

Bilateral plantar rheumatoid nodules

Toshiyuki Yamamoto^{1*} and Shigeki Hagane²

^{1*} Department of Dermatology, Fukushima Medical University, Fukushima, Japan

² Tateuma Clinic, Fukushima, Japan

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TO THE EDITOR,

A 58-year-old woman was suffering from rheumatoid arthritis (RA) for these a few years, and had been treated with non-steroidal anti-inflammatory drugs (NSAIDs). She was engaged in serving at a Japanese hotel (ryokan). She visited the dermatology clinic, complaining multiple painful nodules on the soles. Physical examination revealed firm nodules on the bilateral soles (Figure 1), which summed up five in total. Laboratory examination showed positive rheumatoid factor (RF; 29 U/ml, normal <20) and RAPA (1:80), whereas C-reactive protein was normal (0.29 mg/dl) and antinuclear antibody was negative. Biopsy was performed from both lesions, both of which showed similar histological features showed palisaded granuloma composed of a number of histiocytes surrounding necrobiotic tissues in the deep dermis (Figure 2a, 2b). There were no rheumatoid nodules other sites than the soles. She was treated with oral methotrexate (7.5 mg per week), which was partially effective.

Rheumatoid nodule (RN) is the most representative specific cutaneous manifestation of RA [1]. Classic rheumatoid nodules are firm and mobile subcutaneous nodules which develop most predominantly on the extensor surface of the elbow. Otherwise, olecranon, extensor tendons of the hands, proximal ulna, sacrum, occiput, and sole [2], all of which are sites subjected to frequent mechanical irritation, and may be induced through Koebner phenomenon [3]. However, only a few cases of plantar RN have been reported so far [4,5]. The previously reported cases developed RN especially beneath the metatarsophalangeal (MTP) joints. MTP joints are frequently involved in RA, and MTP joint deformity may lead to the formation of RN through plantar subluxation and/or plantar callus [5]. Our case suggested that RNs were developed on the body weight bearing regions.

Histopathological features show that RN is composed of three parts, namely an inner zone of central necrosis (mostly eosinophilic, but rarely basophilic), a surrounding cellular palisading zone, and an outer area with perivascular infiltration of chronic inflammatory cells. The major

proportion of the palisaded cells consists of macrophages, and T-cells are seen among and surrounding the palisaded macrophages.



Figure 1. Firm nodules on the bilateral sole (arrow) (a: left, b: right)

Corresponding author: Toshiyuki Yamamoto, MD, PhD, Department of Dermatology, Fukushima Medical University, Hikarigaoka 1, Fukushima 960-1295, Japan, Tel./Fax: +81.24.547.1307; E-mail: toyamade@fmu.ac.jp

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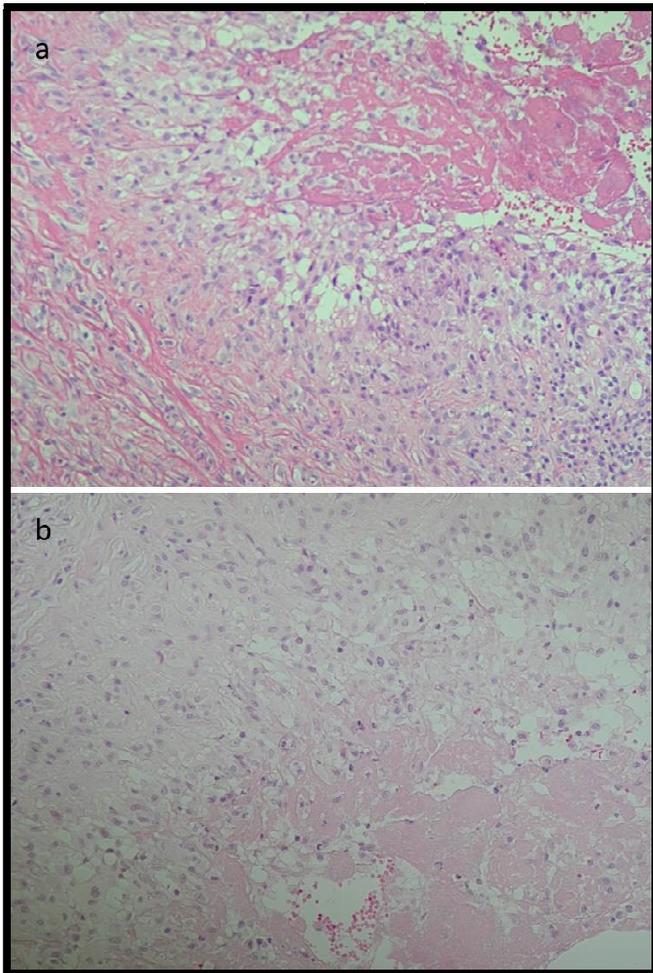


Figure 2. Histological features showing palisading granuloma (a; left sole, b; right sole)

Local secretion of cytokines, mediators, growth factors, proteases, and collagenases from those inflammatory cells lead to inflammation, angiogenesis, necrobiosis, and granuloma formation. Macrophage-derived proinflammatory cytokines such as interleukin-1 β (IL-1 β) and tumor necrosis factor- α (TNF- α) are thought to play a role in the induction of RN [6,7], as well as Th1 cytokines such as interferon- γ (IFN- γ), IL-1 β , TNF- α , IL-12, IL-18, IL-15, and IL-10 [8]. Local vascular damage is supposed to be caused by repeated minor trauma because RNs predominantly occur on the pressured sites. Endothelial cell injury may result in local accumulation of IgM immune complexes on the small vessel walls, which subsequently activate monocytes/macrophages. TNF- α enhances endothelial cells to express adhesion molecules such as intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1) and E-selectin in the blood

vessels, which promote leukocyte migration into the nodules [9].

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