



Pemphigus Vulgaris and Bullous Pemphigoid: Laboratory Testing and Diagnosis

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Autoimmune blistering diseases are a rare group of mucocutaneous disorders that can result in irreversible sequelae and death if accurate diagnosis and treatment are not rendered promptly.^{1,2} Two of the most common diseases in this group are pemphigus vulgaris and bullous pemphigoid, which are disorders characterized by the production of autoantibodies that target structural proteins important to the maintenance of intercellular and cell-to-basement membrane adhesion.^{3,4} Diagnosis of these disorders requires the integration of clinical findings, histopathologic characteristics, immunofluorescent analysis, and further immunologic laboratory testing (eg enzyme-linked immunosorbent assay) if necessary.

Pemphigus vulgaris is the most common subtype of the pemphigus group of disorders, which presents as flaccid mucocutaneous blisters that have a tendency to rupture easily.^{5,6} If left untreated, progression of the disease may lead to death within five years of onset in some cases, due to secondary bacterial infection and sepsis.¹ Bullous pemphigoid is the most common autoimmune blistering skin disease and presents with large, tense, cutaneous blisters.^{1,3} Ruptured bullae may lead to erosions that are susceptible to bacterial infection. Current treatment for pemphigus vulgaris and bullous pemphigoid involves immunosuppressive therapy, which may include both topical and systemic application of steroids, depending on the severity of disease.

Surgical pathologists and dermatologists who are trained in dermatopathology and/or immunodermatology play an important role in the diagnosis of pemphigus vulgaris and bullous pemphigoid. As mentioned earlier, histopathologic characteristics, immunofluorescent analysis, and further immunologic laboratory testing must be integrated with the clinical findings in order to establish an accurate diagnosis. Histopathologically, pemphigus vulgaris displays acantholysis, suprabasal separation of the epithelium, and sparse inflammatory infiltrate.^{1,2,6} These findings occur due to IgG autoantibodies targeting the desmosomal protein *desmoglein 3*, which serves an important role in intercellular adhesion of the epidermis and mucosal epithelium.^{7,8} Direct immunofluorescence on a perilesional mucocutaneous biopsy displays intercellular deposition of IgG antibody and/or C3 complement along the epithelial cell surfaces.^{1,6} Indirect immunofluorescence shows the presence of circulating serum IgG autoantibodies through intercellular deposition on substrates such as human skin or monkey esophagus.^{1,6} Enzyme-linked immunosorbent assay (ELISA) allows for further specificity in the detection of circulating IgG autoantibodies that target desmoglein 3 and in the measurement of antibody titers that correlate with disease activity.⁹ Histopathologic examination of a cutaneous biopsy of bullous pemphigoid shows subepidermal blistering with an inflammatory infiltrate consisting of eosinophils and

neutrophils.^{1,2} These findings are the result of IgG autoantibodies targeting the hemidesmosomal proteins BP230 and BP180, which serve an important role in anchoring epidermal basal cells to the basement membrane.^{10,11} Direct immunofluorescence on perilesional biopsy demonstrates a linear deposition of IgG and C3 along the basement membrane.^{1,2} Indirect immunofluorescence on human skin or monkey esophagus substrates displays serum antibody deposition in a linear fashion along the basement membrane as well.^{1,2} ELISA may be utilized to detect circulating autoantibodies to BP180 as well as to monitor disease activity through the measurement of antibody titers.¹²

In summary, pemphigus vulgaris and bullous pemphigoid are autoimmune blistering disorders, that require the integration of clinical, histopathologic, and immunopathologic findings for diagnosis. Communication between the clinician and the dermatopathologist/immunodermatologist is essential for prompt and accurate diagnosis, allowing for the immediate initiation of immunosuppressive therapy in order to significantly reduce morbidity and mortality.

References

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