A Case of Neumann Type Pemphigus Vegetans Showing Reactivity with the 130 kD Pemphigus Vulgaris Antigen

Sir,

Two major types of pemphigus are defined. Suprabasal clefting is seen in pemphigus vulgaris (PV) and its vegetating form, pemphigus vegetans (PVeg). More superficial bullae are found in pemphigus foliaceus (PF) and its variant form, pemphigus erythematosus. PVeg is a rare variant of pemphigus and characterized by blisters and erosions associated with verrucous vegetations (1–5). Clinical and histologic findings suggest two subtypes. The Hallopeau type starts with circumscribed pustules, which histologically show eosinophilic intraepidermal pustules, and has a relatively benign course. The Neumann type is seen more commonly but develops extensive lesions that are often refractory to therapy (1). In this study, we present a case of Neumann type of PVeg, whose serum reacted with the PV antigen with immunoblot analysis.

CASE REPORT

A 30-year-old Japanese male first noticed acneiform eruptions on the trunk in September 1991. In January 1992, he developed oral mucosal lesions, and the pathologic examination suggested the diagnosis of PV. He was treated with oral prednisolone for about one year. Several psychiatric medications were also administered for the treatment of schizophrenia, insomnia and AIDS phobia. In April 1993, he developed generalized skin lesions and was referred to our hospital. Physical examinations revealed flaccid bullae and erosions with crust formation, up to 2 cm in size, on the entire body, particularly on the upper trunk. The entire oral mucosa was involved, with painful erosive lesions, and vegetating lesions were seen on the tongue and lips. The tongue had a lingua-plicata-like appearance (Fig. 1) (2). Papillomatous vegetating lesions were also seen on the nape and upper back as well as on intriginous areas, such as the armpits, groin and perianal regions.

A skin biopsy taken from the vegetating lesion on the upper back showed hyperkeratosis, acanthosis and spongiform abscess formation in the entire epidermis, as well as acantholysis and villi in the suprabasal area. Direct immunofluorescence demonstrated intercellular deposition of IgG throughout the epidermis and of C3 in the lower epidermis. Indirect immunofluorescence of normal human skin demonstrated IgG anti-intercellular antibodies at a titer of 1:2,560.

To identify the antigen molecules in this case, Western immunoblot analysis was performed using extract of EDTA-separated human epidermis as an antigen source (6) (Fig. 2). With this assay, one control PV serum detected only the 130 kD PV antigen (PVA) (lane 2), another PV serum reacted with the PV antigen and weakly with the 160 kD PF antigen (PFA) (lane 3), and control PF serum reacted with the PF antigen (lane 4). The serum of the present case reacted clearly and exclusively with the PV antigen (lane 1).

Under the diagnosis of PVeg, treatment began with oral prednisolone, 25 mg daily. Erosive lesions gradually disappeared, but with some recurrence. The dose of prednisolone could not be increased because of the existence of bacteremia. Therefore, plasma exchange and oral dapsone were added. This combination treatment was very effective and the skin condition rapidly improved. Thereafter, as psychosis was highly exacerbated, the patient was referred to another psychiatric hospital, where the patient was well controlled on a maintenance dosage of prednisolone. However, the titer of the intercellular autoantibodies was not significantly reduced in spite of the clinical remission.

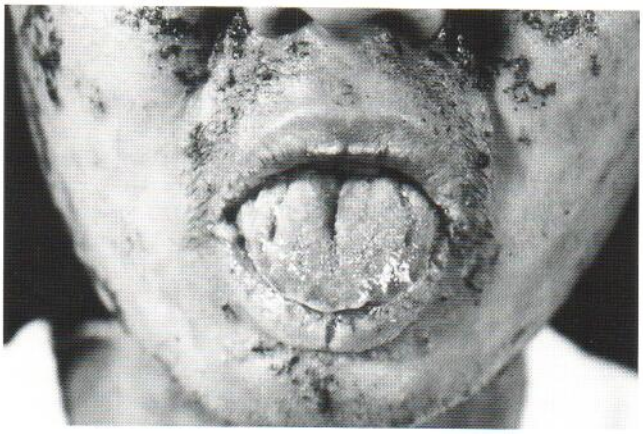

Fig. 1. Clinical appearance. Erosive and vegetating lesions on the tongue and lips.

