

during heat separation cannot be completely ruled out, as previously discussed by us (11).

However, if the changes in psoriasis can be considered as an analogue to the events taking place in the hyperplastic rat skin, as reported by Peters & White, any earlier controversy between the hitherto obtained data may now be ignored.

Sequential changes in a biphasic manner with low cAMP in developing guttate lesions and supranormal levels of cAMP in stable lesions may account for the conflicting data and these may merely reflect the various levels of cAMP in psoriatic biopsy specimens at different developmental stages.

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Ultrastructural Study of Mechanobullous Desquamative Gingivitis: A Case Report

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Received March 16, 1979

Abstract. A 67-year-old female with localized bullous desquamative gingivitis is described. Ultrastructural studies of the perilesional area showed changes similar to those seen in cicatricial pemphigoid and epidermolysis bullosa acquisita.

Key words: Desquamative gingivitis; Cicatricial pemphigoid; Epidermolysis bullosa acquisita

Chronic desquamative gingivitis is a descriptive term for a clinical finding which may result from such diverse conditions as atypical gingivostomatitis, lichen planus, pemphigus, bullous pemphigoid or cicatricial pemphigoid (7, 8). Recently, patients with a chronic form of desquamative gingivitis and a marked sensitivity to trauma and absence of skin or extra-oral involvement have been felt to possibly represent a localized form of cicatricial pemphigoid or acquired epidermolysis bullosa (4).

We wish to describe the ultrastructural findings in a patient who represents this subtype.

CASE REPORT

The patient is a 67-year-old white female who presented with a 2½ year history of sore and bleeding gums. The condition was aggravated by mastication or toothbrushing. Blisters up to 1 cm in diameter, localized to the gingiva, have developed occasionally but no history of lesions involving other mucous membranes was noted.

A biopsy done elsewhere showed separation of the epidermis from the dermis. She had been treated for 1½ years with Prednisone 40 mg per day, which was reduced to 5 mg per day prior to being seen at the Mayo Clinic.

On physical examination, there were two ulcers, each 2 mm in diameter, on the lower inner gingiva surrounded by erythema. Probing of the ulcer edge with a blunt probe resulted in the epidermis being easily lifted from the dermis, with subsequent bleeding. The rest of the physical examination was normal.

Perilesional biopsy of the gingiva showed multiple focal subepidermal bullae associated with a chronic inflammatory infiltrate consisting of plasma cells, lymphocytes and

