

Successful Treatment of Plasmacytosis Circumorficialis with Topical Tacrolimus: Two Case Reports and an Immunohistochemical Study

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Key Words

Plasmacytosis circumorficialis · Tacrolimus · Proinflammatory cytokine · CD163⁺
macrophages · IL-17

Abstract

Plasmacytosis circumorficialis (PLC), a benign chronic inflammatory disease with an unknown pathogenesis, is characterized by erythema, erosion nodules and ulcers around the openings of the human body. In this report, we describe two cases of PLC successfully treated with topical tacrolimus. Interestingly, immunohistochemical staining revealed that prominent CD163⁺ proinflammatory macrophages and IL-17-producing cells were infiltrating around plasma cells, which might suggest the reason for the therapeutic effect of topical tacrolimus on PLC.

Introduction

Plasmacytosis circumorficialis (PLC) is a benign chronic inflammatory disease, characterized by erythema, erosion nodules and ulcers around the openings of the human body [1, 2]. Histopathologically, it is characterized by dense infiltration of the lamina propria by plasma cells. Several treatments for PLC have been reported, but an optimal therapy for PLC has not yet been found [2]. In this report, we describe two cases of PLC successfully treated

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with topical tacrolimus and an immunohistochemical study for PLC focusing on CD163⁺ proinflammatory macrophages and IL-17-producing cells.

Case Reports

Case 1

A 38-year-old Japanese woman visited our outpatient clinic with a two-month history of pruritic erythema on her external genitals. She had been treated with topical steroid at a private gynecologist for one month without any improvement. On her initial visit, physical examination revealed erosive erythema around the labium minor and external urethral meatus (fig. 1a). A biopsy specimen revealed a prominent cellular infiltrate in the superficial to mid dermis (fig. 2a). The infiltrating cells were mainly composed of plasma cells and lymphocytes (fig. 2c). Full blood count and biochemical profile were within normal ranges. Based on the above findings, we diagnosed this patient as a case of PLC. To analyze the pathogenesis of PLC, we performed immunohistochemical staining for CD163 and IL-17, which revealed the dense infiltration of CD163⁺ cells in the superficial to mid dermis (fig. 3a, b) and scattered IL-17-producing cells in the superficial to mid dermis (fig. 3c, d). We treated the patient with topical 0.1% tacrolimus twice a day; 4 weeks later, her pruritus had improved (fig. 1b), but the erythema had only slightly diminished (fig. 1b). Since she was still on tacrolimus, there was no relapsing pruritus nor erythematous plaque.

Case 2

A 69-year-old Japanese woman visited our outpatient clinic with a six-year history of pruritic erythema on her external genitals. She had been treated with topical steroid at a private dermatologist for one month without any improvement. On her initial visit, physical examination revealed erythema around the labium minor with pitted purpura (fig. 1c). A biopsy specimen revealed a prominent cellular infiltrate in the superficial to mid dermis (fig. 2c). The infiltrating cells were mainly composed of plasma cells and lymphocytes (fig. 2d). Full blood count and biochemical profile were within normal ranges. Based on the above findings, we diagnosed this patient as a case of PLC. To analyze the pathogenesis of PLC, we performed immunohistochemical staining for CD163 and IL-17, which revealed the dense infiltration of CD163⁺ cells in the superficial to mid dermis and scattered IL-17-producing cells in the superficial to mid dermis. We treated the patient with topical 0.1% tacrolimus twice a day and though her erythema remained, the pruritus improved two months after the administration of topical tacrolimus.

Discussion

In this report, we describe two cases of PLC successfully treated with topical tacrolimus and an immunohistochemical study. Our present data shed light on the possible mechanisms in the successful treatment of PLC by topical tacrolimus.

