli tespit edildi ve ön planda mastit şüpheliydi. Siprofloksasin ve teikoplanin tedavileri altında 7. günde memede kitle olan bölgeler cilde fistülize oldu, öncelikle doku sıvısı şeklinde akıntı ve ardından ülsere hale geldi. İlgili bölgeden Tru-cut meme biyopsisi alındı. Biyopsi materyalinde nötrofillerden zengin, lenfositler ve histiyositler içeren mikst iltihabi infiltrasyon, granülomatöz formasyonlar ve dev hücreler dikkati çekmiş olup idiopatik granülomatöz mastit düşünüldü. Ayrıcı tanılar açısından gereken değerlendirmeler ardından hastaya metilprednizolon ve metotreksat tedavileri başlandı. 6 aylık tedavi sonunda klinik olarak fayda gören hastanın 3 ay sonra nüks nedeniyle dış merkezde takibe alındığı ve azatiopürin ve metilprednizolon ile tedavi ve takiplerinin devam ettiği öğrenildi.
Sonuçlar: İdiopatik granülomatöz mastit ekartasyon tanısı olup başta malignite olmak üzere diğer olası etiyolojiler açısından doğru değerlendirmelerin yapılması hayati öneme sahiptir. Ayrıcı tanılarda akla gelmesi sayesinde enfeksiyöz mastit şüphesi ile gereksiz antibiyotik kullanımının da önüne geçilmesi mümkündür. Tedavisinin uzun süreli ve immünsüpresif ajanlarla yapılması nedeniyle tanı konulması önemlidir.

Anahtar kelimeler: Eritema Nodosum, granülomatöz mastit, Vaka sunumu

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Introduction

Granulomatous mastitis is a benign inflammatory condition of the breast, most commonly seen in women of childbearing age, particularly during pregnancy and lactation [1]. Although granulomatous mastitis is typically classified as idiopathic, potential etiologic factors may include infectious agents, autoimmune mechanisms, hormonal imbalances, and trauma [2]. It is important to consider granulomatous mastitis in the differential diagnosis, particularly because of its similarity to malignant lesions, and a biopsy is necessary for definitive diagnosis [3]. Diagnostic challenges can result in unnecessary surgical interventions, potentially leading to unfavorable outcomes such as prolonged antibiotic use [4].

This case report aims to review the diagnosis and management of granulomatous mastitis with erythema nodosum (GMEN), a rare condition, in a 34-year-old woman, and to provide guidance for clinicians encountering similar cases.

Case presentation

A 34-year-old woman presented with right breast swelling and chest pain that had been ongoing for two months. She also reported fever and diffuse joint pain over the past two weeks. Her medical history was unremarkable, with no comorbidities, no prior pregnancies, or recent breastfeeding (she had last breastfed one year ago). There was no history of breast trauma, contact with tuberculosis, or a family history of malignancy. At the onset of her symptoms, she had been treated with amoxicillin/clavulanate and ciprofloxacin for 14 days, without any clinical improvement

Physical examination demonstrated, two palpable masses were identified in the lower outer quadrant of the right breast, accompanied by increased warmth and tenderness. Palpable lymphadenopathy was noted in the right axillary region, but no nipple discharge was present. Moreover, numerous erythema nodosum lesions were noted on both lower extremities (Figure 1).

