CASE REPORT – OPEN ACCESS

International Journal of Surgery Case Reports 10 (2015) 8–11

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.casereports.com

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], Prahladbhai 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

ARTICLE INFO

Article history:
Received 24 October 2014
Received in revised form 17 February 2015
Accepted 28 February 2015
Available online 4 March 2015

Keywords:
Granulomatous mastitis
Observation
Management
Prolactinoma

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.

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).

http://dx.doi.org/10.1016/j.ijscr.2015.02.051

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 cephelexin 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

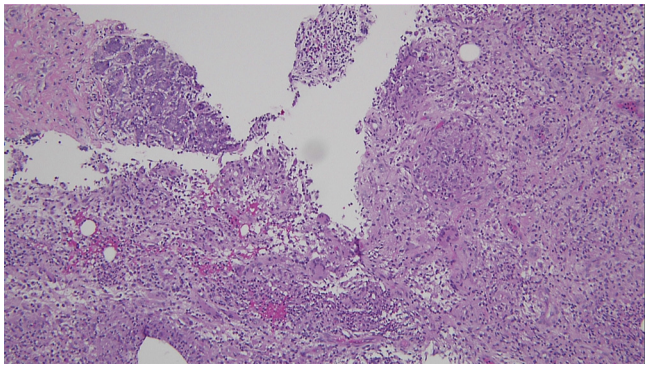

Fig. 1. Hematoxylin and eosin stain showing a normal breast lobule in the upper left corner. The tissue on the right side shows findings of granulomatous mastitis with granuloma and multinucleated giant cell located immediately beneath the granuloma (100× magnification).

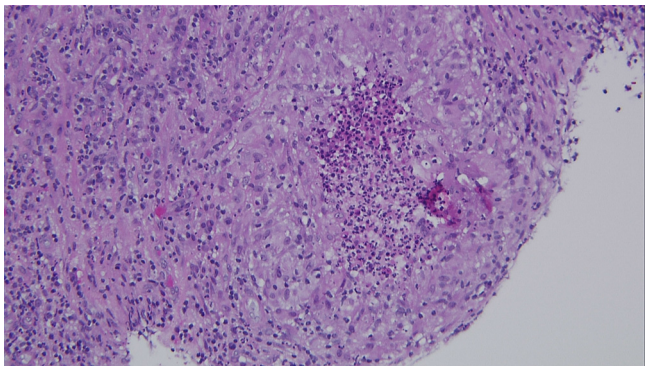

Fig. 2. Hematoxylin and eosin stain showing necrotic granuloma with microabscess formation (200× magnification).

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, Coccidiodomycosis is most often diagnosed via serologic testing of the maternal serum. As with other infections, IGM antibodies are initially positive (in about 75% of

people with primary infection) and later IgG titers become positive. IgG antibodies usually disappear in several months if the infection resolves [13].

The current patient had a known prolactinoma, however, treatment with bromocriptine was stopped by necessity during pregnancy. The course of IGM in this patient appears to correlate with treatment of her prolactinoma. The patient initially demonstrated significant clinical improvement of the mass coinciding with stopping the antifungal medication and then complete resolution after treatment with bromocriptine for her prolactinoma was reinstituted after delivery. In addition, the early signs of the second episode recently seen at 33 months after resolution of the initial episode occurred after being off bromocriptine again for 5 months. This time frame of 5 months was similar to the time that had elapsed prior to her intial episode as she presented at 25 weeks during her pregnancy. During her visit, the patient stated that she felt this second presentation was similar to how her initial episode started. Her prolactin level had been documented to be elevated for at least 5 months.

Although IGM has no known cause, hormones likely play a significant role in the etiology as it is almost exclusively seen in young, fertile, and parous women. It also commonly occurs in pregnancy or during lactation. Review of the literature further demonstrates an unusually high incidence of hyperprolactinemia in these patients [3]. In addition, reports exist of patients with IGM who have prolactinoma [3]. It is possible that at least in some, IGM is caused or exacerbated by prolactin levels, and future inquiry is warranted. The fact that the onset and resolution of this patient's IGM coincided with stopping and restarting bromocriptine on two occasions further supports this possibility.

Treatment recommendations for IGM vary widely but antibiotics and antifungal medications are not recommended. In the past, surgical recommendations have extend from simple excision up to and including mastectomy. Although simple excision of IGM masses was the most frequently reported surgical treatment this may not add assurance for cure as recurrences have been reported to be as high as 21% [14]. There are many reports of mastectomy to treat IGM. Recurrence or residual disease, however, may still occur after mastectomy [15,16]. Most have moved away from surgical management of IGM. Non-surgical recommendations include pharmacologic (i.e., steroids, methotrexate, azathioprine, tuberculosis medications) or close observation [1,3,6,17]. A recent case report in a patient with systemic lupus erythematosus (SLE) and prolactinoma found that treatment of both conditions (immunosuppressive therapy for SLE and bromocriptine for prolactinoma) were necessary to maintain remission of IGM [18]. In the largest series to date, Pandey, et al. reported that 23% of 49 IGM patients had recurrence after corticosteroid treatment [1]. Close observation with reassurance and patient education about the natural history of the process has also been used with similar results [3].

