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Advance in Dermatology II

Immunopathology of Pemphigus Vulgaris:-

Dr. A.V. Ratnam, M.B., Dip. Derm, M.D. (Derm)
Lecturer in Dermatology,
Department of Medicine,
University Teaching Hospital,
LUSAKA

When patients see blisters they believe they are serious. The dermatologist is also concerned because there are more than 30 recognised bullous diseases and many are chronic, needing prolonged and careful management. The early clinical features are often deceptive precluding a correct diagnosis except a few simple ones like bullous impetigo and insect bite reactions.

The aetiology of many remains unknown and the management depends on clinical and especially

histological diagnoses. Since we do not know why but only how a bulla is formed, it is essential to know the early sequence of events and the exact site of bulla formation in the skin. For example, whereas the blister in pemphigus results from suprabasal separation of Malpighian cells with little local inflammatory reaction, pemphigoid results in a sub-epidermal bulla. The bulla of erthema multiforme is also sub-epidermal but shows in addition a massive inflammatory reaction and necrosis of the epidermis. Electron microscopy is useful to define these specific defects.

In the past decade immuno-flourescent (IF) staining techniques have added important new knowledge on pathogenesis of some of the bullous diseases (Fry and Seah 1974; Beutner et al 1973). It is the purpose here to summarise recent advances in pemphigus vulgaris.

Pemphigus is one of the most serious problems the dermatologist has to cope with and before the advent of corticosteroid therapy the prognosis used to be as grave as cancer with certain death in an average period of 14 months from the onset (Sneddon 1972). It is a chronic disease of middle age with world wide distribution. In Brazil, an endemic form of the disease, "Fogo Selvagam" ("wild fire") occurs at younger age with a more serious prognosis.

Large, flaccid blisters appear on apparently normal skin often with involvement of oral mucous membrane as well. The bullae rupture readily leaving raw, oozing indolent areas. When they heal they leave no scar but only dark pigmentation. Inspite of the recurring crops of fresh bullae, the patient remains deceptively well in the initial stages. At the edge of bulla simple sliding pressure on the skin with the thumb easily peels off the superficial layers of skin (Nicolsky's sign). This sign, easy rupturing of the bullae, and absence of scarring provide ample evidence that the abnormality is epidermal.

A biopsy of an early lesion shows abnormal separation of epidermal cells with bulla formation just above the basal layer which remains intact. The dermis shows scanty inflammation of none. Deeper knowledge of the intercellular structure of the epidermis is now required. The epidermal cells are closely held together by two factors: a homogeneous carbohydrate rich cementing substance covering the cell surface, and localised dense structures called desmosomes, which give a prickly appearance to epidermal cells under light microscopy. Electron microscopy shows the initial event in pemphigus to be damage to the intercellular cementing substance which results in loss of cohesion and a bulla forms with wider separation of cells. The epidermal cells lose their prickly appearance, become rounded and float in the cavity. This process is called acanthylysis which is characteristically seen in pemphigus.

The first clue to an auto-immune mechanism causing damage to the intercellular cementing substance was discovered in 1964 when Beutner detected antibodies to the epidermal intercellular substance in patient's sera. If skin biopsies show the presence of 1g.G and complement binding in the intercellular areas of epidermis by direct IF staining. The principle of the procedure is that flouresceinconjugated anti-human 1g G and complement antibodies raised in rabbits are used to stain the biopsy and the resultant binding of the same in the intercellular areas is located by the specific flourescence. Patient's serum also contains circulating antibodies which react with the intercellular substance in vitro. This is demonstrated by indirect I.F. staining using monkey oesophagus as substrate.

With few exceptions pemphigus antibodies are disease specific and their titres are proportional to the severity of the disease (Sams and Jordan 1971). Control of the disease with corticosteroids and immuno-suppressive drugs lends weight to the auto-immune theory. Pemphigus is also found to be coexistent with other known auto-immune disorders like myasthenia gravis and lupus erythematosus (Beutner et al 1968, Chorzelski et al 1968).

Experimentally, passive transfer of pemphigus antibodies by intradermal injections in rabbits, monkeys and guinea pigs has produced intraepithelial microbullae comparable to pemphigus in man and I.F. stainings also gave similar results (Beutner and Chorzelski 1973). However, chronic experimental models of pemphigus, reportedly induced by sensitizing rabbits with epithelial antigens, have not been successful since fixation of such antibodies to the intercellular antigens could not be proved in vivo. Successful results in near future are possible.

Although knowledge gained in pemphigus is considerable we do not as yet know what precipitates the formation of these auto-antibodies. The existence of an endemic form (Fogo Selvagam) suggests an infective agent, possibly with an arthropod vector. Similar auto-antibodies are discovered in sera of some patients following burns. But they do not bind in vivo to epidermis, and thus appear to be non-pathogenic, being similar to myocardial antibodies

developing after an infarction. However, a few cases of pemphigus have developed after burns, and, in isolated cases, in the areas of previous burns. (Chorzelski et al 1973).

Immuno-pathology offers promise to future dermatologists and it has already gained a strong foothold, not only in research but also as an accurate diagnostic tool in pemphigus and many other bullous collagen diseases.

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