

Immunofluorescence Diagnosis in Vesiculobullous Dermatitis

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Overview of Bullous Pemphigoid

Bullous pemphigoid is an autoimmune disease that usually attacks elderly patients. It occurs when the body's defense mechanism produces **autoantibodies** that interact with the bullous pemphigoid antigen [**BPAG1 and BPAG2**] in **hemidesmosomes of basal keratinocytes** (that join the **keratocytes** to the basement membrane zone). This leads to the activation and recruitment of inflammatory cells, such as neutrophils & eosinophils, which make the characteristic skin blisters appear.

While bullous pemphigoid typically affects the skin, it may also involve the eyes, mouth, and genital area. Even though the condition develops insidiously in the majority of the cases, there are some drugs that trigger the development of bullous pemphigoid. Bullous pemphigoid occurs more often in people over 60, but it can also develop in younger persons. This disease is not curable, but treatment can reduce the symptoms.

Symptoms

The condition is characterized by a generalized eruption, with confluent urticarial plaques and multiple tense blisters. The condition is severely pruritic.

Description of the lesion:

Erythematous, pruritic papular or urticarial-type lesions that may precede the formation of the bullae by months. It is characterized by tense blisters, as opposed to the flaccid blisters in pemphigus. The eruption may be localized or generalized around the body. Oral lesions are very rare. At times, these blisters break, leaving an exposed skin that is open and painful.

Diagnosis

A thorough history should be taken to rule out other conditions, along with a skin assessment and blood samples.

Investigations

- Antibasement membrane IgG autoantibodies can be found in the serum.
- Immunofluorescence microscopy of a blood sample will reveal circulating pemphigoid BP180 antibodies.
- Immunofluorescence microscopy of a skin sample will reveal antibodies along the basement membrane that lies between the epidermis and dermis. Neutrophilic infiltrate and eosinophils may also be visible.