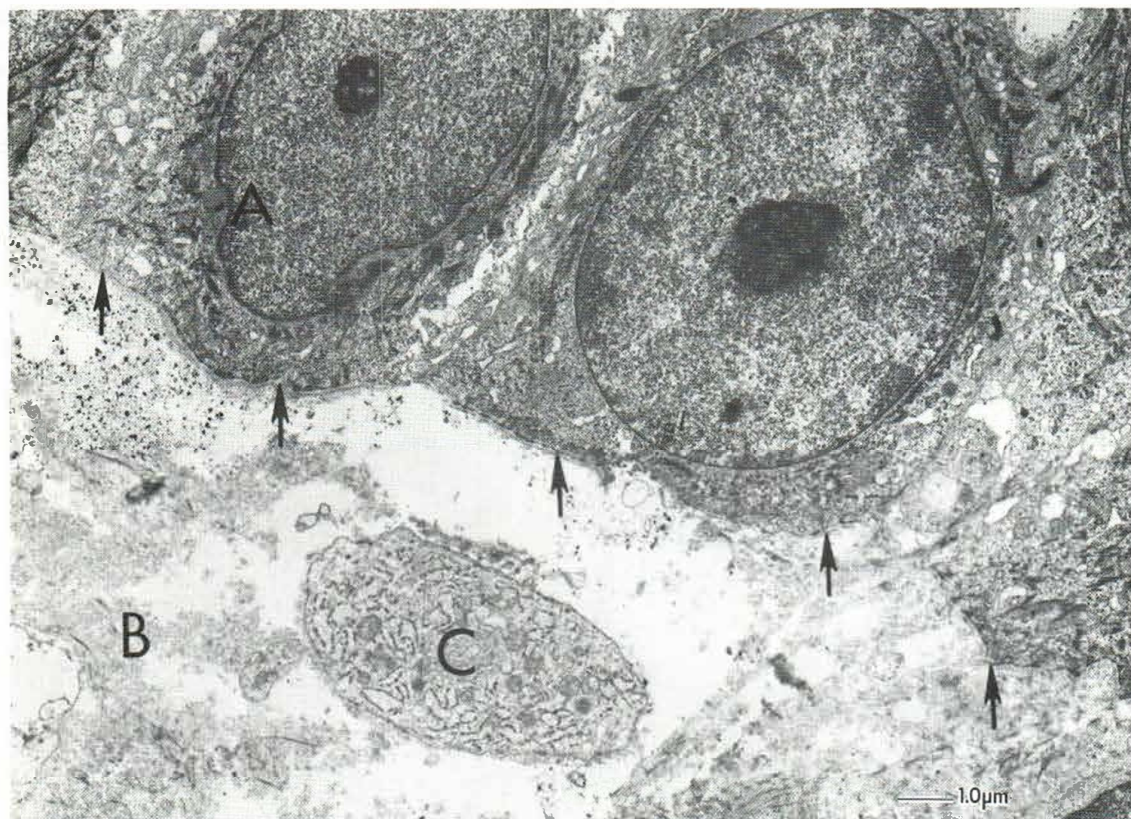


Fig. 1. Bullous area. The basal lamina is adherent to the roof of the subepidermal bulla. (A) Basal cell. (B) debris within bullous cavity. (C) fibroblast. ↑↑↑, basal lamina.

fibrohistiocytes. The periodic acid Schiff stain showed an indistinct basal lamina. Direct immunofluorescence of perilesional mucosa was negative for immunoglobulins and complement on two occasions. Indirect serum immunofluorescence was also negative.

Other normal laboratory studies included complete and differential blood count, blood chemistry, liver enzymes, serum protein electrophoresis, quantitative immunoglobulins, antinuclear antibody, LE clot test, and automated reagin test. The rheumatoid factor was positive, 1:1280.

A specimen was taken for ultrastructural studies.

METHOD

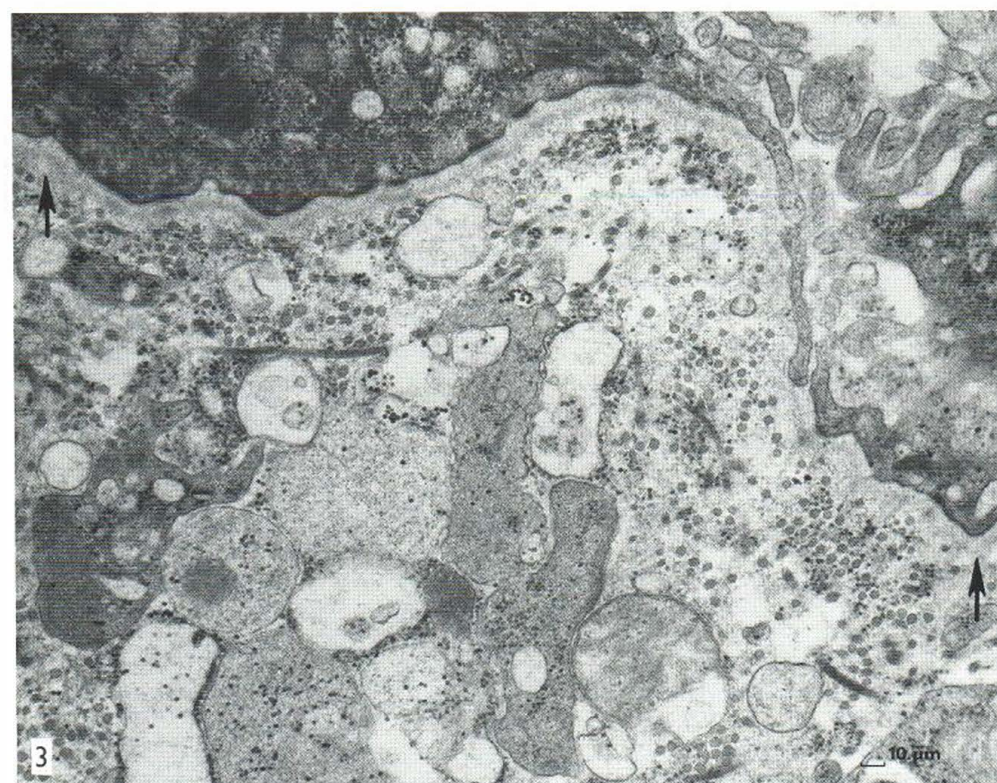
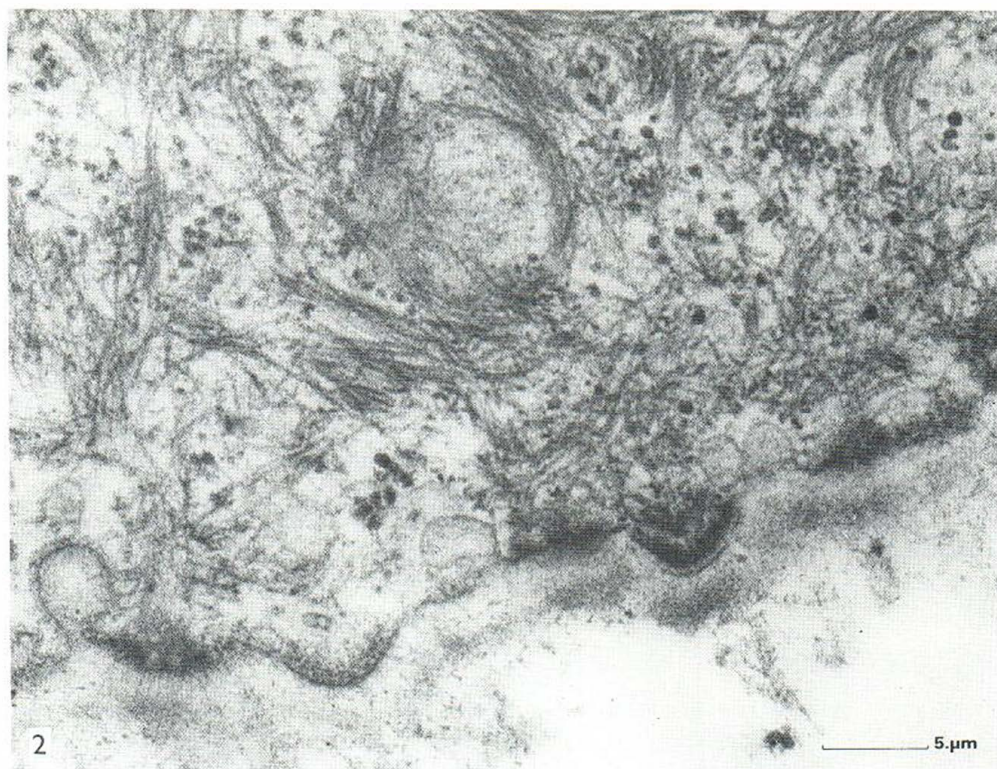
Perilesional gingival biopsy material was fixed in chix solution, postfixated in 10% osmium tetroxide and embedded in epoxy resin. Thick sections were stained with azure II. Selective thin sections 600–700 Å were cut and mounted on copper grids. Sections were stained with uranyl acetate and lead citrate. Sections were examined with an electron microscope, Philips 201 at 60 kV.

