Overview on Idiopathic Granulomatous Mastitis

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1 Introduction

Milward and Gough [1] described granulomatous lesions in the breast that were confused with breast carcinoma in 1970. The entity "idiopathic granulomatous mastitis" (IGM) was first reported by Kessler and Wolloch [2] in five cases. These patients were defined as cases with suspected breast cancer, but characterized by granulomas and abscesses on pathological examination. Later in 1977, Cohen [3] detailed this clinical entity.

Many factors such as α1-antitrypsin deficiency, oral contraceptive drug use, smoking, pregnancy, childbirth and breastfeeding, hyperprolactinemia, ethnic origin, and autoimmunity have been blamed in the etiopathogenesis of IGM until today. However, the etiopathogenesis has not been explained exactly yet. Recently, some associations and findings in IGM, such as coexistence with erythema nodosum and arthritis, which are more common in rheumatological diseases such as Sjögren's syndrome, and the increase in the use of steroids in treatment, suggest autoimmunity and immune dysregulation more likely in the etiopathogenesis [4–11].

Idiopathic granulomatous mastitis is a mysterious disease that continues to attract many researchers' attention, with many unknowns. Unfortunately, the pathogenesis and an ideal treatment approach of IGM, a disease known for nearly half a century, are still unknown. Many unknowns about the etiology of the disease also persist. For example, these questions should be answered: (i) Why is IGM more

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frequently observed in countries such as Turkey, China, South Korea, and Saudi Arabia? (ii) Why is it more common in premenopausal women? As emphasized above, although it has been known for half a century as a clinical entity, it still remains as a mystery.

2 Definition

There are various causes of granulomatous inflammation in the breast. The conditions that cause granulomas are shown in Table 1 [5, 12–14].

Generally, idiopathic granulomatous mastitis, a rare disease, may be confused with breast carcinomas. Patients with IGM present with a mass accompanied by inflammation manifestations such as erythema and pain. In order to diagnose IGM, histologically, there should be a non-caseous granulomatous inflammation. In addition, other causes of granulomatous inflammation should be ruled out including infectious diseases such as tuberculosis, fungi, parasites, or a systemic granulomatous disease, for example, sarcoidosis and Wegener's granulomatosis [5, 10, 12–14]. Briefly, IGM is a diagnosis of exclusion when other causes of granulomatous mastitis cannot be detected after demonstrating non-caseous granulomas histopathologically. The pathological features of IGM are discussed in detail in the "pathology and differential diagnosis" section.

Table 1 Causes of granulomatous inflammation in the breast

Causes
Infectious
Mycobacterium tuberculosis
Blastomycosis
Cryptococcosis
Histoplasmosis
Actinomycosis
Filarial infection
Corynebacterium
Autoimmune
Wegener granulomatosis
Giant cell arteritis
Foreign body reaction
Duct ectasis
Plasma cell mastitis
Subareolar granuloma
Periductal mastitis
Diabetes mellitus
Sarcoidosis
Fat necrosis
Idiopathic

3 Historical Perspective

Granulomatous mastitis was first defined by Milward and Gough [1]. In 1967, the authors performed a biopsy on a patient with a clinical suspicion of breast cancer. They froze this section; however, they could not find any evidence of carcinoma in the patient.

Pathologically, they found granulomatous inflammation in the patient. The authors retrospectively reviewed 691 patients who underwent local or radical mastectomy with a clinical diagnosis of breast cancer between 1960 and 1967 at United Oxford Hospitals. During this period, no evidence of breast carcinoma was detected in eight patients who were operated with a clinical diagnosis of breast carcinoma. The authors found a condition unlike the known noninfective inflammatory breast diseases including fat necrosis and periductal mastitis in four patients. There was a condition in the breast that was accompanied by granulomatous inflammation.

In 1972, Kessler and Wolloch [2] described five patients who were clinically similar to breast carcinoma, but had no evidence of breast carcinoma on pathological examination, similar to Milward and Gough [1]. Multiple granulomas and abscesses were observed in these patients. All patients were women in childbearing age, and they had given birth. The age of the patients was found to be between 27 and 40 years.

In two patients, a preoperative punch biopsy had been performed and they were diagnosed with carcinoma and received preoperative radiotherapy. However, as a result of the definitive surgery of these two patients, no finding of carcinoma had been found. “Lipid crystals” were investigated to rule out fat necrosis. In addition, Ziehl-Neelsen stain for acid-fast bacilli, Gram staining for bacteria, and periodic acid-Schiff reaction for fungi were used. No positivity was found in any of the patients. In conclusion, Kessler and Wolloch [2] used the term “idiopathic granulomatous mastitis” for the first time.

Cohen [3] reviewed 67 patients diagnosed with granulomatous tuberculosis, or fungal mastitis, and revealed five patients with granulomatous mastitis as described by Kessler and Wolloch [2]. The patients with granulomatous mastitis that fit the definition of Kessler and Wolloch accounted for 7.5% of all granulomatous mastitis patients. Cohen’s patients were young women of childbearing age, as were the patients of Kessler and Wolloch [2]. The patients’ age ranged between 17 and 34 years old. Cohen [3] described the pathological characteristics of patients with idiopathic granulomatous mastitis.

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