BRIEF ARTICLES

Granulomatous Mastitis as a Presentation of Sarcoidosis

Andrea D. Maderal MD[a], Daniel G. Federman MD[b], Robert S. Kirsner MD, PhD[a]

[a]University of Miami Miller School of Medicine, Miami, FL
[b]VA Connecticut Healthcare System and Yale University School of Medicine, West Haven, CT

ABSTRACT

Sarcoidosis is an idiopathic inflammatory disease characterized by granuloma formation in various tissues, most commonly the lungs, lymphatics, skin and eyes. Involvement of the breast in sarcoidosis is rare, and can be defined into three subsets, including granulomas localized to the breast, referred to as breast sarcoidosis. Breast sarcoidosis may present with systemic findings such as erythema nodosum, arthritis, and uveitis, and unlike typical sarcoidosis, commonly manifests during pregnancy. In this report, we present a rare case of breast sarcoidosis presenting in a pregnant female with associated erythema nodosum, arthralgias and ocular complaints.

CASE REPORT

A 31-year-old African-American woman, G3P2002, presented 26 weeks pregnant to her Obstetrician with a painful, red tumor in her right breast. A breast ultrasound did not show any drainable collection; she was diagnosed with mastitis and treated with dicloxacillin for 2 weeks. One month later, she was seen at an outside hospital with new onset weakness, arthralgias and myalgias, so severe that she needed a walker for ambulation. She received systemic intravenous antibiotics with cefazolin and oseltamivir. During her hospitalization, she developed red tender nodules on both legs and forearms, as well as redness and discomfort in her right eye. She also had a mild non-productive cough but denied fevers, chills, oral ulcers, dry mouth, shortness of breath, hemoptysis, chest pain, gastrointestinal symptoms or hematuria. She was otherwise in good health. Her only medications included prenatal vitamins. There was no family history of autoimmune disease or sarcoidosis. She denied any recent travel.

On physical examination, she was afebrile but tachycardic with heart rate ranging from 110-120. Her lungs were clear to auscultation, and there was non-pitting edema of her legs to the knees. She did not have joint redness, tenderness or swelling and muscle strength was normal. On skin examination, she had a 5 x 13 cm indurated mass in her right breast with associated tender, rubbery lymphadenopathy in the right axilla, (Fig. 1) as well as red tender subcutaneous nodules on her anterior legs (Fig. 2) and forearms.

She had a normal complete blood count (CBC) and complete metabolic profile (CMP). Her C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were highly elevated at 19.6 and 100, respectively. Quantiferon gold was negative and angiotensin converting enzyme (ACE) level was normal. Further infectious and autoimmune serologies were negative and she had an anti-nuclear antibody (ANA) of 1:40. Chest radiograph (CXR) did not show consolidation or lymphadenopathy. Breast ultrasound and mammogram showed BIRADS 3 (probably benign), likely from an inflammatory process. Breast biopsy showed non-caseating granulomas. (Fig. 3) Swab and tissue cultures for bacterial, fungal and mycobacterial organisms were negative.

The patient was diagnosed with sarcoidosis with a presentation of erythema nodosum, arthralgias, granulomatous mastitis and ocular complaints (ophthalmology had not been consulted at the time of presentation). Treatment with prednisone 20 mg daily resulted in complete resolution of erythema nodosum lesions, ocular complaints, and arthralgias, and significant reduction in the breast mass. Post-uncomplicated delivery, computed tomography (CT) of the chest and electrocardiogram (EKG) were within normal limits, and the patient's symptoms were well maintained on prednisone 10 mg daily.