FINDINGS

The bullous cavity was subepidermal and lay below the basement membrane zone (Fig. 1). The basal lamina could be traced along the roof of the bulla immediately beneath the basal cells. Towards the center of the cavity the basal lamina was disrupted in places. The ultrastructure of the basal lamina at the edge of the bulla and in the perilesional region appeared normal. Anchoring fibrils were attached to the basal lamina, and both hemidesmosomal and anchoring filaments could be identified in the roof of the bulla (Fig. 2). The underlying submucosa was

Fig. 2. Detail showing intact basal lamina above bullous cavity; anchoring fibrils hang from lamina. Tonofilament hemidesmosome complex and basal membrane filaments appear normal.

Fig. 3. Detail of peribullous area showing complex array of cytoplasmic processes of activated fibroblasts below basla membrane zone, ↑↑, basal lamina.



not limited by any membrane and the collagen fibers were separated by edema. The basal cells at the edge of the bulla did not show degenerative changes and had a normal complement of tonofibrils which retained their desmosomal attachment. The intercellular spaces of the epidermis were focally widened and contained vacuoles and amorphous granular material.

The area subjacent to the bullous cavity showed an increased number of fibroblasts with well developed rough endoplasmic reticulum. Cytoplasmic processes from the cells formed a complicated network in the area immediately below the basement membrane zone (Fig. 3). Multiple dermal vacuoles which separated the collagen fibrils were visible in the area. Free ribosomes, prominent mitochondria, large vacuoles and amorphous granular material distended the fibroblast cytoplasmic processes.

DISCUSSION

Glickman & Smulow (6) separated the lichenoid and bullous forms of desquamative gingivitis on a histopathological basis. Immunofluorescent studies of the bullous variety have shown the frequent presence of immunoglobulins or complement at the basement membrane zone but negative indirect serum immunofluorescence (8). This finding, in addition to localized involvement of the mucous membranes and evidence of scarring, suggests that some patients with desquamative gingivitis are afflicted by a localized form of cicatricial pemphigoid. Recently, Forman & Nally (4) described fourteen patients with a similar clinical presentation and suggested that it may also represent a localized form of acquired non-dystrophic epidermolysis bullosa.

