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Temporal resolution of idiopathic granulomatous mastitis with resumption of bromocriptine therapy for prolactinoma



Marcia E. Bouton^a, Lisa M. Winton^a, Sonal G. Gandhi^b, Lakshmi Jayaram^a,
Prahlabhai N. Patel^a, Patrick J. O' Neill^a, Ian K. Komenaka^{a,c,*}

^a Maricopa Medical Center, Phoenix, AZ, USA

^b New Horizon's Women's Care, Phoenix, AZ, USA

^c Arizona Cancer Center, University of Arizona, Tucson, AZ, USA

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ABSTRACT

INTRODUCTION: Idiopathic granulomatous mastitis (IGM) is becoming more commonly recognized and reported more often. Currently, many recommend corticosteroids in its management.

PRESENTATION OF CASE: A 34-year-old G3P2 Hispanic female, 28 weeks pregnant, presented with a 19 cm right breast mass. She had a known prolactinoma treated with bromocriptine which was discontinued during her pregnancy. Ultrasound guided core biopsy procedure revealed granulomatous mastitis. The patient was told that the mass would resolve with observation. The patient seen at another institution by an infectious disease specialist who started treatment with amphotericin for presumptive disseminated coccidioidomycosis. Repeated titers were negative for coccidioides antibody. Repeat cultures were negative as well. Due to the persistence of the infectious disease specialist, tissue cultures were performed on fresh tissue specimens, which did not grow bacterial, fungal, nor acid fast organisms. The amphotericin regimen resulted in no improvement of her breast mass after 10 weeks. Within two weeks of stopping the antifungal therapy, however, the mass diminished to 6 cm. The patient delivered at 39 weeks. Bromocriptine was restarted, and within 4 weeks, the lesion was no longer palpable. She had not shown signs of recurrence for 32 months.

DISCUSSION: Treatment recommendations for IGM vary widely but antibiotics and antifungal medications are not recommended. Corticosteroid treatment is most commonly recommended, however, outcomes may not be different from management with observation. Prolactin may be involved in the pathophysiology of the process.

CONCLUSION: IGM is becoming recognized more frequently. Observation and patience with natural history can be an effective management.

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1. Introduction

Idiopathic granulomatous mastitis (IGM) was an uncommon disease of the breast that is now being recognized and reported more commonly [1–3]. It occurs most often in fertile, parous women, in the fourth decade of life, can have a prolonged natural history, and can be recurrent [4–9]. By definition, IGM is a disease with no known cause and can only be diagnosed when other etiologies have been ruled out (i.e., malignancy, infection most notably

tuberculosis, and the systemic diseases sarcoidosis or Wegener's granulomatosis) [4,9].

Patients with IGM have a variety of presentations. Most commonly a breast mass with or without pain and sometimes with associated skin ulcerations and sinus tract formation. Most concerning is that, IGM may present with findings suspicious for breast cancer such as a large palpable mass and associated skin changes. As with nearly all palpable masses, because of the dangers inherent in the differential diagnosis, histologic diagnosis with needle biopsy is necessary. On biopsy, IGM shows characteristic non-caseating granulomas, inflammation, and microabscess formation confined to the lobule. Following diagnosis, treatment modalities vary widely. These include excision of lesion, steroid therapy, chemotherapy such as methotrexate, and observation. None of

* Corresponding author at: Hogan Building, 2nd Floor, 2601 E Roosevelt Street, Phoenix, AZ 85008, USA. Tel.: +1 602 344 5368; fax: +1 602 344 1299.

E-mail address: Komenaka@hotmail.com (I.K. Komenaka).

these modalities has been shown to be superior to close observation [1–3,9].

The case presented is the management of a pregnant woman with a prolactinoma and a large mass determined to be idiopathic granulomatous mastitis.

2. Presentation of case

A 34-year-old G3P2 Hispanic female born in Mexico presented with a painful enlarging right breast mass for one month. She presented at 25 weeks intrauterine pregnancy. She previously was given a course of cephalexin followed by dicloxacillin at an unaffiliated institution with minimal subjective improvement. Her past medical history was significant for a prolactinoma treated with bromocriptine. The medication, however, had been discontinued during her pregnancy. On review of systems she had a one week history of erythema nodosum on bilateral lower legs; and denied fever, chills, cough, nausea and vomiting.

Physical examination revealed a non-ill appearing, well nourished, pregnant female with a 19 cm right breast mass with breast skin edema, induration, and some nipple distortion. Ultrasound did not identify a distinct mass and mammography was not performed. An ultrasound guided vacuum assisted core biopsy procedure was performed and 12 core samples were taken from various portions of the lesion. Breast tissue was submitted to pathology and microbiology for bacterial, fungal and acid fast bacilli (AFB) cultures. Histologic diagnosis revealed granulomatous mastitis characterized by granulomatous inflammatory reaction centered on lobules and composed of epithelioid histiocytes, multinucleated giant cells with admixed lymphocytes, plasma cells and eosinophils (Figs. 1 and 2). All cultures and stains were negative for organisms. The patient was told that the mass would resolve with observation and that no further treatment would be necessary. She was also told that the course of the disease process, however, can have periods of exacerbation and require up to 18 months to resolve.

