Chapter 2
Overview of Pemphigus Vulgaris

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Introduction

Pemphigus is originated from the Greek word *pemphix* meaning bubble or blister. Pemphigus vulgaris (PV) is a life-threatening chronic autoimmune disease where the serum autoantibodies respond to the cell surface antigens resulting in a loss of epidermal cell cohesion [1]. This can be characterized as the manifestation of circulating autoantibodies against the intercellular adhesion structures, desmosomal protein desmoglein (DSG) 3, and in some cases DSG1. However, there is accumulating evidence that indicates that pemphigus vulgaris also targets other, nondesmoglein, molecules. The functional role of these other specificities and their impact on disease expression are yet to be fully elucidated [2–4].

Disruption of the cell-cell and cell-matrix adhesion due to the circulating autoantibodies results in acantholysis, which could result in Tzanck phenomenon—the rounding of single epidermal cells due to the loss of cell-cell attachment [1].

Desmoglein proteins are a type of cadherin, which is a transmembrane protein that binds with other cadherins to form junctions known as desmosomes between cells [5]. These desmoglein proteins thus hold cells together, but when the body starts producing antibodies against desmoglein, these junctions break down, and this results in subsequent blister or vesicle formation.

Initially, PV is expressed in the form of intraoral lesions, which then spread to other mucus membranes and skin, causing cutaneous and mucosal blistering. This disease is commonly seen in the elderly population, and 50 % of the cases primarily display oral lesions in the form of blisters (within the epidermis) that quickly rupture causing patients to suffer excruciating erosions [6]. Patients can develop lesions anywhere within the oral cavity; however, the soft palate, buccal mucosa, and lips are shown to be more commonly involved [6].

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There are two dominant clinical variants of pemphigus vulgaris: one is the mucocutaneous variant and the other is the mucosal dominant variant [7]. The mucosal dominant variant of pemphigus vulgaris involves autoantibodies against only desmoglein 3, whereas the mucocutaneous variant involves autoantibodies against both desmoglein 1 and 3. Pemphigus vulgaris has the two variants, and the clinical features of these two variants can also be explained based on desmoglein expression. The mucocutaneous variant that involves autoantibodies against desmoglein 1 and 3 causes mucosal erosions and deep skin blisters. The mucosal dominant variant that involves antibodies against desmoglein 3 only causes mucosal erosions and no skin lesions, because the desmoglein 1 in the lower epidermal layers makes up for the lack of desmoglein 3. However, in the mucous membranes, there is not enough desmoglein 1 to make up for the lack of desmoglein 3, since desmoglein 3 is expressed in greater quantity than desmoglein 1 in the mucous membranes. There are, however, a small group of patients that never had mucosal lesions (no current or history of mucosal lesions), classified as cutaneous-only pemphigus vulgaris, whose disease presentation cannot be fully explained by the distinct expression patterns of desmoglein 3 or 1. It remains to be determined if this group of patients is linked to the presence of autoantibodies to nondesmoglein targets.

If left untreated, pemphigus vulgaris can be fatal. This may be due to the complications of ulceration. For instance, if the erosions get infected, it may cause the patients to become septic [8]. The erosions stem from a lack of cohesion among the epidermal or mucosal layer of cells, and this disrupts the function of these cells to retain water, thus resulting in fluid loss as a complication of the disease [7]. Since the blisters are very fragile and rupture easily, physicians rarely are able to find intact blisters [7].

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