PLC is a skin disorder characterized by a chronic course and benign plasma cell infiltration around the openings of the human body, such as the lips, oral mucous, pudendum and anus [1, 2]. It is histologically characterized by dense plasma cell infiltration of the lamina propria. Clinical signs typically include glossy redness, edematous swelling, erosions and ulceration. The pathogenesis of PLC is still unclear. Several hypotheses have been suggested: (1) chronic exogenous stimuli (dental metal, sunlight, smoking); (2) senile changes in elastic

fibers; (3) endocrine secretions; (4) hypertension or change of blood pressure, and (5) metabolic abnormalities such as diabetes mellitus [2, 3]. More recently, Saruya et al. [2] reported the efficacy of fucidic acid for PLC and concluded that fucidic acid might suppress cytokines such as IL-2, interferon-gamma, IL-1, IL-6 and others. This recent report suggested the contribution of proinflammatory cytokines to the pathogenesis of PLC.

For the above reasons, we used immunohistochemical staining for CD163, which was reported to produce proinflammatory cytokines such as IL-23 [4] and IL-17-producing cells, which are differentiated under the control of IL-1 β , IL-6 and IL-23 [5]. As in our previous report suggested [6], we treated all cases with topical administration of tacrolimus ointment, which is reported to increase the number of IL-10-producing cells and enhance the production of TGF- β [7], which might suppress the production of proinflammatory cytokines. In one of our present cases, indeed, the eruption diminished during two months of topical administration of 0.1% tacrolimus. In the other case, though slight erythema was still observed, there was a substantial improvement of the pruritus. In the aggregate, topical administration of tacrolimus might suppress proinflammatory cytokines and induce immunosuppressive cells in PLC. Further studies including more patients are needed to confirm the potential effect of topical administration of tacrolimus ointment on CD163⁺ macrophages and IL-17-producing cells in the pathogenesis of PLC.

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Fujimura et al.: Successful Treatment of Plasmacytosis Circumorificialis with Topical Tacrolimus: Two Case Reports and an Immunohistochemical Study



Fig. 1. Case 1: erosive erythema around the labium minor and external urethral meatus before (a) and after (b) the administration of topical tacrolimus. Case 2: erythema around the labium minor with pitted purpura (c).

