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Review

Diagnosis and classification of autoimmune blistering diseases

Sharon Baum *,[1], Nicole Sakka [1], Ofir Artsi, Henri Trau, Aviv Barzilai

Department of Dermatology, Chaim Sheba Medical Center, Tel-Aviv University, Sackler School of Medicine, Tel Hashomer, Israel

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ABSTRACT

Blistering skin diseases are a group of autoimmune disorders that are characterized by autoantibodies against structural proteins of the epidermis or the dermal–epidermal junction and clinically by blisters and erosions on skin and/or mucous membranes. Since clinical criteria and histopathological characteristics are not sufficient for diagnosis, direct immunofluorescence microscopy of a biopsy specimen or serological tests are needed for exact diagnosis. The differentiation between the various disorders became more important since prognosis as well as different treatment options are nowadays available for the various diseases. Moreover, some bullous diseases may indicate the presence of an underlying malignancy. The detection of serum autoantibodies have been shown to correlate with disease activity and thus may be helpful in deciding treatment options for these patients.

Contents

1. Introduction

Autoimmune blistering dermatoses comprise a heterogeneous group of diseases that are characterized by autoantibodies directed against adhesion molecules of the skin and adjacent mucous membranes.

* Corresponding author at: Department of Dermatology, Chaim Sheba Medical Centre, Tel Hashomer, Tel Aviv, Israel, 52621. Tel.: +972 52 666 6182; fax: +972 3 530 3515.
E-mail address: Sharon.Baum@sheba.health.gov.il (S. Baum).
[1] Contributed equally.

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According to the skin level at which the blister occurs and by the structural proteins that the autoantibodies target, autoimmune blistering diseases can be categorized into different groups i.e. in pemphigus group, autoantibodies target desmosomal proteins that results in loss of cell adherence between keratinocytes, in pemphigoid diseases, hemidesmosomal proteins of the dermo-epidermal junction are targeted, and in dermatitis herpetiformis, autoantibodies bind to epidermal and tissue transglutaminase (Diagram 1).

The diagnosis of autoimmune blistering dermatoses is based on a constellation of clinical and laboratory findings and due to their rarity and heterogeneous clinical features, they often pose a major diagnostic challenge. Diagnosis cannot be based solely on clinical signs and the histopathological findings and requires the detection of tissue bound and circulating autoantibodies which still remains the diagnostic gold standard in the detection of autoantibodies. Furthermore, sensitive and specific serological assays have been developed to allow the detection of serum antibodies which are used as diagnostic tools as well as for disease activity monitoring.

