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Bullous Pemphigoid Accompanied by Aplastic Anemia: The Induction of IL-17-Producing Cells in the Affected Areas of the Skin

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Key Words

IL-17 · Aplastic anemia · Bullous pemphigoid

Abstract

Th17 cells, characterized by IL-17 production, play a critical role in the pathogenesis of autoimmune diseases, including autoimmune bullous disorders and aplastic anemia (AA). In this report, we describe a 58-year-old Japanese man with bullous pemphigoid (BP) accompanied by AA. Interestingly, immunohistochemical staining revealed the existence of IL-17-producing cells in the skin biopsy specimens from BP. Our findings might suggest relationships between IL-17 and the pathogenesis of these autoimmune diseases, and, to our knowledge, this is the first English report of BP accompanied by AA.

Introduction

T helper 17 (Th17) cells, characterized by interleukin-17 (IL-17) production, play a critical role in the pathogenesis of autoimmune disease [1]. In dermatological fields, previous reports suggested that Th17 cells are associated with various dermatological disorders, including autoimmune bullous disease such as pemphigus vulgaris (PV) and bullous pemphigoid (BP) [2, 3]. Aplastic anemia (AA), characterized by peripheral blood pancytopenia and bone marrow hypoplasia, is an immune-mediated disorder [4, 5]. Recently, it was reported that the Th17 immune response contributes to the AA pathophysiology [4]. In this report, we describe a case of BP accompanied by AA. Interestingly, biopsy specimens from involved skin lesions included IL-17-producing

cells in the superficial dermis, which might suggest a relationship between IL-17 and the pathogenesis of BP accompanied by AA.

Case Report

A 58-year-old Japanese man visited our outpatient clinic with a half-month history of pruritic bullous erythema on his trunk and extremities. He had been treated for aplastic anemia (AA) by a hematologist for twenty years in another institute. On his initial visit, physical examination revealed large tense bullae and erosion arising on erythematous plaque on the trunk and extremities ([fig. 1](#)). A biopsy specimen revealed prominent subepidermal blister formation and dense infiltration of eosinophils in the upper dermis ([fig. 2a](#)). Direct immunofluorescent study revealed IgG deposition on the epidermal side of the basement membrane zone. A full blood count and biochemical profile revealed a prominent decrease of white blood cells (2,500/ μ l), platelets (20,000/ μ l) and red blood cells (2.26×10^4 / μ l). In addition, high levels of serum anti-BP180 IgG (2,180 index) and platelet-associated IgG (375 ng/ 10^7 cells) were detected. From the above findings, we diagnosed this patient as BP accompanied by AA. To further investigate the correlation between AA and BP, we employed immunohistochemical staining for IL-17 (R&D system, Minneapolis). Immunohistochemical staining revealed IL-17-positive cells were infiltrating around the blister and upper dermis ([fig. 2b](#)). We treated him with oral prednisolone 30 mg/day for two weeks without any improvement. Then, we administered oral prednisolone 50 mg/day with cyclosporine 2.5 mg/kg/day. Two weeks later, the initial eruptions had disappeared and his disease was under control.

Discussion

AA, a disease characterized by peripheral blood pancytopenia and bone marrow hypoplasia, is an immune-mediated disorder and, in most cases, with active destruction of hematopoietic cells by effector T cells [4, 5]. Recently, de Latour et al. [4] reported the significance of the Th17 immune response in AA pathophysiology, especially at the early stage in the disease progression. They reported an increased number and frequency of Th17 cells in bone marrow and peripheral blood in patients with AA along with a reduction of regulatory T cells (Tregs). They concluded that the Th17 immune response may contribute to the recruitment of Th1 cells and may be important for the proinflammatory cytokine milieu in the bone marrow during the early stages of bone marrow failure.

Th17 cells have been characterized in mice as a novel subset of CD4⁺ T cells that produce IL-17A and IL-17F, and IL-22, and serve as immune effectors in autoimmunity [6]. In human, Th17 differentiation is under the control of IL-1 β , IL-6 and IL-23. Several studies have reported the association of IL-17 with autoimmune diseases, such as rheumatoid arthritis, multiple sclerosis, and lupus erythematosus [1, 4]. In bullous disorders, recently, Arakawa et al. [2] reported the significance of lesional Th17 cells in BP. They mentioned that BP shows more Th17 cell-related inflammation and less Treg-related regulation compared with pemphigus [2]. In aggregate, Th17 seems to contribute the pathogenesis of both AA and BP.

For the above reasons, in this report, we employed immunohistochemical staining for IL-17. As we expected, we detected IL-17-positive cells in superficial dermal areas of the BP specimens. Though we did not examine IL-17-producing cells in the circulating peripheral blood, our present case might suggest relationships between IL-17 and the pathogenesis of BP accompanied by AA.

Fig. 1. Large tense bullae and erosion arising on erythematous plaque on the trunk and extremities.

Fig. 2. Prominent subepidermal blister formation and dense infiltration of eosinophils in the upper dermis (**a**, H&E staining). Paraffin-embedded tissue sample from the BP patient was deparaffinized and stained using anti-IL-17 Ab. The sections were developed with new fuchsin (red) for IL-17 (**b**, **c**). Original magnification $\times 100$ (**a**, **b**), $\times 400$ (**c**).

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