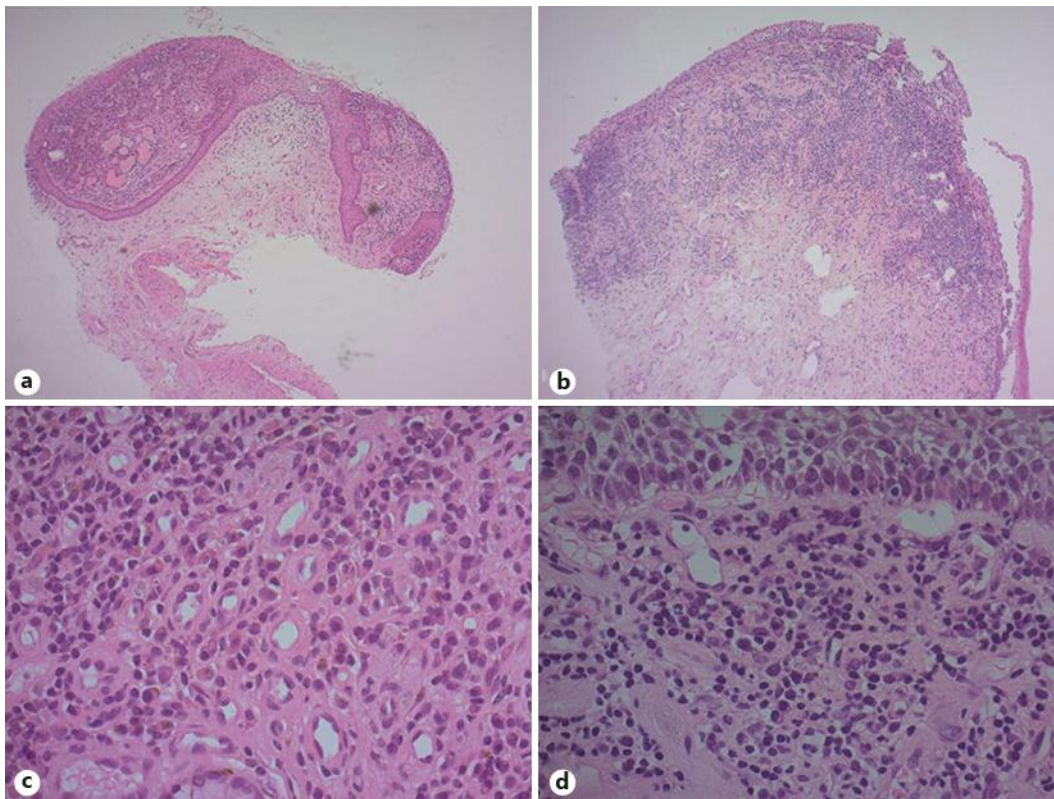


Fig. 2. Prominent cellular infiltrate in the superficial to mid dermis (a, b). The infiltrating cells were mainly composed of plasma cells and lymphocytes (c, d). Original magnification: $\times 50$ (a, b), $\times 400$ (c, d). Case 1: a, c; case 2: b, d.

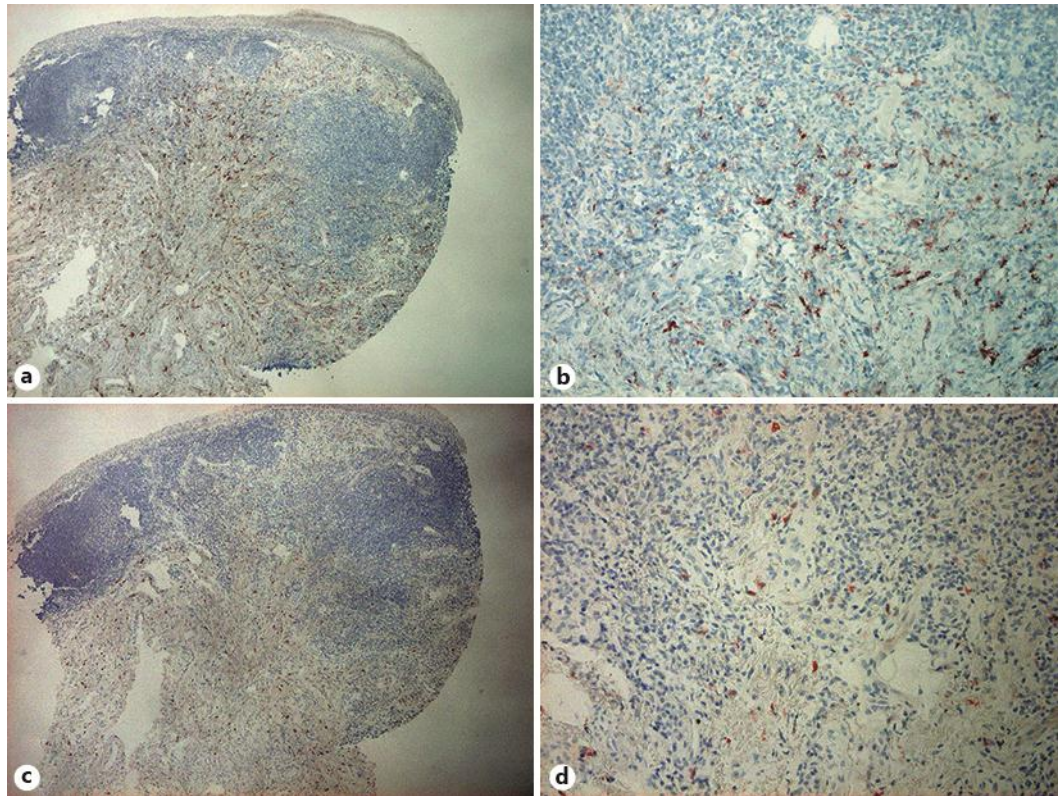


Fig. 3. Paraffin-embedded tissue samples from the patient were stained as follows: the sections were developed with new fuchsin for CD163 (a, b) and IL-17 (c, d). Original magnification: $\times 50$ (a, c), $\times 200$ (b, d).