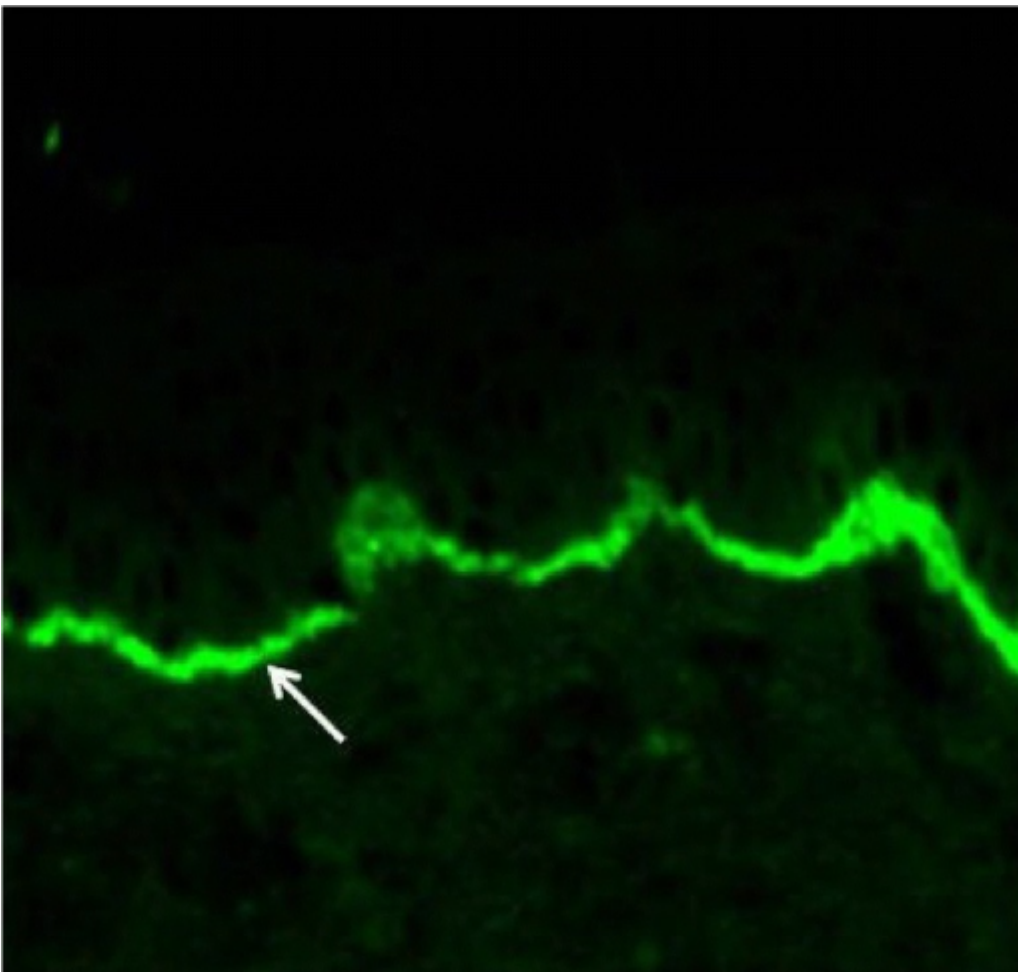


Image: Linear complement 3 (C3) (arrow) fluorescence in immunofluorescence analysis of perilesional skin biopsy is diagnostic for gestational pemphigoid. Primary magnification 200 × . By: Huilaja L, Mäkikallio K, Tasanen K - Orphanet journal of rare diseases (2014). License: [CC BY 4.0](https://creativecommons.org/licenses/by/4.0/)

Treatment

The main aim of therapy is to reduce itching and blisters and assist the proper skin healing. Usually, the choice of treatment depends on the extent of skin involvement.

Immunosuppressive agents

- In very mild cases and for local recurrences, topical glucocorticoid or topical tacrolimus
- Systemic prednisone in severe cases, either alone or combined with azathioprine
- Low-dose MTX is effective & safe in elderly

Overview of Pemphigus Vulgaris

Pemphigus Vulgaris is a rare autoimmune condition that results in blisters on the skin and mucous membranes (mouth, throat, nose, eyes, genitals, lungs), which are usually painful. It is caused by the loss of the normal cell-to-cell adhesion in the epidermis (*acantholysis*) due to circulating auto-antibodies of the IgG class, which bind to desmosomes (desmogleins 3) and join the keratocytes in the epidermis.

Pemphigus Vulgaris is the most prevalent kind of a cluster of autoimmune disorders called pemphigus. Respective kinds of pemphigus are distinguished by blister locations. The condition begins with a blister on the mouth, which then goes to the skin and, at times, the genitals. If left untreated, the condition can be life-threatening.

Pemphigus Vulgaris is mainly genetic and affects individuals of all races, genders, and ages. However, it is more prevalent in individuals from the Mediterranean areas, Eastern European Jews, people residing in the Amazon region of Brazil, and middle-aged and old people.

Symptoms

The main symptoms of Pemphigus Vulgaris are painful blisters. Usually, they first appear in the oral mucosa (rapidly become erosive & painful, preventing eating), and months may elapse before skin lesions occur.

Lesions might be localized for several months; after that, generalized bullae may occur.

Description of the lesion:

It is characterized by flaccid bullae (blisters) that appear spontaneously, after which may rupture. When these blisters rupture, they become *tender and painful* from erosions and can bleed easily.

Diagnosis

Positive Nikolsky's sign: A characteristic sign is if the patient's skin peels away easily when the surface is wiped with a cotton ball. However, a skin biopsy may be necessary to confirm the diagnosis.

Investigations

1. Immunofluorescence microscopy reveals intercellular IgG and/or C3 deposits in the

epidermis

2. IgG Autoantibodies in the intercellular substance of epidermis (IIF).
3. ELISA: More antibodies to desmoglein 3 than desmoglein 1.

