Autoimmune bullous disease

Mariana A. Phillips, M.D.

Disease	Immunology/ Autoantigen	Primary Lesion	Distribution	Distinctive Pathology	Assoctiated Disease	Associated Drugs
Bullous Pemphigoid	BPAg 1(230 kDa) BPAg2-NC16A (180 kDa) IF: Linear C3 & IgG at BMZ IgG4>IgG1	Tense blister on normal or erythematous base Urticarial plaque	Lower abd, inner/ anterior thigh, flexor forearms; may be anywhere 10-35% with oral mucosal involvement	Subepidermal blister with superficial dermal infiltrate with EOS 50% with Eosinophilia	No increase in cancer; age appropriate screening	Furosemide Captopril Enalapril Nalidix Acid PCN Penicillamine Sulfasalazine
Cicatricial Pemphigoid	BPAg2- NC16A & a more distal site Laminin 5- a3 LAD1, a6b4 Type VII collagen IF: Linear IgG and C3 at BMZ	Tense vesicle bulla on erythematous or urticarial base, rupture easily	Mucous membranes Oral & conjunctiva most common; Esophageal, rectal, genital, nasopharyngeal ***1/3 develop skin lesions****	Blister in lamina lucida with mixed infiltrate — may see Plasma cells, EOS, PMNs		Penicillamine Clonidine
Epidermolyis Bullosa Aquisita	IgG to NC1 of Type VII collagen (Anchoring fibrils) a-chain- 290kDa 145 kDa- NC1 domain IF: Linear IgG at BMZ	Blister on non-inflamed skin Scarring and milia cyst formation	**Classic** – acral with alopecia & nail dystrophy **BP-like** – widespread with accentuation in skin folds **Brunsting-Perry** – head & neck involved **Mucosal form**	Subepidermal blister in the sublamina densa PMN predominant May see blister in the lamina lucida because that is the weakest point	Inflammatory bowel disease Diabetes Thyroiditis Myeloma Bullous SLE Lymphoma	
Herpes Gestationis	IgG1 & **C3** BPAg2 NC16A domain **C3** is the main factor! IF: Linear **C3** at BMZ	Erythematous papules Papulo-vesicles Urticaria Tense Bulla Extremely pruritic	Peri-umbilical, abdomen, may involve palms, soles, chest, back Mucosa spared	Necrosis of basal cells with vacuolization Bulbous teardrop shaped blister Edema of dermal papilla	Grave's disease Hydatidiform mole, choriocarcinoma Usually in 4th to 7th month of pregnancy or in post partum period No increase in maternal mortality May recur at delivery, oral contraceptive use, menstruation, and subsequent pregnancy	
Chronic Bullous Disease of Childhood	Linear IgA1 + C3, IgG	Pruritic tense blister on inflammatory base	Perineum, perioral region, "collarette of blister" Lower trunk and thighs +oral lesion		HLA B8	

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Linear IgA Dermatosis	Linear IgA1; antigen unknown LAD-1 (97kDa, 120 kDa); Type VII collagen. IF: Linear IgA at BMZ + IgG/C3	Annular/ grouped papules, vesicles, bulla, urticaria	Pruritic, symmetrical, extensors — elbows, knees, buttocks. 70% with oral lesions	Subepidermal bulla, neutrophills along BMZ; perivascular lymphocytic infiltrate	Lymphoid malignancies Thyroid disease	Vancomycin Lithium Diclofenac
Dermatitis Herpetiformis	IgA1 + C3 granular deposits at BMZ. IF is + in normal appearing skin (IgA & C3 deposits not affected by treatment with dapsone, does decrease with glutean free diet)	Papulovesicle +hemorrhagic Urticarial plaques	Symmetrically on extensor surface; elbows, knees, buttocks, sacral, shoulders	Blister in lamina lucida Neutrophillic microabscesses in dermal papilla + EOS Accumulation of PMN in BMZ Late – necrosis of keratinocytes	Gluten sensitive enteropathy Increased GI lymphoma DM, SLE, vitiligo, non-Hodgkin's, Sjogren's HLA-B8 HLA-DR3 DQ-w2	Iodides aggravate
Pemphigus Foliaceus	IgG to 160 kDa Desmoglien 1 IgG4- complement independent IF: intercellular IgG throughout epidermis Pemphigus Erythematosus: +ANA; +lupus band test, IgG and complement intracellular and at BMZ	Scaly crusted erosions on erythematous base	Seborrheic distribution — face, scalp, trunk Rarely Mucosa inv. Fogo selvagem- endemic to Brazil	Blister just below stratum corneum in granular layer with acantholysis Exocytosis of EOS Perivascular infiltrate with EOS	Myasthenia gravis Thymoma	Penicillamine Captopril Piroxicam
Pemphigus Vulgaris	IgG to Desmoglien 3 in mucosal predominant IgG to both Desmoglien 1 and 3 in mucosal and cutaneous disease IgG4- complement independent	Painful, not pruritic flaccid Blisters on normal skin	Occur anywhere In majority of pts, mucous membrane involvement will be the presenting symptom	Suprabasilar blister with acantholysis and acantholytic cells in the blister cavity Pemphigus vegetans – intraepidermal eosinophilic abscesses	Myasthenia Gravis Thymoma	Penicillamine Captopril (drugs are not implicated as often as in pemphigus foliaceus)
Paraneoplastic Pemphigus	IgG and C3 Dsg 1, DSG 3, Plectin, BPAg1, Envoplakin, Periplakin 250, 230, 210, 190, 170 kDa proteins involved IgG and C3 IF: IgG and C3 intercellular and linear along BMZ	blisters on erythematous skin	Severe oral and conjunctival involvement	Dyskeratosis, suprabasilar acantholysis with basal cell vacuolar change and exocytosis	Non-Hodgkin's Lymphoma Leukemia (CLL) Thymoma (6%) Waldenstrom's macroglobulinemia Castleman's disease (HHV-8)	

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