Fifteen days later, she presented to the breast clinic with a breast fluid collection in the same location as the mass. A drainage procedure was performed through an 11 blade stab incision using a 12 gage vacuum core needle biopsy device in the clinic. The vacuum feature was used to remove the necrotic liquefied tissue. The mass was approximately 15 cm after the drainage procedure. A second fluid collection then occurred and she sought treatment at an emergency room of an unaffiliated hospital. There she was seen by an infectious disease specialist who started treatment with amphotericin for presumptive disseminated coccidioidomycosis. The patient had a second core needle vacuum drainage procedure to remove the fluid collection. Repeated titers were negative for

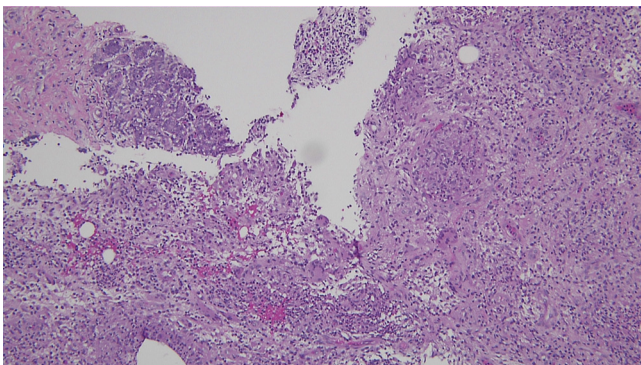


Fig. 1. Hematoxylin and eosin stain showing a normal breast lobule in the upper left corner. The tissue on the right side shows findings of granulomatous mastitis with granuloma and multinucleated giant cell located immediately beneath the granuloma (100× magnification).

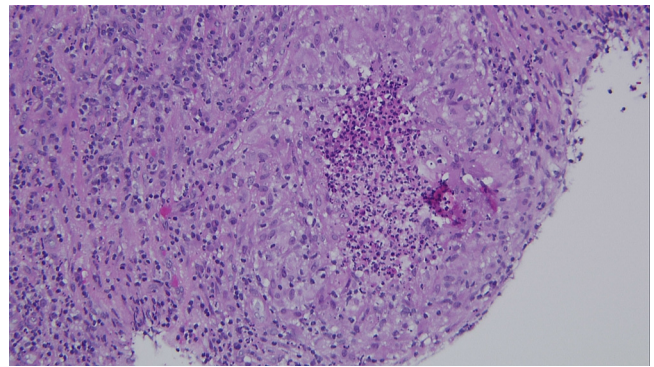


Fig. 2. Hematoxylin and eosin stain showing necrotic granuloma with microabscess formation (200× magnification).

coccidioides antibody. Repeat cultures were negative as well. The infectious disease specialist remained concerned that titers were unreliable due to the patient's pregnancy. *Coccidioides immitis* titers failed to convert over time. The infectious disease specialist felt that fresh tissue was required to reliably rule out *Coccidioides*. Tissue cultures were performed on fresh tissue taken on two subsequent core needle biopsy specimens. These specimens did not grow bacterial, fungal, nor acid fast organisms. In addition, unfixed breast tissue from this patient was submitted to the University of Washington for polymerase chain reaction (PCR) analysis for fungal, AFB and bacterial organisms, and was negative as well. Additionally, *Coccidioides* species was not detected using PCR. The amphotericin regimen was stopped after 10 weeks of treatment with no improvement of her breast mass.

Subsequently, within two weeks of stopping the antifungal therapy, the lesion diminished in size from 15 cm to 6 cm. The patient delivered at 39 weeks. At initial postpartum visit her mass was still 6 cm. Two weeks later bromocriptine was restarted, and within 4 weeks, the lesion was no longer palpable. She had not shown signs of recurrence for 32 months after resolution of the mass.

The patient was then seen at 33 months after resolution. At this time she complained of a new developing area of swelling in her right breast for 1–2 weeks. On examination she did have a 1 cm area of swelling clinically consistent with early granulomatous mastitis. It turned out the patient had missed appointments with her endocrinologist and therefore, had been off bromocriptine for approximately 5 months. This 5 month time frame of being off bromocriptine is similar to her first presentation at about 5 months during her pregnancy. Her prolactin level was again elevated. This was discussed with her endocrinologist and the bromocriptine was reinitiated. The breast changes resolved 1 week after the patient restarted the bromocriptine.

3. Discussion

Idiopathic granulomatous mastitis (IGM) is a disease with no known cause and is diagnosed after other more common etiologies of breast mass have been ruled out (i.e., malignancy, infection most notably tuberculosis). There is no consensus on the recommended treatment.

Coccidioides immitis is an environmental dimorphic fungus endemic to the desert regions. Erythema nodosum is a common finding, and is associated with a more indolent course [10,11]. *Coccidioides* infection is rare in pregnancy, even in endemic areas. Wack, et al. reported 10 cases among 47,120 pregnancies in Tucson, Arizona [12]. In pregnancy, *Coccidioidomycosis* is most often diagnosed via serologic testing of the maternal serum. As with other infections, IGM antibodies are initially positive (in about 75% of

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