DISCUSSION

PVeg comprises less than 1–2% of all cases of pemphigus. All the clinical and histological features and the disease course suggested that the patient presented in this study was a typical case of Neumann type of PVeg.

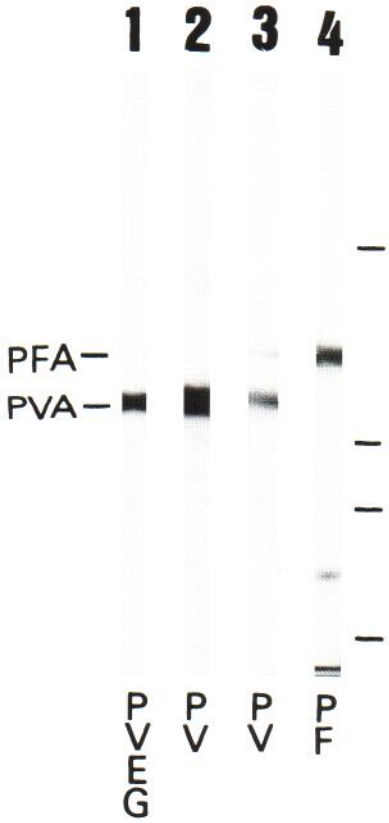

Fig. 2. Results of Western immunoblotting. *Lane 1*: the present case. *Lanes 2–4*: controls. The bars in the right indicate the positions of molecular markers, from top to bottom, 200 kD, 116 kD, 97 kD and 66 kD. *PVEG*: pemphigus vegetans; *PV*: pemphigus vulgaris; *PF*: pemphigus foliaceus.

It is well known that PV antigen is a 130 kD transmembranous desmosomal cadherin-type glycoprotein (desmoglein 3; Dsg3) (6,7), whereas PF sera react with the 160 kD PF antigen (desmoglein 1; Dsg1). There are very few reports concerning antigens with which PVeg sera react. Parodi et al. reported that serum of Neumann type of PVeg reacted with the 130 kD PV antigen, as well as a number of other proteins, with immunoprecipitation assay (3). We also reported that the sera of two cases of Hallopeau type of PVeg reacted with the 130 kD PV antigen with immunoblotting of human epidermal extract (8), although in addition these sera reacted with bovine desmocollin, another group of desmosomal cadherin. These results suggest that the PV antigen is target antigen for PVeg. However, since there are obvious differences between PVeg and PV, it is also possible that other antigen(s) may be involved in the pathogenesis of PVeg.

In the present study, the 130 kD protein detected by our patient's serum co-migrated with the PV antigen reacted by sera of typical PV patients. Although the possibility cannot be completely excluded that our patient's serum detected a different protein with the same molecular size as that of PV antigen in the one-dimensional gel, the strong and exclusive reactivity with the 130 kD protein clearly indicates that this serum reacted with the PV antigen. To the best of our knowledge, this is the first case of Neumann type of PVeg, shown to react with the PV antigen with immunoblotting of epidermal extracts.

The mechanisms by which PV and PVeg develop different clinical manifestations are still unknown, although these diseases show indistinguishable immunological findings. To understand the pathogenesis of PVeg, further examinations for more PVeg cases will be necessary, such as cytokines that induce epidermal proliferation and eosinophilic chemotaxis.

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Yoshiyuki Ohata, Hiroko Komiya, Yoshie Kawahara, Kyoko Watanabe, Takeji Nishikawa and Takashi Hashimoto*
Department of Dermatology, Keio University School of Medicine, 35 Shinanomachi, Shinjuku, Tokyo 160, Japan.
*Reprint requests.