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Perspective

Granulomatous lobular mastitis

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Abstract

Granulomatous lobular mastitis is an unusual breast benign inflammatory disorder with unknown aetiology. It is generally emerged with the clinical symptoms of breast mass, abscess, inflammation and mammary duct fistula. The diagnosis is made by histopathology with a chronic non-necrotizing granulomatous inflammation in lobules of the breast tissue as the microscopic feature. Therapy of granulomatous lobular mastitis consists of surgical, medication treatment or combination of both, but now researches suggest that observational management is an acceptable treatment.

Keywords: Breast; Granulomatous lobular mastitis; Mastitis; Granulomas

Introduction

Granulomatous lobular mastitis (GLM) is an unusual breast benign inflammatory disorder first described by Kessler and Wolloch in 1972.[1] The aetiology of GLM is unknown, but growing evidences suggest that a various of factors, including microbiology agents, hormonal effect, and immunologic disorder, played an important role in disease occurrence.[2] The age range of GLM has been reported from 11 to 83 years old; however it mostly emerges in third and fourth decades women and was more frequently reported in the Mediterranean region and the developing countries in Asia.[2] GLM closely resembles the duct ectasia/periductal mastitis complex (DE/PDM) and tuberculous mastitis in the clinical manifestations and imaging examination.[3,4] In microscopic features, it is a chronic non-necrotizing granulomatous inflammation in lobules of the breast tissue.[5] No standard treatment exists for GLM. The main approaches are surgical, medication treatment or a combination of both, but now some studies suggest that observational management is an acceptable treatment.[6] In this review, we describe the aetiology, clinical presentation, pathologic findings and differential diagnosis, as well as recommendations for treatment.

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Aetiology

The aetiology of GLM is not known exactly. A various of factors, including microbiology agents, hormonal effect, and immunologic disorder have been suggested of playing an important role in disease aetiology.

Microbiology agents

Corynebacteria are Gram-positive bacteria and members of the skin flora. They have been found in some patients with GLM recently and been considered to go deeper into the breast tissue via the ductal system. Taylor et al isolated *Corynebacteria* from breast tissue in 62 patients, who were diagnosed with GLM histologically, and 54.8% patients were bacteria-positive. Paviour et al[7] carrieded on a research of 24 patients, and observed *Corynebacteria* in 12 cases by hostopathological evaluation and diagnosed 9 cases with idiopathic granulomatous mastitis (IGM). *Corynebacterium kroppenstedtii* was the most frequently detected species in the studies mentioned above. In other literature,[8,9] case presentations on *Corynebacterium* species have been mentioned as well, and species including *Corynebacterium amycolatum* and *Corynebacterium tuberculostearicum* were identified. *Corynebacterium accolens* was also proposed as a possible cause of GLM in a 23-year-old female.[10]

Hormonal effect

GLM is usually detected in women with a history of breast-feeding or birth recently. Gestation, breast-feeding and hyperprolactinemia have also been put forward as a possible pathogenesis of GLM. Documents and case reports have confirmed the hypothesis aforementioned. According to a study by Bani-Hani[11] et al, in the overall cases, 16.7% had active gestation, 16.7% had an experience of birth and breast-feeding within 6 months, and only 8.3% did not have a history of pregnancy. In 1984, Rowe[12] indicated co-morbid prolactionma in a GLM case. Cases of GLM with hyperprolactinemia have also been reported in the following decades.[12–14] A relation between GLM and breastfeeding as well as the hyperprolactinemia has been discussed but has never been elaborated in depth. A possible cause of GLM is the hormonal imbalance with a shift of the ratio among gestagen and oestrogen.[15] With a hypothesis of autoimmune reactions to extravasated secretions from lobules, it becomes manifest intraductally by retention of secretions followed by ductal ectasia. The rupture of the ducts results in a persisting stromal cells inflammation.[16,17]

Immunologic disorder

The association between GLM and erythema nodosum and ankle arthritis have been commonly studied recently. It has been proved that treatment with corticosteroid and immunosuppressants is effective for some patients, which are supported that GLM is a kind of autoimmune disease. In the report by Zen et al,[18] one patient of granulomatous mastitis was observed with a lymphohistiocytic infiltrate, fibrosis, epithelioid granulomas without necrosis and an infiltrate of IgG4+ plasma cells. A conclusion of the report is that the GLM and IgG4-related autoimmune syndrome are possible highly correlated. Ogura et al[19] reported 2 similar cases, in which an infiltrate of IgG4+ plasma cells was also observed, and it was proposed that GLM may consist of two subtypes: non-IgG4-related mastitis and IgG4-related mastitis. Although the autoimmunity of GLM has been put forward, tests for rheumatoid factor (RF) and antinuclear antibody (ANA) are negative in general. Ozel et al[20] conducted a research on 8 cases. In the research, 6 cases were RF positive, and only 2 were positive for ANA and anti-double stranded DNA. In consequence, there exists an autuoimmne component in the aetiology of GLM.

The other factors

The other factors when considered about the aetiology of GLM mainly consist of alpha-1-antitrypsin (AAT), oral contraceptives (OCS) and smoking in general. As a member of the serine-protease inhibitor family, AAT is basically synthesised by hepatic cells. The deficiency of AAT causes lung and liver pathologies primarily. In 2001, Schelfout et al[21] reported one GLM case with an AAT deficiency. OCS could promote the breast secretion and is deemed to be a potential aetiological factor of GLM. The range of the correlation between GLM and OCS is reported as 0–42%.[22,23] In addition to AAT and OCS, a recent progress in the considerable studies is that smoking is related to the GLM, while an explicit reason has not yet been determined. Asoglu et al[24] presented that in a research with 18 GLM cases, 14 had a smoking history. According to a study by Baslaim et al,[22] none of their 20 cases was a smoker nevertheless.

Clinical presentation

The GLM mainly occurs in premenopausal females shortly after their last childbirth. It is generally emerged with the clinical symptoms of breast mass, abscess, inflammation and mammary duct fistula. In addition,