Pemphigus

Frank A. Santoro, MD[a,b], Eric T. Stoopler, DMD, FDS RCSEd[c], Victoria P. Werth, MD[b,d,*]

KEYWORDS

• Pemphigus • Paraneoplastic pemphigus • Oral erosions • Stomatitis
• Blistering disorder • Acantholysis • Rituximab

KEY POINTS

- Pemphigus vulgaris and paraneoplastic pemphigus manifest as flaccid mucosal bullae leading to erosions.
- Mucosal biopsy and direct immunofluorescence are necessary to differentiate pemphigus vulgaris and paraneoplastic pemphigus from other mucosal diseases. Indirect immunofluorescence and enzyme linked immunosorbent assays can aid in the diagnosis and be may be useful to monitor disease activity.
- Paraneoplastic pemphigus is normally associated with an underlying malignancy, usually of lymphoid origin. A complete blood count, computed tomography scan of the chest, abdomen, and pelvis, and a bone marrow biopsy may be indicated.
- Immunosuppressive agents can be used as steroid-sparing agents.
- Rituximab, an anti-CD20 monoclonal antibody, helps in treatment-refractory pemphigus vulgaris. Defining the role of rituximab in earlier disease, and well as its safety profile, will require larger prospective studies.

Disclosures for Authors: None.
This material is supported by the National Institutes of Health, including NIH K24-AR 18 02207 (Werth) and by the Department of Veterans Affairs, Veteran Health Administration Office of Research and Development, Biomedical Laboratory Research and Development. A mentorship award from the Medical Dermatology Society supported Dr Santoro.
[a] Department of Dermatology, Henry Ford Hospital, 3031 West Grand Boulevard, Suite 800, Detroit, MI 48202, USA; [b] Department of Dermatology, Philadelphia VA Medical Center, 3900 Woodland Avenue, Philadelphia, PA 19104, USA; [c] Department of Oral Medicine, University of Pennsylvania School of Dental Medicine, 240 South 40th Street, Philadelphia, PA 19104, USA; [d] Department of Dermatology, Perelman Center for Advanced Medicine, University of Pennsylvania, Suite 1-330A, 3400 Civic Center Boulevard, Philadelphia, PA 19104, USA
* Corresponding author. Perelman Center for Advanced Medicine, University of Pennsylvania, Suite 1-330A, 3400 Civic Center Boulevard, Philadelphia, PA 19104.
E-mail address: werth@mail.med.upenn.edu

Dent Clin N Am 57 (2013) 597–610
http://dx.doi.org/10.1016/j.cden.2013.06.002 **dental.theclinics.com**
0011-8532/13/$ – see front matter Published by Elsevier Inc.

INTRODUCTION AND EPIDEMIOLOGY

Introduction

Nature of the problem

Pemphigus is a group of chronic blistering disorders of the skin and mucosal membranes. Autoantibodies are directed against cell-cell adhesion molecules of keratinocytes, thereby causing loss of adhesion or acantholysis. Although there are 5 major categories of pemphigus (pemphigus vulgaris, pemphigus foliaceus, paraneoplastic pemphigus [PNP], drug-induced pemphigus, and IgA pemphigus), only pemphigus vulgaris and PNP typically have oral involvement.

Definition

The word pemphigus originates from the Greek word *pemphix*, which translates into blister or bubble. The blisters result from acantholysis. PNP was recognized as a distinct entity in 1990[1] after various reports[2–6] associated pemphigus and malignancy, usually of lymphoid tissue.

Symptom criteria

Symptom criteria for pemphigus vulgaris

- Painful erosions in the mouth; ± oropharyngeal and/or esophageal involvement. Fifty percent of patients with pemphigus vulgaris have isolated oral lesions.
- Flaccid bullae and erosions on the body can accompany oral disease.

Symptom criteria for PNP[7]

- Painful, progressive stomatitis
- Acantholysis or lichenoid/interface inflammation on histopathology
- Presence of anti-plakin antibodies
- Presence of an underlying lymphoproliferative disorder

Pathogenesis

In pemphigus vulgaris, immunoglobulin (Ig) G autoantibodies against desmogleins, one of the prominent cell adhesion molecules of the desmosome, cause a loss of cell adhesion.[8] This loss of adhesion results in acantholysis. Desmoglein-1 (Dsg-1) is expressed in all layers of the epidermis with a higher concentration in the more superficial layers, whereas desmoglein-3 (Dsg-3) is expressed in the parabasal and basal layers. In the mucosa, Dsg-1 and Dsg-3 are expressed throughout all layers of the epidermis; however, the mucosa has lower concentrations of Dsg-1. Patients with mucocutaneous pemphigus vulgaris have detectable autoantibodies directed against Dsg-1 and Dsg-3, whereas patients with only mucosal disease have antibodies targeted against only Dsg-3.[9,10] The triggering event leading to antibody formation is unknown.

Patients with paraneoplastic pemphigus also have autoantibodies against Dsg-1 and Dsg-3. In addition, PNP has antibodies targeted against proteins in the plakin family (plectin, desmoplakin I, desmoplakin II, bullous pemphigoid antigen I, envoplakin, and periplakin). These plakin proteins are also involved in cell-cell adhesion of keratinocytes.

Prevalence/Incidence and Worldwide/Regional Incidence

The overall incidence of pemphigus is estimated at 0.076 to 5,100,000 person-years.[11] The incidence of pemphigus vulgaris is higher in women (male:female; 1:1.1–2.25) and the Ashkenazi Jewish population. Because there is regional and ethnic clustering of pemphigus, there is likely a genetic component, and recently ST18, a gene regulating