Chapter 4
Epidemiology and Etiology

Epidemiology

Pemphigus vulgaris (PV), an autoimmune blistering disease, is a rare disease with an estimated worldwide yearly incidence of 0.1–0.5 per 100,000 populations [1, 2]. PV is also the most common form of pemphigus. The occurrence is mostly common in middle-aged and older adults between the ages 50 and 60 years, although there have been a few cases in children [1]. PV has a male-to-female ratio of 1:2, showing a higher incidence in women [3]. A study conducted by Gupta et al. in 2011 also found that more women than men suffer from PV and they resonated this to the female predominance reported in several other autoimmune diseases [2]. Nonetheless, it was noted that there are restricted number of studies on pemphigus that do not depict female supremacy. Though PV can occur in people of all racial and ethnic backgrounds, it has the highest incidence in Ashkenazi Jews. PV is known as one of the most common pemphigus diseases, accounting for about 70% of all pemphigus cases in India, China, Malaysia, and the Middle East [4].

Etiology

The etiology of pemphigus vulgaris is still unknown. It is a complex disease, where susceptibility is multifactorial, involving both genetic and environmental factors (most of which are unknown) [5, 6]. PV involves the body creating antibodies to desmoglein cadherin proteins that form the intercellular junctions between epithelial cells, but the specific cause of attack by the immune system is not known [1]. It has been speculated that viral infections may be involved in the production of autoantibodies. The more frequent occurrence of PV in Ashkenazi Jews and those of Mediterranean origin may point toward a strong genetic basis [3]. PV has also been found to demonstrate a strong association with certain human leukocyte antigen

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(HLA) class II alleles [3]. There seems to be a strong genetic link between pemphigus vulgaris and having the HLA-DR4 and HLA-DR6 HLA types, since about 95% of people who have pemphigus vulgaris also have one or both of these HLA types [5, 6].

On the other hand, environmental factors may also play a role in the progression of this life-threatening blistering disease. Some initiating factors include foods with high garlic content, infections, neoplasms, and drugs—in particular those in the thiol group such as captopril, penicillamine, and rifampicin [3]. A survey study of 126 PV patients found that patients who were smoking cigarettes experienced an improvement in PV, while nonsmokers experienced worsening in their condition [7]. This can be explained by the antiestrogenic effects of smoking, which seem to be contributing to the protective effect in PV. Furthermore, activation of nicotinic cholinergic receptors on keratinocytes stimulates calcium influx, which increases cell-cell adhesion and promotes lateral migration of keratinocytes improving the symptoms of PV [7]. The study also found an increase in the risk of developing PV with increased exposure to pesticides and metal vapor. Pesticides may contribute to the disease process due to its estrogenic effect. It is yet to be determined whether preventing exposures to pesticides and metal vapor may be advantageous in the clinical context [7]. There have also been hypothesized drug triggers for PV, which include medications that contain thiol groups, for example, rifampicin. Neoplasms have also been hypothesized to trigger pemphigus vulgaris in some cases. Other environmental factors have also been hypothesized to play a part in autoimmune antibody formation, for example, ultraviolet (UV) rays and stress [4]. All in all, there seems to be an interaction between genetic and environmental factors in the development of PV.

References

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