2. Clinical classification

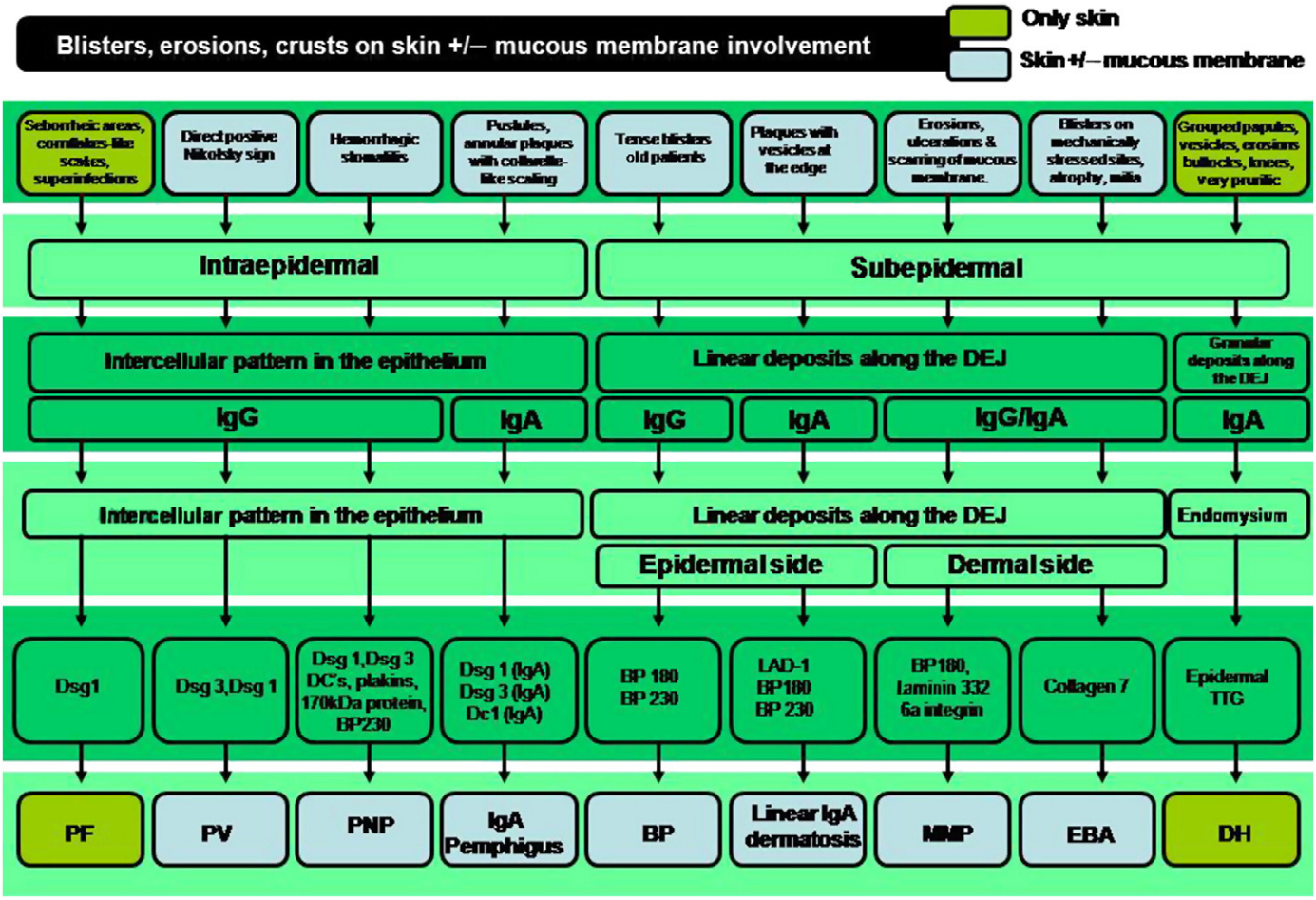
Autoimmune bullous diseases have a broad spectrum of clinical manifestations and a variety of morphological lesions. Based on the level of the skin blister formation — intraepidermal or subepidermal, they can be classified into pemphigus group and pemphigoid group of diseases respectively. Pemphigus is characterized by flaccid vesicles and erosions of the skin and/or mucous membranes, intraepidermal blistering and the production of IgG autoantibodies against the keratinocytes adhesion molecules. The major subtypes are; pemphigus vulgaris and pemphigus foliaceus, and aless frequent form, IgA pemphigus. Pemphigoid diseases are characterized by autoantibodies directed against structural proteins of the dermal–epidermal junction that clinically can manifest with urticarial lesions, tense blisters and erosions which may involve the mucous membranes. Diseases in this group include bullous pemphigoid, dermatitis herpetiformis, mucous membrane pemphigois, linear Ig A bullous dermatosis, herpes gestationis and epidermolysis bullosa acquisita (Table 1, Diagram 1). Paraneoplastic pemphigus, although classified as a type of pemphigus based on its clinical presentation, shows antibodies against both intraepidermal and subepidermal components.

3. Pemphigus group — diseases of intraepidermal loss of adhesion

3.1. Pemphigus vulgaris (PV)

Pemphigus vulgaris ("pemphigus" stems from the Greek word pemphix for "blister") is the most frequent representative of the group of pemphigus diseases with an incidence of 0.1–0.5/100 000 population [1–3]. The mean onset of PV is usually around middle age with an age peak in the fourth and fifth decade of life and a higher prevalence in patients of Jewish or Mediterranean ancestry [1–4]. PV is a chronic autoimmune intraepithelial blistering disease and potentially life-threatening condition. Despite advances in management, the mortality

Table 1
Diagnostic algorithm of clinical, histological, immunofluorescence and autoantibodies against structural antigens for autoimmune bullous disorders. Abbreviations: DEJ: dermo-epidermal junction zone; Dsg: desmoglein; Ig: immunoglobulins; DC: desmocollin; TTG: tissue transglutaminase, LAD-1: soluble ectodomain of BP180; PF: pemphigus foliaceus; PV: pemphigus vulgaris; PNP: paraneoplastic pemphigus; BP: bullous pemphigoid; MMP: mucous membrane pemphigoid; EBA: epidermolysis bullosa acquisita; and DH: dermatitis herpetiformis.



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