

New-Onset Granulomatous Mastitis in a Systemic Lupus Erythematosus Patient While on Immunosuppressive

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ABSTRACT:

Etiology of granulomatous mastitis (GM) mostly unknown, but it may be associated with systemic or local granulomatous diseases. It responds well to immunosuppressive treatments. Here, we reported a case of a 36 year-old female systemic lupus erythematosus (SLE) patient with a new onset breast mass at the first year of the disease. Meanwhile, she was taking azathiopurine, hydroxychloriquine and low dosage steroid treatment during the onset of the breast mass. Then, granulomatous inflammation was found at the biopsy from the breast lesion. After, excluding the possible infectious etiologies, we started high dosage steroid. Thereafter, GM was responded to the treatment and then, she has been free of relapse since reducing the dosage of steroid to moderate level. As far as we know, our patient was the first SLE associated GM case resistant to treatment of azathiopurine and hydroxychloriquine. Moreover, we thought that GM may occur during immunosuppressive treatments in SLE patients and responded to high dosage of steroid.

Keywords: Azathiopurine; Granulomatous mastitis; Hydroxychloriquine; Systemic lupus erythematosus.

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INTRODUCTION:

Granulomatous mastitis (GM) is a pathologic terms that specifies chronic inflammatory granulomatus reaction in breast tissue [1]. In most of the cases, the etiology of the disease is unknown and accepted as idiopathic. Nevertheless, GM may be a manifestation of systemic or local granulomatous diseases such as bacterial, fungal and parasitic infections; rheumatologic diseases such as sarcoidosis, connective tissue diseases, granulomatous vasculitis; drugs and histiocytic disorders [2]. Herein, we presented a patient with systemic lupus erythematosus (SLE) who developed GM while on azathiopurine, hydroxychloriquine and low dosage steroid treatment. Meanwhile, - the patient was responded to high dosage steroid regimen.

CASE REPORT:

Thirty-six years old, female patient with the signs of arthritis, recurrent oral ulcers, deep venous thrombosis and of pulmonary artery thromboemboly was diagnoses as SLE. Furthermore, she had anti-nuclear antibody positivity with 1/320 titration and anti-SSA, anti-SSB, anti-scl 70 positivity. Her lupus anti-coagulant, anti-beta-2 glycoprotein G Ig and anti-cardiolipin G Ig tests were found positive two times in 12 week interval. With these findings, she was also diagnosed as secondary anti-phospholipids syndrome relates to SLE. Then, treatment with azathiopurine 150 mg/day, hydroxychloriquine 400 mg/day and predniolosone 5mg/day were started. At the first year of the treatment, while she was taking azathiopurine and hydroxychloriquine with initial

dosages and prednisolone 2, 5 mg/day, a mass originated from her right breast. At the same time, there were concomitant skin lesions with discharge over the breast mass. The culture of the discharge was negative. C-reactive protein level was normal and sedimentation rate was 28 mm/hour. Furthermore, she had no clinical sign or symptoms related with SLE activation. Complement proteins were in normal range and anti-ds DNA level was negative. Moreover, complete blood count, transaminase and creatinine levels were found in normal rates. In her breast ultrasonography exam, there were abscess-looking hypoechoic masses surrounded by inflammatory hyperechoic borders in an area of 21x12 mm. Furthermore, we did not order mammography wasn't performed due to the non specificity of this imaging in younger age and radiation risk of the procedure. Then, we have started broad spectrum antibiotics for breast mass and skin lesions. But, both lesions did not improve with antibiotic treatment. Following, we conducted biopsy from the mass. Pathologic examination of the specimen revealed granulomatous inflammation (**Figure**).

