Blistering Skin Diseases

Lt. Col. S.L. Rajbhandari
Consultant Dermatologist
Shree Birendra Hospital

The blistering skin diseases present with various aetiopathogenesis. Histopathologically these disorders can be divided into following types according to level of split.

1. Subcorneal the blister here is formed by detachment of stratum corneum. e.g., Bullous impetigo, Miliaria crystallina, subcorneal pustular dermatosis, erythema neonatorum.
2. Intracellular degeneration there is separation of cells from one another due to intense degeneration. Site of formation is upper dermis in spinous cell layer, e.g., friction blister, epidermolytic hyperkeratosis, erythema multiforme-epidermal type.
3. Spangiotic-here the intercellular oedema is severe and site of cleavage is again intraepidermal, e.g. dermatitis, incontinentia pigmenti, miliaria rubra.
4. Acantholytic-here we find dissolution of intercellular substance, the blister cavity is intraepodermal. It can be suprabasaleg pemphigus vulgaris or subcorneal e.g. pemphigus foliaceus.
5. Viral-formation of blister here is due to ballooning degeneration of basal cells, leading to acantholysis, It is intracpidermal e.g. herpes zoster, herpes simplex, chickenpox.
6. Degeneration of basal cells-damaged basal cells have loose contact with dermis. So the blister formed is subepidermal. e.g., epidermolysis bullosa simplex, lichen planus, lupus erythematosus, lichen sclerosus et atrphicus.
7. Degenerative changes in basement membrane zone-damage in structure causing coherence of basal cells with dermis, site is subepidermal, e.g. bullous pemphigoid, urticaria pigmentosa, dermatitis herpetiformis, cicartical pemphigoid, herpes gestationis, epidermal bullosa junctional, porphyria cutanea tarda, erythema multiforme-dermal type. According to age frequency of occurrance is as follows :

During infancy

common-impetigo unusual-epidermolysis bullosa, incontinentia pigmenti, urticarial pigmentosa, acrodermatitis enteropathica, congentital syphilis, congenital porphyria, bullous icthyosiform erythroderma.

Childhood

common-impetigo, bullous papular urticaria, erythema multiforme unsual-bulous drug eruption.

Adult

common-insect bite, erythema multiforme, bullous drug eruption, bullous eczema unusual-bullous morphea lichen sclerosùs, bullous lichen planus, bullous plant dermatitis, dermatitis herpetiformis, pemphigus, porphyria.

Old age

common-pemphigold unusual-leukemic bullae, cicatrical pemphigoid, diabetic bullae.

Autoimmune blistering diseases

These diseases are characterised by target antigen whose function is either cell to celkl adhesion within epidermis or adhesion of statified squamous epithelium to dermis. These target antigens are components of desmosomes or functional units of basement membrane zone known as adhesion complex. Here the blister is epidermal or dermalin origin. Accordingly, the target antigen can be epidermal or dermal.

Antigen is any substance when introduced into the body stimulates the production of antibodies and with which the antigen reacts specifically and in a observable manner. Specificity means the antigen which if intoruced reacts with B lymphoeytes or T lymphocytes which express specific marker for that antigen. Antibody so produced will react with that particular antigen.

Antibody-serum protein contain soluble albumin and insoluble globulin. Antibodies are globulins. These globulins are synthesised by plasma cells and lymphocytes. Clobulin constitutes 25% of total

serum proteins. Five classes of antibodies found in human body arc Ig G, Ig A, IG M, IG D, IG E.

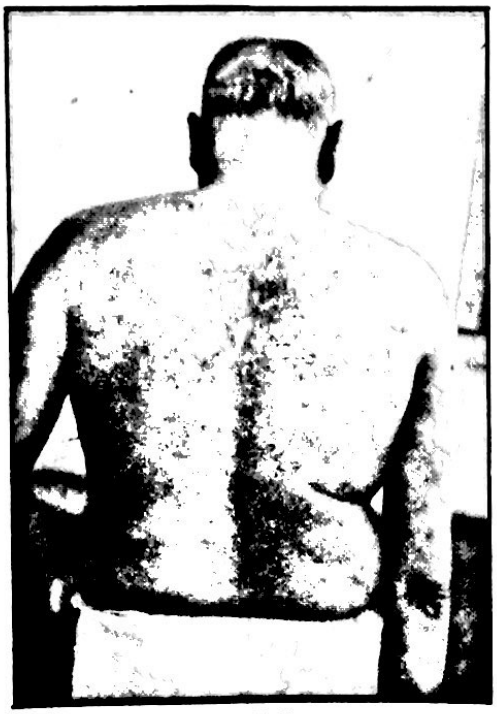
Antigen-Antibody reaction-ag and ab combine with each other in a specific and observable manner. Reaction between them result in antibody mediated immunity in infectious diseases or result in tissue injury as in auto immune diseases.

Some like pemphigus and pemphigoid have ag and ab combination resulting in localised or generalised blister formation. These blister formation may lead to fluid loss and or superinfection.

Pemphigus

It is a collective term for a group of chronic bullous dermatoses characterised by intra epidermal cleft and presence of circulating autoantibodies against cell surface of epidermal cells. In 1953, Lever distinguished pemphigus from bullous pemphigoid on the basis of clinical, histopathological and natural course.