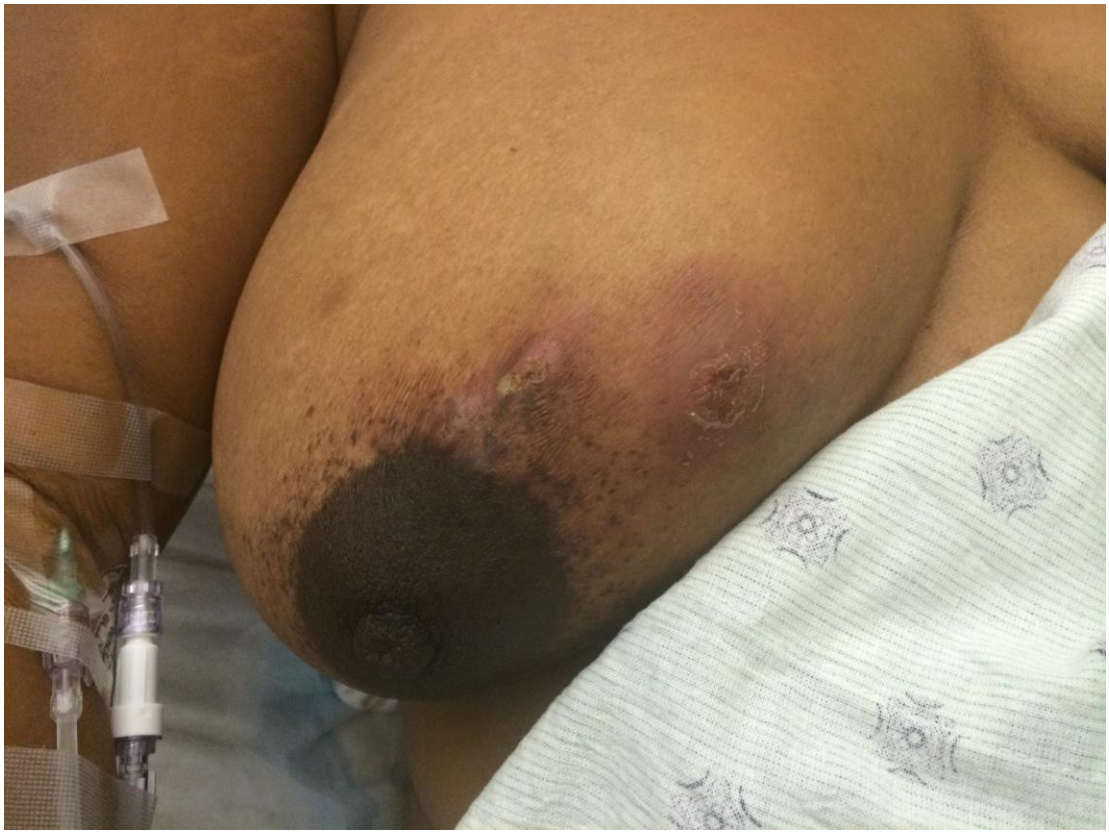

Figure 1. Red to violaceous ulcerated plaques on the right breast.

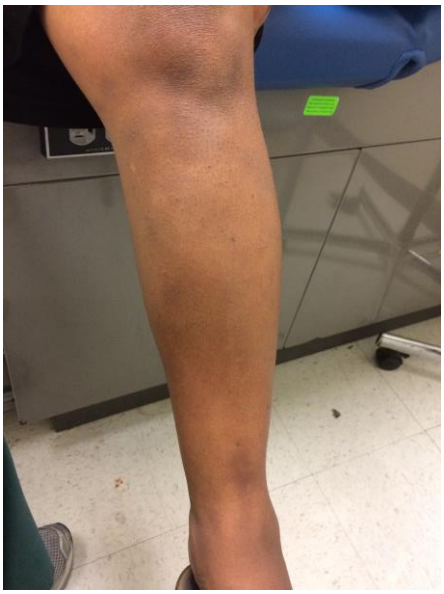

Figure 2. Red subcutaneous nodules on the anterior leg.

