

Granulomatous Mastitis in a Systemic Lupus Erythematosus Patient: Case Report

Lais Zanlorenzi^{2*}; Nelzi Ferreira de Queiroz Junior¹; Thiago Alberto Fernandes Gomes dos Santos²; Barbara Stadler Kahlow²; Thelma Larocca Skare²

¹Resident of Rheumatology, Service of Hospital, Mackenzie Evangelical University (HUEM), Brazil.

²Professor and Doctor of Rheumatology, Service of Hospital, Mackenzie Evangelical University (HUEM), Brazil.

Corresponding Author: Laís Zanlorenzi

Professor and Doctor of Rheumatology, Service of Hospital, Mackenzie Evangelical University (HUEM), Brazil.

Email: laiszn@gmail.com

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Abstract

Granulomatous Mastitis (GM) is an uncommon form of mastitis frequently associated with autoimmune diseases. This entity requires a differential diagnosis with breast tumor and infections and may be treated with glucocorticoids and methotrexate. We report a case of GM in a patient with systemic lupus erythematosus already using high doses of prednisone and immunosuppressants that responded to the use of doxycycline. Some pathophysiological, histological and treatment aspects are discussed.

Keywords: Granulomatous mastitis; Systemic lupus erythematosus; Glucocorticoid, Antibiotics.

Introduction

Granulomatous Mastitis (GM) is considered a subtype of autoimmune mastitis that may present as a diagnostic challenge [1]. This entity is defined by its histological pattern that shows lobulocentric non-necrotizing granulomas, and epithelioid histiocytes and should be differentiated from infectious and neoplastic breast lesions [1]. Local inflammation induces the infiltration of immunocompetent cells to react with delayed-type hypersensitivity forming the granulomatous structure [2]. The concomitance of GM with other autoimmune disease seems to have prognostic value; according to Basim et al. [3]. The association with rheumatic diseases increases 4.5 times the risk of recurrence. Even in the cases which the GM appears isolated, the presence of arthralgias, erythema nodosum [4,6] and circulating autoantibodies such as antinuclear antibodies and rheumatoid factor are found, highlighting the underlying autoimmune nature [7]. Herein we describe a case of GM associated with Systemic Lupus Erythematosus (SLE) that offered treatment difficulties but finally answered to the use of thalidomide and doxycycline.

Case description

A 27 years old female was diagnosed having Systemic Lupus Erythematosus (SLE) based on presence of recurrent fever, photosensitive rash, non-cicatricial alopecia, vasculitis in the fingers, thrombocytopenia, positive antinuclear antibodies, anti-Sm and anti-dsDNA. She was treated with antimalarials and high dose glucocorticoid followed by mophetyl mycophenolate. She had no history of abortions and have had one child in 2018; she was using Intramuscular medroxyprogesterone since then. In November 2021, while on 60 mg of prednisone/day, hydroxychloroquine 400 mg/day and 3 g/day of mycophenolate, she noticed a breast lump (Figures 1 and 2). Mammography and thorax MRI suggested a BIRADS 4 lesion, with no pulmonary findings. A core biopsy was performed and showed chronic granulomatous mastitis. The material was negative for acid fast bacilli and cultures also negatives. ANCA-c and p, IGRA (Interferon Gamma Release Assay) and ACE (Angiotensin I-Converting Enzyme) were negative. Prolactin level was normal (<10 ng/mL). As the patient was already using prednisone and mycophenolate, an attempted treatment with thalidomide was

done. After 2 months of thalidomide use, some improvement was noted: the lesions seem softer, less painful and slightly smaller and paler. A biopsy review was done and the presence of some cystic spaces filled with neutrophils associated to the granulomas came into attention, reclassifying the lesion as cystic neutrophilic granulomatous mastitis, with *Corynebacterium* species possibly correlated. Long-term doxycycline was added with constant improvement until now.



Figure 1: Initial breast lump.



Figure 2: Evolution before treatment.

Discussion

The present case has at least some peculiarities that need to be noted. The first one was the association with SLE. When a patient with SLE presents with mammary involvement the first diagnosis to be excluded is lupus panniculitis also known as lupus profundus [8]. This is a predominantly lobular panniculitis with a dense lymphoplasmacytic infiltration of lobules and hyaline fat necrosis that usually occurs in patients with a previous diagnosis of systemic or discoid lupus but that can also be the initial presentation of the disease [8]. Histological examination and the presence of overlying discoid skin lesions are some aspects used for differentiation between lupus panniculitis and GM [9,10]. A second interesting observation is that GM has been frequently described in patients with high levels of prolactin. [11]. GM has been associated to prolactinomas [12], high levels of prolactin due to anti-psychotic drugs use [11] and in breastfeeding women [12]. Nikolaev et al. [13]. Described four cases of prolactin secreting tumor in patients with GM that had a complete resolution along with normalization of prolactin levels. Thus, abnormal levels of this hormone may be implicated in the physiopathology of GM. The prolactin has hormonal and a cyto-

kine functional roles; it affects the immune system modulation preventing the negative selection of autoreactive B lymphocytes [14]. Moreover, high prolactin levels have been described in relation to the pathogenesis and activity of several autoimmune disorders, among them, the SLE [14]. Nevertheless, this was not the present case in which prolactin levels were normal. A third interesting observation is about patient's clinical response to treatment. Because its autoimmune background, glucocorticoids and methotrexate have been proposed as first line treatment [2,15]. The patient described presently was already using glucocorticoid and immunosuppressants for SLE treatment when she developed the GM. So, an attempted use of thalidomide was done. The rationality for using thalidomide was grounded in the presence of granulomas in which TNF-alpha is essential for the orderly enrolment of cells. Thalidomide has immunomodulatory properties; amid them, the suppression of TNF alpha effects [16]. In the described case, despite some improvement observed with thalidomide use, the response was considered very modest and doxycycline was added. More recently, the presence of *Corynebacteria*, especially *Corynebacterium kroppenstedtii*, has been implicated in the appearance of GM [2]. These microorganisms have been identified locally by culture and RNA gene sequencing and, according to some authors, they mark a subtype of GM called Cystic Neutrophilic Granulomatous Mastitis (CNGM) [2,17]. The CNGM has a peculiarity from histological point of view: it has vacuoles filled with neutrophils concomitant with the granulomas [2,18]. The role of *Corynebacteria* in this context is not clear. This microorganism is part of normal skin flora and their presence may be just the result of colonization [2]. Moreover, there is also the possibility that this bacteria offers an independent immunogenic factor or that is causing a secondary infection in a tissue with decreased local immune resistance, as an epiphenomenon [2]. Despite this uncertainty, the identification of *Corinebacterium* should lead to antibiotic use [2]. No microorganism has grown in the cultures of the presently described patient, nevertheless in the review of biopsy findings, some cystic spaces were detected suggesting CNGM and grounding the antibiotic use. Finally, the authors would like to bring to attention the association of GM with other autoimmune diseases. The knowledge of this association will help clinicians who cares for these patients to readily recognized and treat this disease.

Declarations

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