Incidence common in middle age, common in Jews. Sex almost equal in ratio Aetiopathogenesis-circulating autoantibodies are directed against a component of cell surface of stratified squamous epitheloim. Experssion of pemphigus antigen is highest in buccal mucosa, scalp, scalp, axill, midface, complexes of polypeptides named desmoglein 3 (130 kd) combine with plakoglobin 85 kg. Certain genes HLA DR4 express this disease, stimulation for production of auto antibodies Ig G ? Mechanism of Acantholysis ? directly by altered physiology at assembly of intercellular junction or indirectly by release of proteases by keratinocytes or by both. Plasminogen activators convert plasminogen to plasmin which leads to lysis of intercellular substances and subsequent acantholysis. Complement activation may enhance pathogenicity of antibodies.



Pemphingu Follaceous

Bullous Pemphigoid

Patients present with large tense blisters and arise in urticarial and erythematous base or normal skin. The course of disease is chrome and benign. Each crop of lesion amy last for 2-3 weeks and heal without scarring. Nickolsky's sign is negative. Upon application of pressure by finger on normal looking skin there is no seperation of dermis from epidermis. Lesion involve trunk, extremeties, intertriginous areas. Oral mucosa may be involved in 1/3 cases and readily get resolved. May start as nonspecific eruption. Commonly affect above 60 years of age.

Bullons Pemphigoid

Histopathological exam shows in early blister papillary dermal ocdema with perivascular lymphocytes and eosinophils. Blister arises at dermoepidermal junction. Ab is located lamina lucida. Blister roof consists of basal keratinocytes. Antibody binds to lower basal keratinocytes. Pathogenesis-Unknown immunological signal from BP Ag cause formation of B clone cells. These are activated to form plasma cells. The plasma cells produce monoclonal Ig G against BMZ. a Mostly Ig G4 gets bind to BP Ag. These AG-Ab get deposited in LL. Complement is activated, C3a, C4a,Ig G 4 deposited. Mast cells degranulate.

release inflammatory mediators-ECF, NCG, LB4, proteolytic enzymes, Eosinophils appear with release of MBP and other enzymes. LL seperation occurs from injury of basal keratinocytes, disruption of hemidesmosomes, and protcolysis, thus seperate at DEP junction.

Adjuvants in management of Pemphigus

Based on Mode of Action

(1) Immunosuppressivedrugs, cyclophosphamide, azathioprine eyclosporine, methotrexate-do not diminish immunoglobulin

(2) Antiinflammatory drugs-gold, dapsone, antimalaria

(3) Immunomodulatory-plasmapheresis, photopheresis down regulate production of pemphigus ab.

With adjuvant use after 1970 mortality rate reduced to 5.9%. Other factors are earliner initiation of therapy, diagnosis of early and mild forms, better treatment of complications. Now treatment induced complications are major problems.

With rapid effect

1. pulse steroid therapy (a) with methyl prednisolone iv 1 gram/day in 2 hours for 5 days, control achieved, treat with mtralesional steroid. Other adjuvants can be used to reduce need for steroid and have more remissions. Cyclophosphamide more (b) DCP (100 mg Dexona equivalent to 667 mg prednisolone) + 500 mg CPM in 500 ml 5% Dextrose in 2 hours-day 1st During next 2 days 100 mg Dexona OD only given. Repeat it every month. Remaining days of every month give CPM 50 mg/day oral. There are 4 phases. 1st phase-give this cycle till remossion (6 month-1 year). Within 3 days crosions dry up but fresh lesions appear with milder recurrences. 2nd phase-Continue for next 6 month even if no eruption. 3rd phase-only oral CPM continue for next 1 year. 4th phase stop treatment & follow up with ab titre if possible. It was first tried successfully in Pyoderma gangrenosum. Indicated in Pemphigus, bullous pemphigoid. SCPD, erythema multiforme, TEN, behcet's disease, wagener's aganulomatosis, lupus erythematosus. Side effects of pulse therapy-secondary bacterial infection, oral candida, septicemia pharyngitis, tonsillitis, amnorrhoea, azoospermia, electrolyte imbalance, MI, arrhythmia, HTN.

2. plasmapheresis-effectiveness depends on balance between amount removed and amount of ab reproduced. So, in turn depends on frequency and amount of plasma removed and steps taken to prevent new ab synthesis,eg, cyclophosphamide damage rapidly replicating cells and achieve long lasting remissions by selectively and permantly destroying clones of cells.

With delaved effects- Dapsone-effective for superficial forms of poinphigus. Improve by stabilising lysosomal enzymes, inhibiting neutrophil toxicity & acting as steriod sparing agent.

Extra corporal photopheresis-6 mg/kg methoxalen administered 2 hours later 240 ml wbc entiched blood treated to UVA at 2 J/cm2. Reintroduced into body, stimulate clones of spcific immune responses with downregulatory activity for B cells. This process is done for 2 successive days in each month. Concurrently treat with steroids and immunosuppressive drugs. Improve after many months.

Immunosuppressive drugs tried are-cyclophosphamide, azathioprine, cyclosporine, methotrexate.

Anti malarial drugs have some beneficial effect because of photo protective effect. Nicotinamide 1.5 gm/day & tetracycline 2 gm/day with or without prednisolone do complete remission in less than 50% cases.

Few mild pemphigus showed improvement with gold therapy alone.

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