Blistering skin diseases

Blisters are accumulations of fluid within or under the epidermis. Blistering skin diseases is a broad, complicated subject, but diagnosis depends on the site of the intercellular split:

Subcorneal: Very thin roof breaks easily. Examples include impetigo, miliaria, staph scalded skin.

Intra-epidermal: Thin roof ruptures to leave denuded surface. Examples include acute eczema, varicella, herpes simplex, pemphigus.

Subepidermal: Tense roof often remains intact. Examples include bullous pemphigoid, dermatitis herpetiformis, erythema multiforme, Stevens-Johnson syndrome/toxic epidermal necrolysis, friction blisters

Inherited blistering diseases

Epidermolysis bullosa (EB) refers to a group of inherited disorders in which there are mutations in specific keratin proteins (EB simplex), hemidesmosomes (junctional EB), anchoring filaments or type VII collagen (dystrophic EB). Minor trauma results in blisters and erosions, the split site and severity depending on the specific defect.

Autoimmune bullous eruptions

There are multiple distinct immunobullous diseases due to autoantibodies directed at differing components of the desmosome complex. Skin biopsy and direct immunofluorescence are diagnostic and there may be detectable circulating skin antibodies. Bullous pemphigoid is the most common immunobullous disease and affects the elderly. Early signs include a very itchy rash which may not even look blistery.

Dermatitis herpetiformis mostly affects young adults but may present at any age as a chronic itch. It mainly affects scalp, elbows, buttocks, knees and shoulders. Diagnosis is made by skin biopsy and rapid improvement on dapsone. Dermatitis herpetiformis (DH) is associated with gluten-sensitive enteropathy in most cases (at least 85%) although this may be asymptomatic.

Pemphigus has at least 7 subtypes caused by pathogenic IgG antibodies to intraepidermal cell adhesion molecules. It is diagnosed by clinical presentation and skin biopsy. Pemphigus vulgaris is potentially fatal, and usually presents with acute or subacute extensive oral ulceration followed by widespread cutaneous denudation. Pemphigus foliaceus affects the elderly and presents with erosions affecting primarily seborrhoeic areas (scalp, face, chest). It is much less severe than pemphigus vulgaris. Pemphigoid gestationis: bullous eruption of pregnancy (autoantibodies directed against BP180 antigen) Cicatricial (benign mucosal) pemphigoid: blisters affecting mouth, nose, eyelids and genitocrural sites that form scars (autoantibodies directed against anchoring filaments)

Epidermolysis bullosa acquisita is blistering following trauma (autoantibodies directed against NC1 domain of type VII collagen)

Linear IgA dermatosis is annular blistering

Investigations

Skin biopsy and direct immunofluorescence (DIF) are crucial for diagnosis of immunobullous diseases.

Other tests

There may be circulating ‘skin antibodies’ in immunobullous diseases. These are detected by indirect immunofluorescence of serum. If dermatitis herpetiformis is suspected, additional investigations to detect gluten enteropathy can include antibodies to transglutaminase and endomysium.

Management

Control of dermatitis herpetiformis is usually a gluten-free diet and oral Dapsone. Control of other immunobullous diseases can be very challenging and can involve immunosuppressive agents like prednisone, azathioprine, mycophenolate, methotrexate, rituximab and/or intravenous immunoglobulin. Maintenance therapy is usually required for years if not lifelong and is likely to result in significant complications. Alternatively, sometimes, the oral antibiotics doxycycline or minocycline can help or the supplement niacinamide can help.