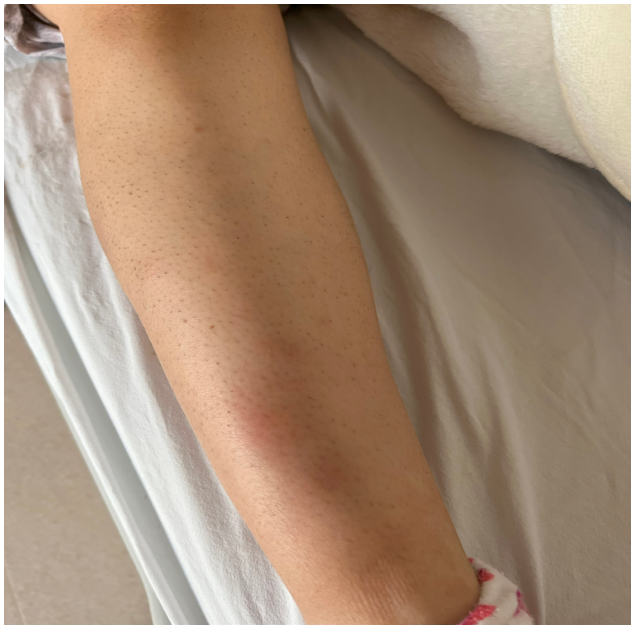

Figure 1. Erythema nodosum on the leg

In light of the presenting symptoms and clinical findings, a breast ultrasound was conducted. The ultrasound demonstrated heterogeneity in the fatty tissue of the outer half of the right breast, along with a significant increase in ductal diameter (6.1 millimeters at its widest point) and dense content within the lumens, suggesting mastitis (BIRADS category 3: Probably benign and shorter interval follow-up should be performed to determine stability. The risk of malignancy is less than 2% (5)). No abscess formation was noted. Moreover, a 25x13 millimeter (mm) reactive lymph node was noted in the right axilla. The results of the investigations performed upon admission are summarized in Table 1.

Table 1: Examinations performed on admission

Parameters	Value
Leukocyte (/μL)	14520
Neutrophil (/μL)	11180
Lymphocyte (/μL)	2210
Platelet (x10^3/μL)	479
Hemoglobin (g/dL)	14.1
C-reactive protein (mg/dL)	83
Erythrocyte sedimentation rate (mm/hour)	53
Antistreptolysin O (IU/mL)	648
Rheumatoid factor (U/mL)	10.4
Rose Bengal test	Negative
Brucella tube agglutination	Negative
HbsAg antibody	0.16 (Negative)
Anti HIV antibody	0.08 (Negative)
Anti HCV antibody	0.06 (Negative)
Blood culture	No growth detected
Tuberculin skin test (mm)	0
Angiotensin-converting enzyme (μg/L)	5
HLA B27 gene test	Negative
ANA (Index)	0.32 (Negative)
Anti-CCP antibody (IU/mL)	16.7 (Negative)
Anti Cardiolipin IgM antibody (MPL-U/mL)	1.07 (Negative)
Anti Kardiyolipin IgG antibody (GPL-U/mL)	1.05 (Negative)
Anti SSA antibody (IU/mL)	2.56 (Negative)
Anti SSB antibody (IU/mL)	0.68 (Negative)
PR3 ANCA antibody (U/mL)	2.88 (Negative)
MPO ANCA antibody (U/mL)	0.6 (Negative)
Anti ds DNA antibody (U/mL)	2.5 (Negative)
Anti Histon antibody (IU/mL)	2.6 (Negative)
Anti Sm/RNP antibody (U/mL)	1.6 (Negative)
Anti-centromere antibody (U/mL)	0.8 (Negative)
Anti Scl-70 antibody (IU/mL)	3.7 (Negative)
Anti Jo-1 antibody (IU/mL)	2.4 (Negative)

The patient was admitted to the hospital and intravenous (i.v.) treatment was initiated with ciprofloxacin 400 mg twice daily and teicoplanin 400 mg twice daily as a loading dose, followed by 400 mg once

daily for maintenance. A blood culture was obtained prior to starting antibiotic therapy. Nonsteroidal anti-inflammatory drugs (NSAIDs) were administered concurrently. On the seventh day of treatment, the mass areas in the breast fistulized to the skin, initially discharging tissue fluid, followed by ulceration. A Trucut breast biopsy was conducted on the affected area, and aspirate samples from the discharge site were obtained. Both Gram staining and cultures were negative. Dermatology consultation led to the addition of topical mupirocin for the ulcerated wound and topical clobetasol for the erythema nodosum lesions. After a total of 10 days of i.v. antibiotic therapy and symptomatic treatment, the patient was discharged with instructions for biopsy follow-up. The biopsy demonstrated mixed inflammatory infiltration, lobulocentric inflammation, granulomatous formations, and giant cells, rich in neutrophils, lymphocytes, and histiocytes, suggesting idiopathic granulomatous mastitis. Acid-resistant bacillus (ARB) staining was negative, and Mycobacterium tuberculosis polymerase chain reaction (PCR) was also negative in the biopsy sample. Based on the biopsy results and differential diagnoses, the patient was diagnosed with idiopathic granulomatous mastitis, with input from the rheumatology team. During follow-up, absence of growth of M. tuberculosis was detected in the biopsy culture.

