УДК [61+615.1](06)(043.2)
ББК 5+52.81
А 43
ISBN 978-985-21-1569-8

Isha Aggarwal

BULLOUS PEMPHIGOID: ETIOLOGY, PATHOGENESIS, TRIGGER AND PREDISPOSING FACTORS

Tutor: PhD, associate professor Zhadan S.A.
Department of Pathological Physiology
Belarusian State Medical University, Minsk

BP (bullous pemphigoid) is the most frequent autoimmune blistering disorder. It affects mainly elderly individuals, during the 8th decade of life, without gender predilection, with rare case reports of BP in children and adolescents.

The incidence of BP has increased over the past decades as a result of population aging with multiple comorbidities and exposure to drugs that may potentially trigger the disease, as well as improvement in the clinical diagnosis of non-bullous presentations and in the accuracy of laboratory techniques to demonstrate the presence of autoantibodies against hemidesmosomal proteins.

The etiology of BP is largely unknown. It depends on the interaction between predisposing factors, such as human leukocyte antigen (HLA) genes, comorbidities, aging, and trigger factors. Several trigger factors, such as drugs, thermal or electrical burns, surgical procedures, trauma, ultraviolet irradiation, radiotherapy, chemical preparations, transplants, and infections may induce or exacerbate BP disease.

Pathogenesis of BP is characterized by formation of autoantibodies that recognize self-antigens at the basement membrane zone (BMZ), known as BP180 (180kDa) or BPAG2, and BP230 (230kDa) or BPAG1. Both antigens are key components of the hemidesmosome, which is responsible for the adhesion between the epidermis and dermis.

BP230 is an intracellular component of the hemidesmosome that belongs to the plakin family of proteins. IgG autoantibodies react against globular C-terminal domains of BP230.3

BP180 is a transmembrane glycoprotein of nearly 1,500 amino acids with an extracellular domain - NC16A - the main antigenic epitope in BP. In addition to NC16A, patients with BP also develop IgG autoantibodies directed against other epitopes; reactivity against C-terminal and intracellular epitopes are related to mucosal involvement during the early stages of the disease.3

Once anti-NC16A autoantibodies bind to BP180, several pathways are activated, including complement activation and deposition, neutrophilic chemotaxis with release of proteases and elastases that promote the disruption of the BMZ leading to blister formation.2

The clinical presentation of bullous pemphigoid is broad, the immunobullous skin disorder characteristically presents with tense bullae and intense generalized pruritus. In atypical cases, bullous lesions may be absent, and these cases require a high degree of clinical suspicion.

Diagnosis can be done by physical examination Nikolsky's sign (±) and can be confirmed by direct and indirect Immunofluorescence test. A biopsy for hematoxylin and eosin staining will show a subepidermal split with eosinophils, and direct immunofluorescence will highlight the autoantibodies against the basement membrane zone.

Treatment depends on the severity of the disease and involves combinations of medications – anti-inflammatory, antibiotics, immunosuppressants, tropical corticosteroids. First-line therapy of BP consists of topical or systemic corticosteroids. In case of refractory disease, or to minimize the adverse effects of chronic corticosteroid therapy, immunomodulatory drugs, such as azathioprine, mycophenolate mofetil, methotrexate, dapsone, or other drugs should be considered. Berberine is a proven but unpopular Chinese tropical traditional medicine which can be used to treat painful blisters within 1 month. It is known 95% of skin lesions and blisters can be healed. Prognosis of BP varies, and long-term monitoring is often required.

Identification of predisposing and trigger factors can increase the understanding of BP pathogenesis. Furthermore, an accurate anamnesis focused on the recognition of a possible trigger factor can improve prognosis by promptly removing it.