Dear Editor,

Bullous pemphigoid (BP) is an autoimmune blistering disease of the skin with autoantibody against components of basement membrane zone (BP 180 and BP 230) whereas in pemphigus vulgaris (PV) autoantibodies are directed against desmosomal proteins (Dsg 1 & Dsg 3).[1] Patient diagnosed with BP having autoantibody against desmoglein (Dsg) with no manifestation of pemphigus has been reported and transition between BP and PV and vice versa has also been reported.[2] We report a case of bullous pemphigoid coexisting with anti-desmoglein autoantibodies. A 60-year-old female presented with the history oral and genital ulcers followed by bulla over the chest, back and extremities since 4 months. History revealed bulla ruptured on its own without peripheral extension and healed with pigmentation. On examination—multiple flaccid and tense bullae, crusted plaques and healed erosions with perifollicular pigmentation were present over trunk and both arms. Erosions were present over right buccal mucosa and labia majora. Bulla spread sign was positive and Nikolsky sign was negative around the flaccid bulla. On investigation, Tzanck smear—showed lymphocytes and eosinophils. No acantholytic cells seen. Biopsy showed sub-epidermal bulla with neutrophils and eosinophils. The mid and deep dermis showed perivascular mixed inflammatory infiltrate of lymphocytes, neutrophils, and eosinophils. Direct immunofluorescence (DIF) from perilesional skin demonstrated prominent homogeneous linear deposits of C3 along the basement membrane. IgG, IgM, IgA, and fibrinogen were negative. BIOCHIP mosaic-based indirect immunofluorescence (IIF) revealed overlap pattern of staining—intercellular deposits in primate esophagus, linear basement membrane deposit in roof pattern in salt split skin [Figure 1], positive for both target antigens desmoglein 3 and BP 180. Desmoglein 1 and BP 230 were negative. Autoimmune findings and assessment of sera of the patient for indirect immunofluorescence, enzyme-linked immunosorbent assay (ELISA) and immunoblotting was done in the University of Lübeck, Germany.

IIF on monkey esophagus showed circulating IgG-autoantibodies that bind with an intercellular pattern in the epithelium and no IgA-autoantibodies detected.

IIF on rat/monkey bladder showed circulating IgG-autoantibodies that bind to epithelium.

IIF on humanNaCl-split skin showed no circulating IgG and IgA autoantibodies detected.

ELISA studies for recombinant desmoglein 3 and BP180 NC16A was positive. ELISA with recombinant envoplakin (IgG) was negative.

Immunoblotting with extract of cultured keratinocytes showed no circulating IgG autoantibodies.

The serological finding was compatible with bullous pemphigoid with additional desmoglein 3 autoantibodies which is explained by an epitope spreading (ES) phenomenon.

The patient was diagnosed as BP because of clinical, histological, DIF, and IIF findings. The presence of additional anti-Dsg-3 antibody suggest that it could be due to ES.[3] An epitope is an antigenic determinant, on the surface of an antigenic molecule, to which a single antibody binds.[4] The ES phenomenon is when tissue damage from a primary inflammatory process causes the release and exposure of a previously sequestered antigen, leading to a secondary autoimmune response against the newly released antigens.[5] It represents the process of diversification of T-cell and/or B-cell response from the initial dominant epitope to a secondary epitope over time. It can occur within a single antigen or involve different antigens and manifest at various stages of the disease. ES phenomena may also lead to disease transition. It can occur between PV and pemphigus foliaceus, whereas transition between BP and PV and vice versa are rare.[5] A few cases of transition from PF to BP[6] or the simultaneous existence of these conditions[7] have been described. Tie D et al.[3] reported a case of 79-year-old Japanese woman with clinical and histopathological features of bullous pemphigoid, ELISA, and immunoblotting showed antibodies against both BP180 and Dsg 3. Julio et al.[8] reported four patients with BP, out of which three had anti-Dsg1 antibodies and...
one had both anti-Dsg 1 and 3 in addition to BP antibodies. In BP inflammatory process leads to skin damage, which may expose other antigens such as Dsg and desmocollin. The coexistence of anti-Dsg autoantibodies in BP patients may suggest the immunological ES phenomenon as seen in our patient.[9] Dsg1 is expressed to a higher degree in the superficial epidermis, Dsg3 is expressed in the lower portion of the epidermis, close to the basement membrane zone, where BP180 and BP230 are located. Moreover, BP mucosal impairment may expose Dsg3 to the immune system which can be explained by the presence of anti-Dsg3 antibody as seen in our patient.[9]

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Conflicts of interest

There are no conflicts of interest.

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