Paraneoplastic Pemphigus with Widespread Mucosal Involvement

Mami Wakahara[1], Takahiro Kiyohara[1], Masanobu Kumakiri[1], Takanori Ueda[2], Kazumori Ishiguro[1], Tomozo Fujita[3], Masayuki Amagai[4] and Takashi Hashimoto[5]
[1]*Department of Dermatology and* [2]*1st Internal Medicine, Faculty of Medical Sciences, University of Fukui, 23-3 Shimoaizuki, Matsuoka-cho, Yoshida-gun, Fukui 910-1193* [3]*Fujita Memorial Hospital, Fukui,* [4]*Department of Dermatology, School of Medicine, Keio University, Tokyo and* [5]*Department of Dermatology, School of Medicine, Kurume University, Fukuoka, Japan. E-mail: kinari@yo.mitene.or.jp*
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Sir,

Paraneoplastic pemphigus (PNP) was first characterized as a distinct entity in 1990 by Anhalt et al. (1). The term was proposed to describe an autoimmune mucocutaneous disease linked to an underlying lymphoproliferative neoplasm. Unlike pemphigus vulgaris (PV), patients with PNP have circulating autoantibodies reactive to desmoplakins, and desmosomal plaque proteins present in all epithelia. It is therefore not surprising that PNP may involve more extensive epithelial surfaces than PV (2). We here describe a patient with PNP who presented with widespread mucosal involvement of oral mucosa, oesophagus, stomach and bulbus duodeni.

CASE REPORT

A 70-year-old man presented with widespread annular erythemas with peripheral blisters on the entire body and oral

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erosions (Fig. 1). An oesophagogastroduodenoscopy demonstrated panoesophagitis with multiple ulcerations (Fig. 2a). In addition, there were flare and erosions in the stomach and bulbus duodeni. A skin biopsy specimen showed liquefaction degeneration and suprabasal cleft accompanied by eosinophilic spongiosis. Biopsy specimens from the oesophagus and bulbus duodeni revealed suprabasal clefts and acantholytic cells with tombstone appearance (Fig. 2b). A stomach biopsy specimen showed liquefaction degeneration and eosinophilic spongiosis. Direct immunofluorescence of the skin lesion showed deposits of complement at the cell surface of the epidermis and the dermal–epidermal junction. Indirect immunofluorescence was positive on rat bladder epithelium. Immunoprecipitation studies demonstrated a complex of four proteins with molecular weights of 250 kDa, 230 kDa, 210 kDa and 190 kDa, confirming the diagnosis of PNP. A computed tomography scan of the abdomen showed a large retroperitoneal mass around the abdominal aorta. A biopsy specimen from the intra-abdominal mass revealed diffuse large B-cell lymphoma. The pemphigus lesions disappeared after multi-agent chemotherapy for lymphoma.

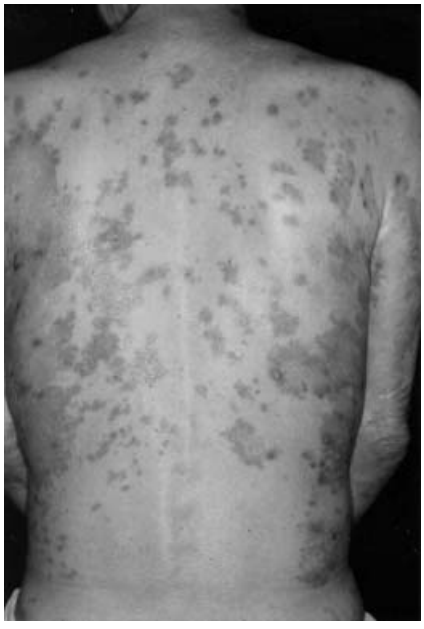

Fig. 1. Widespread annular erythemas with peripheral blisters on the entire body.

DISCUSSION

Histopathological changes of PNP involve keratinocyte necrosis, intra-epidermal acantholysis and interface vacuolar dermatitis. Direct immunofluorescence shows cell surface deposits of IgG and complement, and often linear or granular deposits of complement at the dermal–epidermal junction. Indirect immunofluorescence demonstrates circulating antibodies binding to simple, columnar and transitional epithelia in addition to the typical pemphigus pattern. These circulating autoantibodies immunoprecipitate a high molecular weight protein complex of 250 kDa, 230 kDa, 210 kDa, 190 kDa and 170 kDa. It is the gold standard for the diagnosis of PNP. Furthermore, rat bladder epithelium has been found to be a particularly useful substrate and is highly specific for PNP (3).

The distinctive clinical findings in PNP include intractable stomatitis and polymorphous skin lesions. Mucosal involvement is almost always present (4), such as the conjunctiva, oral mucosa, pharynx, larynx and vulva. Refractory stomatitis is the most constant clinical feature in PNP patients (5). PNP may also involve all surfaces of the oropharynx and extend onto the vermilion border of the lips. The skin lesions may be generalized or limited in distribution. Involvement limited to the oral mucosa has also been described (6).

Oesophageal involvement has been reported in PV (7). There have been five case reports of PNP with oesophageal involvement (1, 2, 4, 8, 9). However, only two cases have demonstrated oesophageal lesions histopathologically (2, 4). To our knowledge, this is the first description of PNP with widespread mucosal involvement of the oral mucosa, oesophagus, stomach and bulbus duodeni. An oesophagogastroduodenoscopy examination and biopsy specimens from oesophagus, stomach and bulbus duodeni demonstrated widespread involvement by PNP. Multi-agent chemotherapy (CHOP) regimen improved the lymphoma mass followed by the disappearance of PNP lesions, which suggested that the PNP lesions in the present case were a definite paraneoplastic condition.

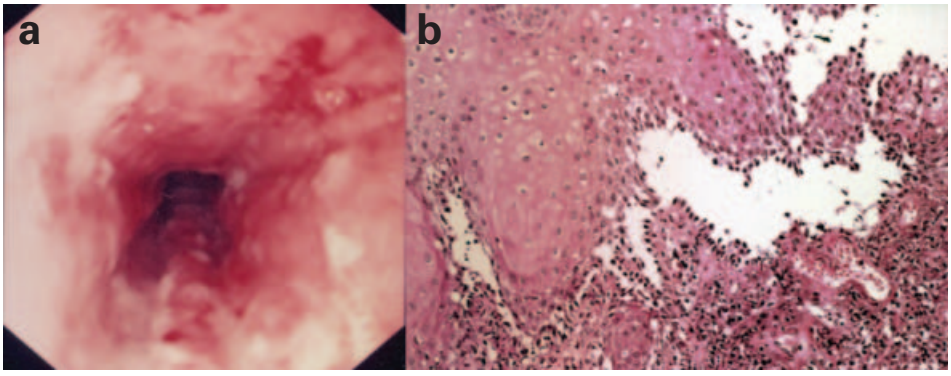

Fig. 2. (a) An oesophagogastroduodenoscopy demonstrated panoesophagitis with multiple bullae and ulcerations. (b) An oesophageal biopsy specimen revealed suprabasal cleft formation and acantholysis with tombstone appearance.

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