Following the diagnosis, the patient was initiated on methylprednisolone 16 mg daily and methotrexate 15 mg once a week. After six months of treatment, a follow-up breast ultrasound demonstrated a 19x12 mm hypoechoic area at the 8 o'clock position in the right breast, which was interpreted as a sequela of mastitis (BIRADS category 3). No enlarged lymph nodes were found in the axillary region. After the six-month treatment period, rheumatology discontinued the patient's treatment because of the resolution of her symptoms, full compliance with the regimen, and the absence of side effects. The erythema nodosum lesions also revealed regression. Three months later, the patient was assessed for recurrence and was subsequently managed with azathioprine and methylprednisolone at an external center. Her follow-up care is still persistent.

Discussion

Idiopathic granulomatous mastitis is a benign, chronic, and rare breast condition. It has an annual prevalence of 2.4 cases per 100,000 individuals and an incidence rate of 0.37 [6]. Most cases occur in individuals in their thirties with a history of pregnancy or breastfeeding within the past five years. The lesions are typically unilateral, located outside the areola, and may fistulize, form microabscesses, or ulcerate. Non-specific symptoms, such as fever and malaise, are commonly observed. A reactive lymph node is present in approximately 28% of cases [7–9]. Rarely, erythema nodosum may accompany [10]. Our patient was a 34-year-old woman with a lesion in the right breast, accompanied by a reactive lymph node on the same side, and a history of breastfeeding one year prior. During follow-up, the lesion fistulized to the skin, leading to the development of an ulcerated area. Erythema nodosum was noted in both lower extremities.

The exact pathogenesis of granulomatous mastitis remains unclear. However, the favorable response to corticosteroid therapy in some patients, along with the co-occurrence of erythema nodosum and other autoimmune conditions, supports the prevailing hypothesis that it is an autoimmune disorder [11]. It is proposed that elevated levels of circulating immune cells contribute to the development of septal panniculitis in the subcutaneous tissue, particularly in the pretibial region, thereby leading to erythema nodosum [12].

During the diagnostic process, breast ultrasound may reveal lobulated, heterogeneous hypoechoic masses; however, these findings are non-specific [13]. The gold standard method for diagnosis is biopsy. Since breast cancer is part of the differential diagnosis, biopsy is essential. Histologically, it is characterized by multinucleated giant cells, lymphocytes, plasma cells, non-caseating granulomas confined to the breast lobules, and negative ARB staining [14]. In our case, the biopsy findings were consistent with idiopathic granulomatous mastitis.

It is typically a diagnosis of exclusion, and potential underlying causes should be investigated and ruled out first. These include tuberculosis, breast cancer, and sarcoidosis [6]. Tuberculous mastitis exhibits clinical, radiologic, and even histologic features that are similar to those of granulomatous mastitis [15, 16]. Histologically, tuberculous mastitis is characterized by epithelioid cells, caseating granulomas, and positive ARB staining [14]. The histology of breast carcinoma is characterized by the presence of malignant epithelial cells [17]. In our case, the diagnosis of tuberculosis was excluded based on negative ARB staining, M. tuberculosis PCR, and culture results in the biopsy material. Malignancy was ruled out through the biopsy findings. Autoimmune etiologies were excluded as the tests for autoimmune diseases returned negative results. Sarcoidosis was ruled out because of the absence of pulmonary symptoms and a normal angiotensin-converting enzyme (ACE) level. Potential infectious causes were excluded with negative anti-HIV tests, aspirate culture, and blood culture results.

Definitive treatment strategies for idiopathic granulomatous mastitis have not yet been established. Current management options include antibiotics, non-steroidal anti-inflammatory drugs, corticosteroids, methotrexate, azathioprine, and surgical interventions. The treatment outcome remains uncertain, with potential for both remission and recurrence [9]. Relapse rates have been reported as high as 5-78% [18, 19]. Velidedeoğlu et al. reported that the presence of erythema nodosum was associated with higher rates of fistula formation and disease recurrence [20]. Similarly, Liu et al. demonstrated that the presence of abscess and sinus significantly increased the likelihood of chronic disease and relapse [21]. In the present case, both erythema nodosum and fistula formation were observed concurrently. It is noteworthy that our case experienced a recurrence following approximately six months of immunosuppressive treatment.

Conclusion

In conclusion, idiopathic granulomatous mastitis is a diagnosis of exclusion, and thorough evaluation of other potential etiologies, particularly malignancy, is essential. A biopsy is necessary for a definitive diagnosis. Considering this condition in the differential diagnosis can help prevent unnecessary antibiotic use when infectious mastitis is suspected. Timely diagnosis is crucial because of the need for long-term treatment with immunosuppressive agents.

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Informed consent was obtained from the patient shared in the case presentation.

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