4. Conclusion

IGM is a previously rare clinical entity that is becoming more commonly recognized. Management with observation is a reasonable option and can help avoid unnecessary testing and treatment. Prolactin is one of the hormones which may play a role in the pathophysiology of the disease process.

Conflict of interest

All authors report no conflict of interests.

Funding

No funding was used for this research.

Ethical approval

Maricopa Medical Center Institutional review board approval was obtained.

Consent

We have obtained consent from the patient and can provide this, should the Editor ask to see it. No personal information or identifiable images of patients were used in the manuscript.

Author contribution

Concept or design: All authors.
Data Collection: NA.
Data analysis or interpretation: NA.
Writing the paper: All authors.

Guarantor

Ian Komenaka.

Acknowledgement

None.

References

[1] T.S. Pandey, J.C. Mackinnon, L. Bressler, A. Millar, E.E. Marcus, P.S. Ganschow, Idiopathic granulomatous mastitis–a prospective study of 49 women and treatment outcomes with steroid therapy, Breast J. 20 (May–June (3)) (2014) 258–266.
[2] K.A. Joseph, X. Luu, A. Mor, Granulomatous mastitis: a New York public hospital experience, Ann. Surg. Oncol. 21 (December (13)) (2014) 4159–4163.
[3] M.E. Bouton, L. Jayaram, P.J. O'Neill, C.H. Hsu, I.K. Komenaka, Management of idiopathic granulomatous mastitis with observation, Am. J. Surg. (2014) (in press).
[4] E. Kessler, Y. Wolloch, Granulomatous mastitis: a lesion clinically simulating carcinoma, Am. J. Clin. Pathol. 58 (1972) 642–646.
[5] B. Al-Khaffaf, F. Knox, N. Bundred, Idiopathic granulomatous mastitis: a 25-year experience, J. Am. Coll. Surg. 206 (2008) 269–273.
[6] K.E. BaniHani, R.J. Yaghan, S. Matalka, Idiopathic granulomatous mastitis: time to avoid unnecessary mastectomies, Breast J. 10 (2004) 318–322.
[7] G. Gurleyik, A. Aktekin, F. Aker, H. Karagulle, A. Saglamc, Medical and surgical treatment of idiopathic granulomatous lobular mastitis: a benign inflammatory disease mimicking invasive carcinoma, J. Breast Cancer 15 (March (1)) (2012) 119–123.
[8] K.Y. Kok, P.U. Telisinghe, Granulomatous mastitis: presentation, treatment and outcome in 43 patients, Surgeon 8 (August (4)) (2010) 197–201.
[9] G.M. Tse, C.S. Poon, K. Ramachandram, T.K. Ma, L.M. Pang, B.K. Law, et al., Granulomatous mastitis: a clinicopathological review of 26 cases, Pathology. 36 (June (3)) (2004) 254–257.
[10] E.L. Arsura, W.B. Kilgore, S.N. Ratnayake, Erythema nodosum in pregnant patients with coccidioidomycosis, Clin. Infect. Dis. 27 (1998) 1201–1203.
[11] L.G. Mark, W.R. Heymann, J. Berth-Jones, I. Coulson, Treatment of skin disease: comprehensive therapeutic strategies, 45, fourth ed., Saunders, 2014, pp. 147–149.
[12] E.E. Wack, N.M. Ampel, J.N. Galgiani, D.A. Bronnimann, Coccidioidomycosis during pregnancy. An analysis of ten cases among 47,120 pregnancies, Chest 94 (August (2)) (1988) 376–379.
[13] D.A. Stevens, Coccidioidomycosis, N. Engl. J. Med. 332(16 (April (20)) (1995) 1077–1082.
[14] J.P. Wilson, N. Massoll, J. Marshall, R.M. Foss, E.M. Copeland, S.R. Grobmyer, Idiopathic granulomatous mastitis: in search of a therapeutic paradigm, Am. Surg. 73 (August (8)) (2007) 798–802.
[15] M. Hladik, T. Schoeller, F. Ensat, G. Wechselberger, Idiopathic granulomatous mastitis: successful treatment by mastectomy and immediate breast reconstruction, J. Plast. Reconstr. Aesthet. Surg. 64 (December (12)) (2011) 1604–1607.

[16] R. Taghizadeh, O.P. Shelley, B.K. Chew, E.M. Weiler-Mithoff, Idiopathic granulomatous mastitis: surgery, treatment, and reconstruction, Breast J. 13 (September–October (5)) (2007) 509–513.
[17] E.C. Lai, W.C. Chan, T.K. Ma, A.P. Tang, C.S. Poon, H.T. Leong, The role of conservative treatment in idiopathic granulomatous mastitits, Breast J. 11 (2005) 454–456.
[18] L.N. Zhang, T.Y. Shi, Y.J. Yang, F.C. Zhang, An SLE patient with prolactinoma and recurrent granulomatous mastitis successfully treated with hydroxychloroquine and bromocriptine, Lupus 23 (April (4)) (2014) 417–420.