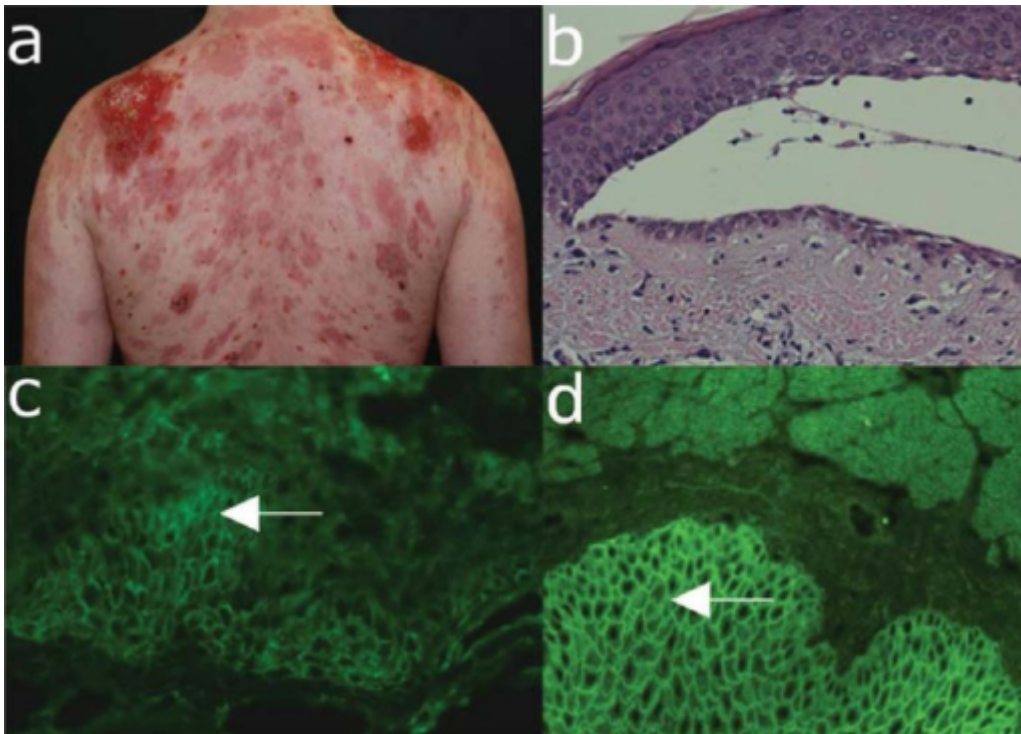


Image: Major clinical and laboratory findings in pemphigus vulgaris. (a) Extensive erosions with crusts and hyperpigmentation on the back of a 34-year old male patient with muco-cutaneous pemphigus vulgaris. (b) Histopathological examination reveals suprabasal acantholysis with modest inflammatory infiltrate. A single layer of basal keratinocytes remains attached to the basement membrane as a "row of tombstones". (c) Direct immunofluorescence microscopy analysis of a perilesional skin biopsy shows deposits of IgG with an intercellular pattern in the epidermis. (d) Serum IgG autoantibodies binding with an intercellular pattern are detected by indirect immunofluorescence microscopy on monkey oesophagus (all magnification 200x). By: Otten JV, Hashimoto T, Hertl M, Payne AS, Sitaru C - Current molecular medicine (2014). License: [CC BY 2.5](https://creativecommons.org/licenses/by/2.5/)

Treatment

The most effective and important treatment for this disease is corticosteroids. High doses are needed initially, which can then be lowered as the blisters reduce.

Additional drugs, such as azathioprine and methotrexate, which can reduce immune system activity, can also be used with prednisone.

Using Immunofluorescence to Differentiate Between Bullous Pemphigoid and Pemphigus Vulgaris

The direct immunofluorescence examination (DIF) is usually best for examining skin lesions, depending on the disease being investigated. The biopsy should be at least 4 mm deep so that the epidermis and dermis can be gathered equally. Furthermore, the biopsy sample will produce better results with minimal trauma. The most recent lesions should be used while taking a sample for biopsy. These biopsies are usually taken around the joints, where a high quantity of BP antigen is found.

Direct immunofluorescence examination

Pemphigus Vulgaris

Patients with pemphigus Vulgaris present with IgG autoantibodies against desmosomes, indicating a poor prognosis.

Direct immunofluorescence examination shows intercellular deposits (net-like band) of IgG and C3 in the epidermis. If the patients' mucous membrane is involved and the disease is still active, the C3 is mostly found in the lower parts of the epithelia.

Bullous pemphigoid

Direct immunofluorescence examination in all patients with bullous pemphigoid reveals linear collections along the hemidesmosomes (dermal-epidermal junction) with anti-C3 conjugate and IgG. It is very rare to see IgA and IgM with DIF.

References

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