Single Case

The Rare Case of Pemphigus Vegetans in Association with Malnutrition Children in the Multidisciplinary Management

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Keywords
Autoimmune disease · Malnutrition · Pemphigus vegetans

Abstract
Pemphigus vegetans is a clinical variant of pemphigus vulgaris, accounting for 1–2% of all very rare pemphigus cases in children. The involvement of the oral mucosa in this disease is usually accompanied by severe pain that aggravates the patient’s malnourished condition. Conversely, malnutrition may also reduce vulnerability towards autoimmune diseases. Although pemphigus vegetans has never been reported to develop in a child with marasmus before, we encountered a case of pemphigus vegetans in a severely malnourished patient. A 12-year-old boy in marasmic condition presented with painful, clear, fluid-filled blisters, accompanied by erosions, crusts, and vegetative lesions on almost all parts of the body. Histopathological examination of the lesions revealed a suprabasal cleft, and direct immunofluorescence staining showed deposits of immunoglobulin G in the epidermal intracellular spaces. The patient was treated with a multidisciplinary approach, and intravenous corticosteroid was administered for 2 weeks with an appropriate diet. There were significant improvements in the skin lesions and his nutritional status. Although pemphigus vegetans may occur in children with malnutrition, the underlying mechanism for the development of autoimmune diseases in malnutrition remains unclear.

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Published by S. Karger AG, Basel
Introduction

Pemphigus is an autoimmune disease of the skin and mucous membrane characterized by blisters [1]. The occurrence of autoimmune bullous disease in a child is very rare [1–3]. Pemphigus vegetans is the rarest form of pemphigus, occurring only in 1–2% of all cases [2, 3]. It is characterized by vegetative plaques in the inguinal folds, flexural areas, and oral mucosa accompanied by the presence of autoantibodies against desmoglein 3 [4, 5]. The involvement of oral mucosa is usually associated with severe pain, eventually leading to weight loss and malnutrition. Malnutrition in general may reduce vulnerability towards autoimmune diseases [6]. Marasmus, a type of protein-energy malnutrition [7], could affect immunity and increase the risk of infection [8]. In this report, we would like to present the first case of pemphigus vegetans in a child with marasmus. Even though the exact underlying mechanism is yet to be fully understood, we try to describe the possible mechanisms in this condition and stress the importance of a multidisciplinary approach for a successful treatment.

Case Presentation

A 12-year-old boy in marasmic condition presented with painful, clear, fluid-filled blisters accompanied by crusts on almost the entire body. He suffered from malnutrition due to parental neglect since he was 8 years old. Three and a half years later, he complained of extreme pain in the mouth, which resulted in poor ability of oral food intake. Blisters and vegetative lesions soon followed. There was no history of bullous disorder in the patient and his family. Physical examination showed a slender body, with a height of 130 cm, a weight of 22 kg, and a BMI of 13.01. Blisters, erosions, and hemorrhagic crusts with hypertrophic verrucous vegetative plaques were found on the armpits, trunk, extremities, and in the perianal region (Fig. 1). Histopathological examination on the vegetative lesions found on the extremities revealed a suprabasal cleft with scattered acantholytic cells and hyperkeratosis. The subepithelial layer was filled with lymphocytes (Fig. 2a). Direct immunofluorescence (DIF) staining showed deposits of immunoglobulin G on the surface of the keratinocytes (Fig. 2b), which supported the diagnosis of pemphigus vegetans. The patient received 6 mg/day intravenous dexamethasone for 2 weeks. He was given a diet of 1,500 kcal/day, consisting of soft food (3 times/day) and an extra liquid diet (3 times 100 mL) as a collaborative treatment from the pediatric and nutrition departments. Significant improvements in the skin lesions and nutritional status were observed within 15 days after the start of treatment.

Discussion

Pemphigus vegetans is a rare variant of pemphigus. In certain patients, erosions have a tendency to develop into granulation tissue and crusting, known as vegetative lesions [1], often found on the groin, armpits, thighs, hands, eyelids, and in the perioral region [4]. This lesion was caused by intercellular autoantibodies against desmoglein 1 and 3 as adhesion molecules in the desmosomes of keratinocytes [1, 2]. The diagnosis of pemphigus vegetans was based on clinical features, histopathology examination, and a DIF test. Most patients initially present with stomatitis [9], which was also the case in our patient. Diagnostic findings for pemphigus vegetans included eosinophilic spongiosis, suprabasal acantholysis, epi-
dermal hyperplasia, and intraepidermal abscesses filled with eosinophils as the lesions age [10], while DIF examination showed deposits of immunoglobulin G and complement C3 on the keratinocytes [2], which were evident in the biopsy of our patient’s vegetative lesions.