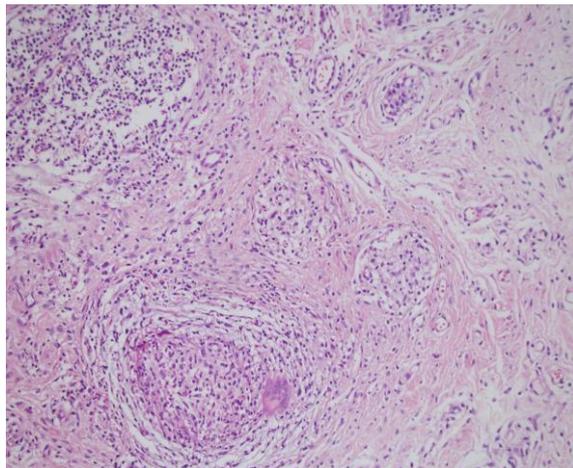


Figure: Granulomatous inflammation in the specimen from the breast mass (**Hematoxylin eosin stain**); objective magnification X100.

Tuberculosis, fungal and parasitic staining of the specimen were all negative. Moreover, tuberculosis skin test was lower than 5mm and serologic tests for brucellosis was found negative. There was no pathologic finding in her chest computerized tomography scanning. Lastly, anti-cytoplasmic neutrophil antibody tests were found negative. Also, she had no any concomitant drug use over the last six months. According to these findings, we thought that granulomatous inflammation in her right breast might be related with SLE or accepted as concomitant idiopathic granulomatous inflammation of the breast. Thereafter, we increased the steroid dosage to 40 mg/day prednisolone equivalent while she was

continuing to take both azathiopurine and hydroxychloroquine with initial dosages. Three months later, both breast mass and skin lesions were disappeared. Moreover, she was in remission both for SLE and GM after reducing the dosage of steroid to moderate levels.

DISCUSSION:

The pathophysiology of the chronic granulomatous inflammation in the breast was unknown. Damage to ductal epithelium via autoimmune processes is thought to be the triggering event. Then, leak of luminal protein rich material and fat into lobular connective tissue may cause granulomatous inflammation in the breast[3]. Palpable mass and pain/tenderness in breast was the most prominent symptoms of GM as our case. Mammography, breast ultrasonography and breast magnetic resonance imaging (MRI) may be used in diagnosis of GM. Focal asymmetry and irregular masses are the most frequent findings in mammography. Also, irregular and hypoechoic masses would be seen ultrasonography [4]. Moreover, most frequent findings in breast MRI are non-mass enhancement, distortion, skin thickening and focal skin enhancement [5]. We diagnosed the case as GM mainly according to the patient's clinical findings. However, hypoechoic masses in her breast ultrasonography support our clinical decision. Steroids and steroid sparing immunosuppressive agents such as methotrexate and azathiopurine are the mainstay treatment[6]. Due to the autoimmune nature of both lupus and idiopathic GM, co-occurrence of them would be expected. But it was hard to say that GM in our patient was secondary to SLE. Owing to our patient's medical history and ongoing immunosuppressive treatment, we firstly exclude possible infectious diseases. We also put emphasis on other systemic granulomatous diseases and excluded them. There were reports about SLE and GM association [7, 8]. But, diverse from our case, all reported patients were not taking any medication for SLE during the diagnosis of GM. Furthermore, hydroxychloroquine treatment with or without low dosage steroid were successfully remitted the disease. Interestingly, in our case, GM was diagnosed while our patient was taking azathiopurine, hydroxychloroquine and low dosage prednisolone. In the study of Konan et al., 2/13 (15.3 %) of the idiopathic GM patients on azathiopurine plus steroid treatment relapsed. Herein, these patients responded either surgical drainage or high dosage steroid treatment [9]. Likewise, our case would be accepted as first SLE associated GM patient resistant to azathiopurine and hydroxychloroquine combination therapy. Also, high dosage steroid was required for

removing the granulomatous inflammation.

CONCLUSION

In conclusion, our case was the first case that GM occurred in a SLE patient during immunosuppressive treatment containing azathiopurine and hydroxychloroquine. In the circumstance, high dosage steroid treatment should be feasible after excluding infectious etiologies.

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CONFLICT OF INTEREST:

The Authors declare that there is no conflict of interest.

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