PEMPHIGUS VULGARIS

The blistering oral and skin lesions of vesiculbullous Pemphigus

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The most common of the pemphigoid disorders, pemphigus vulgaris, is a potentially fatal autoimmune condition characterized by blistering lesions.

What is Pemphigus Vulgaris?

Pemphigus vulgaris (PV) is a rare autoimmune mucocutaneous (affecting skin and mucous membranes) disorder characterized by blistering of the skin and mucous membranes. The disorder is caused by a loss of integrity of the normal intercellular attachments within the skin's epidermis and the mucosal epithelium, which are associated with autoantibodies to desmoglein-3. The blisters in PV resemble burn-like lesions and their severity ranges from mild to severe and life-threatening.

What are Pemphigoid Disorders?

The word pemphigus is derived from the Greek word pemphix, which means bubble or blister. Pemphigus disorders are chronic bullous or blistering diseases in which patients have circulating antibodies directed against the cell surface of tissue cells known as keratocytes. Pemphigus vulgaris is the most common of the pemphigus disorders and accounts for about 70 percent of all cases of pemphigus. The other forms of pemphigus are described in my recent blog article on Pemphigus Disorders. For information on other causes of autoimmune bullous skin disease, see Autoimmune Bullous Skin Disease.

Disease course

Untreated, PV runs a chronic course with lesions occurring all over the body. Untreated, the sores may not heal or they may require a long time for healing. Untreated, PV is usually fatal with most morbidity occurring as a consequence of infection. With treatment, the blisters in PV are able to heal although blisters tend to recur for life. Treatment does not cure PV, but it lessens the effects of the disease, relieves pain, and slows the immune response. Still, mortality is high at 5-15 percent with most mortality caused by consequences of high-dose corticosteroid therapy treatment.

Symptoms

Most people diagnosed with PV first notice blisters in their mouth or on their skin. The blistering lesions of PV resemble flaccid blisters containing clear fluid that erupt on normal or reddened skin. These lesions may be confused with and misdiagnosed as fungal or bacterial infections. Affected skin is usually painful, but it does not itch. The blisters are fragile and are rarely found intact. Ruptured blisters result in erosions.
Besides the skin, the nails may be affected. Ordinary PV erosions may develop vegetation in the form of excessive granulomatous skin folds, particularly on the scalp or face.

The Nikolsky sign suggests a diagnosis of PV. Patients with this sign have active blistering, and firm sliding of the finger over an affected area causes erosions or tears in the skin. Another characteristic sign, the Asboe-Hansen sign, occurs when pressure applied to the edge of a blister spreads the blister into the skin.

In 50-70 percent of patients PV blisters occur on the mucous membranes. Most patients with oral involvement develop ill defined, irregular erosions appearing on the gums, buccal cavity (inner cheeks, jaw) or upper palate. Other sites of mucosal involvement include the conjunctiva (inner lining of the eye), esophagus, penis, labia, urethra, and anus.

Who is Affected?

Similar to other autoimmune diseases, PV occurs in people who are genetically predisposed to developing it (association with DRB1 MHC II alleles) who are exposed to certain environmental triggers. Pemphigus vulgaris affects people of all races although the highest prevalence is seen in regions where there is a high Jewish population especially those of Ashkenazi descent and in the populations of northern India and Asia. In Jerusalem, the prevalence of PV is estimated to be 1.6 cases for every 1 million people. In Finland the prevalence is 0.76 per million.

Males and females are affected equally, and the mean age of onset is 40-60 years although people of all ages, including children, may be affected. When PV is seen in newborns, it is usually a transient condition related to maternal passive transfer of antibodies. When these antibodies leave the circulation (within 2-3 months), symptoms resolve.

Environmental Triggers

Several drugs have been implicated in causing PV. Drug-induced PV is most likely to occur in patients on rifampin, penicillamine and other thiol-containing compounds. Stress is also reported to trigger PV. PV often develops in people with other autoimmune diseases, especially myasthenia gravis. Mercury contamination is also linked to PV. Studies in rural areas of South America and Tuynisia suggest that pemphigoid disorders can be triggered in susceptible individuals by a form of antigenic mimicry that occurs between demoglein and an unidentified infectious agent.

In one recent report, an Israeli man developed severe PV after being treated with glibenclamide for diabetes and the ACE inhibitor cilazapril for hypertension. Researchers determined that both medications caused the PV. After discontinuing these medications, symptoms resolved.
**Diagnosis**

Tissue studies of blisters as well as normal-appearing skin are examined in patients suspected of having PV by immunofluorescent techniques. Characteristic changes include antibodies to skin components (desmyoglein) and changes in keratinocytes. The earliest changes are seen in the basal cell layer. The superficial dermis contains a mild increase in eosinophil cells. Blood tests for IgG desmoglein-3 autoantibodies are also used to diagnose PV.

**Treatment**

The blistering in PV is treated in a manner similar to that of treatment for burns. Patients with severe blistering may be hospitalized and treated with intravenous fluids or plasmaphereisis or antibiotics if infection has developed. High-dose corticosteroids, cytotoxic agents such as Imuran, anti D20 monoclonal antibody (rituximab), and chemotherapeutic agents such as azathioprine are used alone or in various combinations as a mainstay of treatment to decrease inflammation and suppress the activity of the immune system, thereby reducing autoantibody production.

Tumor necrosis factor agonists such as Etranacert (http://www.harvardskinstudies.org/pemphigusvulgaris.asp) are also being studied in clinical trials and appear to offer benefits. Peptide immunotherapy (PI-0824) is also being used in clinical trials. While the development of these treatments has reduced the high mortality previously associated with PV, today most mortality in PV is caused by the consequences of treatment particularly that of high-dose corticosteroid therapy.

Alternative therapies include ginger, nicotinamide, zinc, and gold.

**Resources**


Joo Chuan Tong, Jeff Bramson, Modeling the bound conformation of Pemphigus vulgaris-associated peptides to the MHC Class II D and DQ alleles, Immunome Research, 2006, 2:1.


On the trail...a search for the "guilty party" in pemphigus, INFOCUS, publication of the American Autoimmune Related Diseases Association; 14(2) June 2006.

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