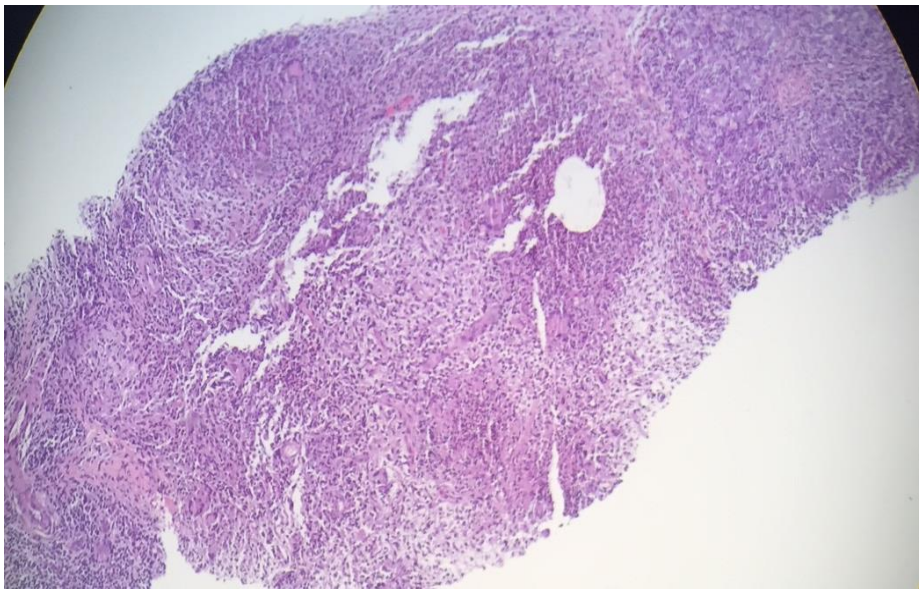

Figure 3. Histopathologic specimen taken from the breast revealing non-caseating granulomas.

DISCUSSION

This patient presented with breast involvement of sarcoidosis, which is rare. Breast involvement in sarcoidosis is classified into three categories: sarcoidosis patients with breast cancer, breast cancer patients showing sarcoidosis-like breast reactions, and sarcoidosis patients with breast granulomas, which is referred to as breast sarcoidosis.[1] The latter presentation of breast sarcoidosis is rare and accounts for less than 1% of cases of breast involvement of sarcoidosis. A total of 51 cases of breast sarcoidosis have been reported with approximately one quarter (23%) as the initial presentation.[2] In those 51 cases, the mean age of onset was 48 years and the most frequent presentation is of a palpable mass concerning for breast cancer. Diagnosis is achieved by core biopsy revealing non-caseating granulomas, without evidence of adjacent malignancy. Numerous reports of idiopathic granulomatous mastitis, occurring most frequently in parous young women between the ages 30-40, usually within a few years after giving birth or during pregnancy exist.[3] In some of these patients, extra-mammary findings including erythema nodosum, arthralgias and episcleritis have been reported and these may represent a form fruste of sarcoidosis.[4] Though sarcoidosis is typically reported to be rare in pregnancy, reports of idiopathic granulomatous mastitis occurring during pregnancy are likely presentations of breast sarcoidosis, and thus the prevalence of sarcoidosis in pregnancy may be underestimated.[5]

Sarcoidosis is an idiopathic systemic disease characterized by the formation of granulomas in various tissues, most commonly the lungs, lymphatic tissue, skin and eyes. The prevalence ranges from 4.7-63 in 100,000, and is more common in women, and in African-Americans.[6] The pathogenesis is largely unknown, but is thought to be due to an exaggerated immune response to unidentified antigens,

either through an autoimmune phenomenon, or as reaction to underlying infection, including possibly mycobacteria. The inflammatory response is characterized by upregulation of Th1 CD4+ cells, causing increased production of IL-2, IFN-gamma and TNF-alpha, with resultant epithelioid granuloma formation.[7]

