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Case Study

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IDIOPATHIC GRANULOMATOUS MASTITIS: A THERAPEUTIC AND DIAGNOSTIC CHALLENGE

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ABSTRACT

Granulomatous mastitis (GM) is a rare benign chronic inflammatory breast disease that affects women of childbearing age with a history of breastfeeding. GM presents with variable clinical presentations, and its diagnosis is usually made by exclusion. There are no clear guidelines for the management of GM. Since the first description of the disease, it has proved itself to be a great diagnostic and therapeutic challenge. It usually presents as a breast mass that can greatly mimic breast cancer .The only way to reach a definitive diagnosis is by core needle biopsy and histology. This manuscript describes the management of a patient with recurrent idiopathic GM at our setting. The patient was treated with a combination of steroids and antibiotics.

INTRODUCTION

Since granulomatous mastitis (GM) was first described as a benign disease entity in 1972 by Kessler and Wolloch[1], hundreds of cases have been reported from all over the world. Nevertheless, GM is a rare diagnosis with an estimated incidence of 2.4 per 100,000 women and 0.37% in the US.[2] The fact that the majority of cases in the US are predominantly in non-white patients, suggests that the incidence in Europe (and specifically Germany) is even less.[3]

The disease most frequently appears in the 3rd or 4th decade of life[4], and reports have shown that the youngest female diagnosed with GM was 11 years and the oldest was 83 years.[5] It typically affects young women between 17 and 42 years of age within the reproductive and post-childbearing period. GM constitutes 24% of all inflammatory breast diseases.[6] The etiology of GM is still hypothetical, and no consensus on disease management exists.[7] Therefore, the diagnosis and treatment of a patient with GM still remains a challenge for the clinician as well as for the patient who often has to suffer a protracted disease course with a significant impact on quality of life. Different causes of mastitis and malignancy are to be excluded before the diagnosis of GM is considered.[8]

GM can present as a palpable mass, abscess formation, peau d' orange or axillary lymphadenopathy, nipple retraction, skin retraction, as well as nipple discharge, have also been reported, but are less common findings. This mass or lump can be later complicated by abscess formation. The main aim of therapy is palliation of symptoms. Granulomatous mastitis will usually take 1-2 years to resolve on its own if left untreated.[9]

CASE REPORT

A 33 year old female presented with a right breast mass and associated breast pain, gradually increasing in severity for the past 15 days. This was accompanied by fever, chills and night sweats, along with skin changes. She underwent ultrasound of the bilateral breasts which revealed ill-defined area of abnormal echogenicity with internal echoes in the right breast. Fine needle aspiration was done and its cytology showed the findings suggestive of granulomatous mastitis, with histiocytes and other inflammatory cells. No evidence of malignancy was found in cytology. A diagnosis of right breast abscess was made and incision and drainage was planned. She underwent incision and drainage of the right breast abscess and was started on oral antibiotics. Pus from her breast drainage was cultured and also sent for cartridge based nucleic acid amplification test (CBNAAT). As her symptoms worsened and pus discharge continued despite drainage and antibiotics, she was started on oral Prednisone (40 mg/daily for 14 days). The steroids resulted in significant improvement of the disease, with the resolution of pain, erythema, and pus discharge. Her steroid dose was slowly tapered over 2 months but the disease recurred after 4 months and she was again started on corticosteroids and gradually dose tapering was done.

History of her current illness dated back to 2018 when she felt a mass in her right breast which upon further investigation, was diagnosed as breast abscess that was drained . Fine-needle aspiration was done in 2018, and was found to be negative for malignancy and was reported to have abscess formation. The slides revealed a heavy inflammatory infiltrate predominantly composed of polymorphonuclear leukocytes. Core biopsy done at that time, didn't reveal any granulomas. The Ziehl–Neelsen stain for acid-fast bacilli was negative. This led to the diagnosis of idiopathic granulomatous mastitis which was a diagnosis of exclusion. The patient continuously followed up at the clinic. In July 2020 she presented with swelling, pain and erythema in the same breast away from the previous scar site without any nipple discharge . The lump was almost 10 x 8 cm in size. She again underwent incision and drainage of the abscess with culture and CBNAAT of the pus. Culture was sterile and CBNAAT did not detect any mycobacteria. Incision biopsy was done which revealed granulomatous mastitis. It was concluded that she had recurrence of the disease which is typical of granulomatous mastitis.

DISCUSSION

GM and mastitis are commonly misdiagnosed since the clinical presentation of GM is consistent with infectious mastitis. As the infection is presumed based on physical exam findings, antibiotic therapy is usually initiated without microbiological proof. GM is by definition a sterile inflammatory disease; therefore, antibiotic therapy usually fails.[10,11] This would explain the lack of success with the initial pharmacotherapy. Mastitis affects 3–20% of lactating women. Although mastitis can occur at any time during lactation, the majority of cases occur in the first 6 weeks.[12] The patient was not breastfeeding, so the inflammatory and infectious diseases resulting from lactation, usually observed in mastitis, were ruled. Also, it was remarkable that the patient reported a similar episode in her right breast 2 years back. This fact lowered the suspicion of a cancer.

