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Single Case

Palisaded Neutrophilic and Granulomatous Dermatitis in a Patient with Granulomatosis with Polyangiitis

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Keywords
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Abstract
Palisaded neutrophilic and granulomatous dermatitis (PNGD) shows various clinical features and is histologically characterized by palisaded granulomas surrounding degenerated collagen. PNGD is known to be associated with a variety of systemic conditions such as rheumatoid arthritis and systemic lupus erythematosus. Furthermore, PNGD has been reported to be associated with antineutrophilic cytoplasmic antibody-associated vasculitis, including granulomatosis with polyangiitis (GPA) and microscopic polyangiitis. Here, we report a case of PNGD associated with GPA, which showed the infiltration of CD163-positive M2 macrophages in the skin lesion with elevated serum level of soluble CD163 (sCD163). The serum sCD163 level was reduced to normal range after systemic steroid therapy. Thus, M2 macrophages may play a role in the pathomechanisms of PNGD associated with GPA.

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Introduction

Palisaded neutrophilic and granulomatous dermatitis (PNGD) is a rare dermatological condition, which shows various clinical and histopathological features [1]. In 1994, PNGD was proposed to unify the conditions in which immune complex molecules, such as IgM and C3, were present, and a similar distribution pattern of neutrophils was seen upon histologic examination [2]. PNGD has been reported to be associated with a variety of systemic conditions, such as rheumatoid arthritis (RA) [3–5], and systemic lupus erythematosus (SLE) [2, 6]. Moreover, PNGD has been reported to be associated with antineutrophilic cytoplasmic antibody (ANCA)-associated vasculitis, including granulomatosis with polyangiitis (GPA) [7] and microscopic polyangiitis [8]. Here, we report a case of PNGD associated with GPA, which showed the infiltration of M2 macrophages.

Case Presentation

A 33-year-old Japanese female who was in remission state after a 15-year history of PGA presented papules or vesicles on her finger pads that had appeared in the prior 2 months. The skin eruptions expanded to all finger pads (Fig. 1a), palms, the lateral sites of the fingers, the bilateral elbows (Fig. 1b), and the lateral malleolus (Fig. 1c). Two months after the skin lesions had initially appeared, GPA recurred with symptoms including fever and pulmonary hemorrhage. Laboratory examination revealed an elevated proteinase 3-ANCA titer, which was >350 U/mL (normal <3.5). The serum level of soluble CD163 (sCD163) was measured using commercially available enzyme-linked immunosorbent assay (ELISA) kit according to the manufacturer's instructions (R&D Systems, Minneapolis, MN, USA). Serum sCD163 level was 1,526 ng/mL, which was higher than that of the healthy controls [9, 10]. Both biopsy specimens taken from the papules on the finger pad of the left middle finger and left elbow showed an infiltration of lymphocytes, histiocytes, and neutrophils with nuclear dust surrounding degenerated collagens throughout the dermis (Fig. 1d, e). Degenerated collagens were histologically demonstrated by Elastica Masson stain. Immunostaining showed an abundance of CD163- and CD68-positive cells surrounding degenerated collagens (Fig. 1f). Based on the histological findings, the patient received a diagnosis of PNGD associated with GPA. Although prednisolone (PSL) 25 mg/day was given for GPA, the skin eruptions remained unchanged. Steroid pulse therapy with methylprednisolone (1,000 mg/day for 3 days) followed by PSL (30 mg/day) and azathioprine (50 mg/day) was carried out, which was effective for both GPA and PNGD. The fever, pulmonary hemorrhage, and skin eruptions disappeared, and the PSL dose was reduced. The titer of PR3-ANCA was decreased to 154.0 U/mL with a normal serum level of sCD163 (301 ng/mL) after 2 months.

Discussion

Early lesions of PNGD show a dense neutrophilic infiltration with or without cutaneous small-vessel vasculitis (leukocytoclastic vasculitis), and collagen degeneration, and lesions are clinically similar with erythematous macules or urticaria-like annular plaques with crusting. Fully developed lesions are characterized by palisaded granulomas surrounding degenerated collagen with interstitial fibrin and mucin deposits, sparse neutrophils, and nuclear dust that

can be visualized through histological examination. Furthermore, the resolving lesions show palisaded granulomas with dermal fibrosis and rare neutrophilic debris [11].