Clinical manifestations of sarcoidosis vary based on degree and location of tissue involvement. Lung disease is seen in approximately 90% of patients with sarcoidosis.[8] Lymphatic involvement is also common, and typically presents with bilateral hilar lymphadenopathy. Skin disease is seen in 30% of patients, and histologic specific lesions include papules, nodules, plaques or subcutaneous nodules due to granuloma formation in the skin.[9] Nonspecific lesions include erythema nodosum. Bilateral ankle arthritis can be seen in 7-28% of patients.[10]

Sarcoidosis is diagnosed by clinical and radiological presentation, evidence of non-caseating granulomas on histology, and lack of evidence for other diseases.[10] As a diagnosis of exclusion, other granuloma-forming conditions, including infections (most commonly tuberculosis or fungal disease), occupational or environmental induced granulomas, drug-induced granulomas and other idiopathic granulomatoses should be considered and excluded.[6]

Diagnostic work-up in patients with sarcoidosis includes a thorough history and physical examination. If any cutaneous lesions are present, skin biopsy should be performed. Laboratory studies can include a CBC, CMP (to evaluate for renal or liver involvement), ESR and ACE level. Elevated ACE levels are seen in 60% of patients with sarcoidosis and can be used to monitor disease activity. Internal organ involvement should be screened for with an ophthalmology evaluation, chest X-ray, pulmonary function tests, and EKG. Treatments for sarcoidosis are most commonly employed with oral corticosteroids. Other treatments that can be effective include immunosuppressive agents such as methotrexate, azathioprine, leflunomide, cyclophosphamide, mycophenolate mofetil; TNF-alpha suppressants such as pentoxyfilline, thalidomide, and TNF-alpha inhibitors; and anti-inflammatory antimicrobial agents such as antimalarials and tetracycline derivatives.[6]

Conflict of Interest Disclosures: none.

Funding: none.

Corresponding Author:
Robert S. Kirsner, MD, PhD
1600 NW 10th Avenue
RMSB 2023A
Miami, FL 33136
rkirsner@med.miami.edu

References:

1. Lower EE, Hawkins HH, Baughman RP. Breast disease in sarcoidosis. *Sarcoidosis Vasc Diffuse Lung Dis.* 2001;18:301-6.

2. Mona el K, Pascal C, Charley H, Francoise B, Veronique B, Marie-Madeleine P. Quiz case. Breast sarcoidosis presenting as a metastatic breast cancer. *Eur J Radiol.* 2005;54:2-5.

3. Altintoprak F, Kivilcim T, Ozkan OV. Aetiology of idiopathic granulomatous mastitis. *World J Clin Cases.* 2014;2:852-8.

4. Fahmy J, Halabi-Tawil M, Bagot M, Tournant B, Petit A. Erythema nodosum during the course of idiopathic granulomatous mastitis. *Ann Dermatol Venereol.* 2015;142:46-9.

5. Hadid V, Patenaude V, Oddy L, Abenhaim HA. Sarcoidosis and pregnancy: obstetrical and neonatal outcomes in a population-based cohort of 7 million births. *J Perinat Med.* 2015;43:201-7.

6. Valeyre D, Prasse A, Nunes H, Uzunhan Y, Brillet PY, Muller-Quernheim J. Sarcoidosis. *Lancet.* 2014;383:1155-67.

7. Kataria YP, Holter JF. Immunology of sarcoidosis. *Clin Chest Med.* 1997;18:719-39.

8. Sheffield EA. Pathology of sarcoidosis. *Clin Chest Med.* 1997;18:741-54.

9. Judson MA. Extrapulmonary sarcoidosis. *Semin Respir Crit Care Med.* 2007;28:83-101.

10. Joint Statement of the American Thoracic Society (ATS) the European Respiratory Society (ERS) the World Association of Sarcoidosis and Other Granulomatous Disorders (WASOG) adopted by the ATS Board of Directors and by the ERS Executive Committee, February 1999. *Am J Respir Crit Care Med.* 1999;160:736-55.