Concurrent development of autoimmune bullous disease and marasmus indicated the variability of the immunological mechanisms of the disease. Gerriets et al. [6] presented a case of malnutrition leading to decreased adipocyte mass, thus changing the CD4+ and CD8+ count and by extension, their functions. This condition is associated with a decrease in Th1 cytokines interleukin-2 and interferon-γ, eventually resulting in an increased susceptibility to infection and protection against autoimmunity. On the other hand, a case report by Bull et al. [11] showed an association between human immunodeficiency virus (HIV) infection and autoimmune bullous diseases. One possible underlying mechanism for autoantibody production in this disease was as a part of nonspecific polyclonal stimulation seen in the early-stage HIV disease. Another possible underlying mechanism was that the loss of specific immunomodulatory CD4+ allows the expansion of B-cell clones responsible for the production of autoantibody. Assuming that patients with malnutrition have similar conditions as HIV-infected patients, alteration of CD4+ function may be considered as one possible underlying mechanism for the development of autoimmune disease in malnutrition. However, this does not explain autoantibody production in malnourished conditions.

This finding suggests that marasmus may have several effects on the immune system, leading to the development of autoimmune bullous disease. Other related cases could further enlighten us of the complex association between autoimmune diseases and marasmus.

Treatment of pemphigus vegetans is similar to that of pemphigus vulgaris. Systemic corticosteroids are the treatment of choice for these diseases. Prednisone is usually administered in a dosage of 1–2 mg/kg body weight/day [12]. This patient received 6 mg/day intravenous dexamethasone (equals to 2 mg/kg body weight/day of prednisone) for 2 weeks, and there was a significant improvement in his skin condition, indicated by the lack of new lesions. An appropriate ongoing intravenous fluid regimen was started under the guidance of the medical team. From the pediatric and nutrition departments, the patient was given an appropriate nutritional plan. The patient’s initial weight at admission was 22 kg, and after 2 weeks of treatment, it had increased to 23.7 kg. With this case report we hope to add to the knowledge of the underlying mechanism of pemphigus vegetans in marasmus patients and the importance of a multidisciplinary approach to improve outcomes.

Acknowledgements

The authors thank the staff of the Departments of Dermatology and Venereology, Department of Pediatrics, and Department of Nutrition, Dr. Hasan, Sadikin Hospital Bandung, for helpful assistance, and Hermin Aminah Usman, MD, for histopathology expertise.

Statement of Ethics

The authors have no ethical conflicts to disclose.
Disclosure Statement

The authors have no conflicts of interest to disclose.

References

1. Stanley JR, Payne AS: Pemphigus; in Wolff K, Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffel DJ (eds): Fitzpatrick's Dermatology in Medicine, ed 8. New York, McGraw-Hill 2012, pp 585–599.
2. Cozzani E, Christina K, Mastrogiacomo A, Rampini P, Drosena M, et al: Pemphigus vegetans Neumann type with anti-desmoglein and anti-periplakin autoantibodies. Eur J Dermatol 2007;17:530–533.
3. Korman NJ: Pemphigus. Dermatol Clin 1990;8:689–700.
4. Yuen KL, Yau KC: An old gentlemen with vegetative plaques and erosions: a case of pemphigus vegetans. Hong Kong J Dermatol Venereol 2012;20:179–182.
5. Son YM, Kang HK, Yun JH, Roh JY, Lee JR: The Neumann type of pemphigus vegetans treated with combination of dapsone and steroid. Ann Dermatol 2011;23(suppl 3):S310–S313.
6. Gerrits VA, Maciver NJ: Role of T cells in malnutrition and obesity. Front Immunol 2014;5:379.
7. Buchanan A, Marquez M: Pediatric nutrition and nutritional disorders; in Nelson Essentials of Pediatrics, ed 7. Philadelphia, Elsevier 2015, pp 86–105.
8. França TGD, Ishikawa LLW, Zorzella-Pezavento SFG, Chiuso-Minicucci F, da Cunha MLRS, Sartori A: Impact of malnutrition on immunity and infection. J Venom Anim Toxins Incl Trop Dis 2009;15:374–390.
9. Sillevis Smitt JH, Mulder TJ, Albeda FW, Van Nierop JC: Pemphigus vegetans in a child. Br J Dermatol 1992;127:289–291.
10. Wu H, Brandling-Bennet HA, Harrist TJ: Noninfectious vesiculobullous and vesiculopustular diseases; in Elder DE, Elenitsas R, Johnson BL Jr, Murphy GF, Xu X (eds): Lever’s Histopathology of the Skin, ed 10. Philadelphia, Lippincott Williams & Wilkins, 2009, pp 250–251.
11. Bull RH, Fallowfield ME, Marsden RA: Autoimmune blistering diseases associated with HIV infection. Clin Exp Dermatol 1994;19:47–50.
12. Gupta MT, Jerajani HR: Control of childhood pemphigus erythematosus with steroids and azathioprine. Br J Dermatol 2004;150:163–164.
Fig. 1. Clinical appearance before and after therapy. Ventral trunk (a), dorsal trunk (b), face(c), and hypertrophic verrucous vegetative plaques on the armpit (d).
Fig. 2. a Histopathological results of the vegetating lesions on the extremities revealed a suprabasal cleft with scattered acantholytic cells and hyperkeratosis. The subepithelial layer was filled with lymphocytes (hematoxylin and eosin. ×100). b Direct immunofluorescence staining (DIF) showed deposits of immunoglobulin G (green color) in the epidermal intracellular spaces, which is characteristic of pemphigus (DIF. ×400).