It has been reported that the infiltrated cells were mainly positive for CD68 and CD163, which are a phenotype suggestive of M2 macrophages, with neutrophils and lymphocytes in PNGD associated with SLE [12]. CD163 is a glycoprotein belonging to the scavenger receptor cysteine-rich superfamily, and is expressed only in monocytes and a subpopulation of tissue macrophages [13]. Moreover, CD163 is a specific marker for M2 macrophages, which are involved not only in the suppression of immune responses and tissue repair and remodeling, but also in the development of type II immune responses and tumor progression. It is known that M2 macrophages are highly induced in active SLE, as SLE lesions contained CD163-positive cells, and a high concentration of sCD163 was found in SLE plasma [12, 14]. Serum sCD163 levels are also reported to be associated with the disease activity of RA [15]; thus, M2 macrophages may play an important role for PNGD formation in RA.

Abundant M2 macrophage infiltration in PNGD lesions was observed with elevated serum level of sCD163 in the present case, suggesting that M2 macrophages may play a role in this condition. However, serum sCD163 levels in GPA [16, 17] have not been defined, and the pathomechanisms for PNGD in GPA and ANCA-related angiitis are still unknown [7, 8]. Further study will be necessary to reveal the pathogenesis of PNGD in GPA.

Statement of Ethics

The patient has given informed consent to publish her case, and the study was done in accordance with the Declaration of Helsinki.

Disclosure Statement

The authors have no conflicts of interest to disclose.

Author Contributions

M.A. collected the data and wrote the initial manuscript draft; T.M. gave her the advice about the histological findings; and M.S. revised the manuscript and acts as the corresponding author. All authors provided critical feedback and contributed to the final version of the manuscript.

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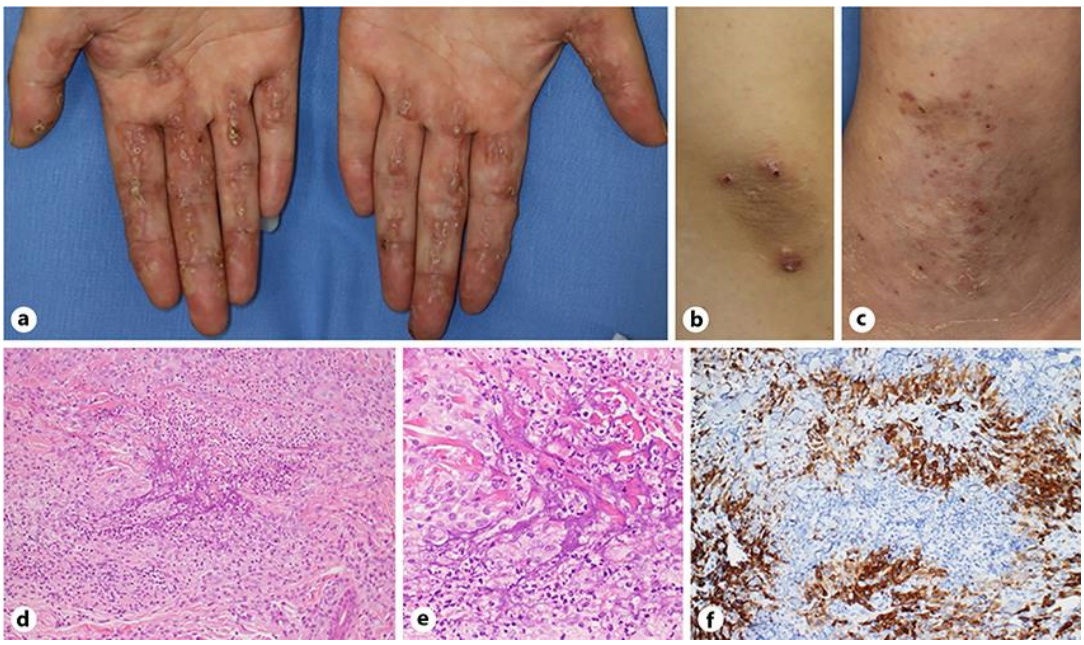

Fig. 1. Clinical findings at the first consultation. **a** Vesicles and papules on the finger pads, papules on the elbow (**b**), and purpura on the lateral malleolus (**c**). **d**, **e** Histological findings of the specimen from the papules **d** on the finger pad of the left middle finger (HE. ×100), and **e** on the left elbow (HE. ×200). **f** Histological findings with immunostaining of the specimen from the left finger pad of middle finger (anti-CD163 antibody; original magnification ×100). Abundance of CD163-positive cells are observed around the degenerated collagens in the dermis.