Antibiotics present the lowest efficacy in the treatment of mastitis in the absence of bacterial infection, with improvement rates ranging from 6 to 21%.[13] By comparison, corticosteroid therapy has a success rate of between 66 and 72%. In a meta-analysis by Lei et al.[8], a pooled recurrence rate of 20% was reported for oral steroid therapy. Surgery alone or in combination with corticosteroids seems to have the lowest recurrence, with rates of 6.8 and 4%, respectively. There are limited data in the literature and a lack of consensus on the use of antibiotic therapy for the treatment of GM.[14] The literature supports empirical therapy with antibiotics, anti-inflammatory agents, and surgery.[8,13,14] Although our patient's response was not optimal, the combination of surgical procedures, corticosteroids (methyl prednisolone or prednisone), and antibiotics resulted in overall clinical improvement.

The diagnosis of GM requires a high index of suspicion after other causes of granulomatous mastitis have been excluded. These include causes like mycobacterial infections, sarcoidosis, foreign body reactions, and fat necrosis. Tuberculous mastitis must be ruled out because steroids are the mainstay of treatment of IGM, which can aggravate mycobacterial infections. All specimens must undergo Ziehl acid-fast staining.[15]

A definitive diagnosis of GM is based on histopathological examination of the tissue specimen. FNA has been historically used but is now losing favour in the diagnosis of IGM due to its lower sensitivity. Studies have shown that the diagnostic yield of FNA may be as low as 21%-39%.[15] For a definite diagnosis, FNA must often be followed by a core biopsy. Core needle biopsy has a higher diagnostic yield and often has sensitivity upwards of 94% based on studies.[16] In some cases, where core needle biopsy is not diagnostic, an open biopsy can be considered.[15,16] The treatment options, which have been tried include observation, steroids, antibiotics, immunosuppressive agents like methotrexate and surgery. Observation can be sometimes used as an initial approach in patients who present with an initial episode of GM. Lai et al. in their study reported spontaneous resolution of GM in 50% of cases and stable disease in the other half.[17] However, the issue with the observational method is that the resolution can sometimes take a long period of time, as seen in the study by Lai and colleagues (approximately two years). This may be troublesome in the clinical setting. Also, observation may not be appropriate in patients with symptomatic disease.

Antibiotics have also been used in treatment. Although, this is controversial as no direct relation has been established between bacterial infiltration and GM. Antibiotic use can be guided by microbiological data available, with chosen agents being directed against gram-positive organisms.[15] Antibiotics can also be used in conjunction with incision and drainage, especially where abscesses have formed.

At this time, corticosteroids are the mainstay of treatment for GM. Several studies have shown promising results with steroid use. In a prospective study by Pandey et al., of the 44 patients treated with steroids, there was complete resolution of disease in 35 patients (79.5%).[18] The median time to resolution was 5.3 months. A total of 23% had a recurrence of the disease and all of them resolved with the second course of steroids.[17] In a retrospective study done by Oran et al., 25 out of 46 patients with GM were treated with steroids. Of these 25 patients, only three (7%) failed to respond to steroids and required surgical excision.[19] Other studies have demonstrated a similar benefit with steroid therapy. The most commonly recommended duration of steroid treatment is three to six months. Doses as high as 60mg of prednisone daily can be used with a gradual taper.[15] However, long-term steroid therapy leads to several side

effects, which include weight gain, hypertension, glucose intolerance, Cushing's syndrome, and steroid myopathy. Immunosuppressive agents like methotrexate and azathioprine can also be used in cases that are resistant to steroid therapy and can function as steroid-sparing agents.[17]

Before the introduction of steroids, GM was managed primarily with surgery. In a retrospective study done by Oran et al., out of 46 patients, wide local excision with negative margins was performed in 18 cases. Of these 18 cases, only three recurred who were then treated successfully with steroids and re-excision.[19] The authors emphasized the importance of wide local excision with negative margins to decrease the risk of recurrence. However, surgical excision has been falling out of favour because of the good response of GM to steroid therapy and also the fact that surgical treatment is associated with a high rate of disfigurement, fistula formation, and poor wound healing.[19]

CONCLUSION

GM is a chronic and often debilitating disease. If a patient presents with symptoms of chronic mastitis, one should always keep the possibility of GM as the underlying disease. This makes it necessary to perform a core needle or excisional biopsy to obtain a histopathologic diagnosis. With no accepted guidelines for the treatment of the disease, it becomes extremely challenging to adequately treat the condition. Authors recommend a corticosteroid regimen of 40 mg prednisolone once a day for 2 weeks, tapering gradually based on clinical findings. Every-2-week follow up should take place to evaluate treatment response and possible side effects. Corticosteroids should be administered for a minimum of 8 weeks and a maximum of 6 months to minimize possible side effects.[20] Further larger studies are needed to understand the most appropriate way of managing this condition.

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