The ultrastructural findings in our patient showed a dermolytic bullous process with the presence of an intact basement membrane in the roof of the bulla. The intense fibroblastic activity within the perilesional papillary dermis may represent an attempt at microscopic repair of subclinical bulla formation. Our findings confirm those of Whitten (11) who examined three patients with bullous desquamative gingivitis and found the primary change to be subepithelial, beneath an intact normal basement lamina, identical with the ultrastructural appearance of cicatricial pemphigoid (3, 10). This contrasts with the intermembranous split in bullous pemphigoid. The latter, however, has been demon-

strated by Brusati & Brachetti (2) in one patient with desquamative gingivitis, but no immunofluorescence data were reported in their case.

Although the direct and indirect skin immunofluorescence was negative in our case, this may occur in at least 15% of patients with the clinical and histopathologic picture of cicatricial pemphigoid (9).

The ultrastructural changes in our case are similar to those described in epidermolysis bullosa acquisita (1, 5) but lack the changes in anchoring fibrils which have been described in this condition. Insufficient data are available on this aspect and molecular changes may exist in the anchoring complex which defy ultrastructural analysis.

Our findings and those of Whitten (11) are most compatible with a form of cicatricial pemphigoid. However, the localized nature of the process and lack of scarring in this patient are unusual features for cicatricial pemphigoid and may signify an independent process involving the stability of the anchoring region of the basement membrane zone in the area.

The ultrastructural study in our case did not provide a definitive answer to these alternatives.

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Mixed Bullous Disease with Labile Erythrocyte Sedimentation Rate

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Received March 23, 1979

Abstract. A woman, aged 66, fulfilled all the usual criteria of dermatitis herpetiformis. Subsequently, she developed circulating IgA and IgM basement membrane zone antibodies, a labile erythrocyte sedimentation rate (ESR), and the clinical picture changed to one of bullous pemphigoid. Her labile ESR was obviously caused by a factor related to the erythrocytes. Direct Coombs test was positive.

Key words: Mixed bullous disease; Dermatitis herpetiformis; Bullous pemphigoid; Labile erythrocyte sedimentation rate

In most cases, differentiation between dermatitis herpetiformis (DH) and bullous pemphigoid (BP) is feasible, based on the clinical findings, biopsies of skin and jejunum (4), immunofluorescence test (IFT) (8), therapeutic response to sulphones in DH, and HLA typing (7). However, coexistence or overlap of DH and BP may occur ("mixed bullous disease") (3). This article presents a patient with the clinical picture of DH which subsequently changed to BP accompanied by a highly labile ESR.

CASE REPORT

A 66-year-old woman had suffered from coeliac disease since the age of 17. When hospitalized in September 1977, she had developed a pruritic polymorphic vesiculo-bullous dermatitis on her limbs, abdomen and around the natal cleft. The clinical diagnosis of DH was confirmed by cutaneous biopsy of the pathological skin, and direct IFT of involved and "normal" skin, both showing linear deposition of IgA along the basement membrane zone

(BMZ). Suction biopsy of the jejunal mucosa revealed subtotal villous atrophy, and absorption of an oral vitamin A test dose was pathologically impaired. A daily oral dose of 100 mg dapsone healed her skin lesions within 2 weeks. She was discharged on a dose of 50 mg dapsone daily and an iodine- and gluten-free diet.

Recurrence of the exanthema in Jan. 1978 led to a new direct immunofluorescence test (IFT) of involved and "normal" skin; both showing a linear, continuous band-like fluorescence of IgA along the BMZ. Unexpectedly, the indirect IFT on this occasion was found to be positive, demonstrating circulating antibody of the IgA class (titre: 1/128) against BMZ in sections from monkey oesophagus. In addition, a considerable variation in ESR values was noted. On 4 consecutive days, the following values were recorded: 105, 5, 80 and 5 (mm/h).

Increase of the dapsone dose to 100 mg daily, supplemented with nicotinic acid 300 mg daily, alleviated the skin symptoms for some weeks.

However, in March 1978, typical clinical signs of BP appeared, in the form of non-pruritic large and tense bullae on the scalp, neck, axillary folds, abdomen and limbs. A new indirect IFT showed circulating IgA and IgM antibodies against BMZ (titre: 1/32). The ESR estimations continued to fluctuate widely (see below). Direct Coombs test was positive (++).

Dapsone medication was discontinued and oral prednisone treatment with a dose of 60 mg daily was started on 7th April 1978. A week later, the prednisone dose was increased to 80 mg daily, and the daily medication of 300 mg nicotinic acid was continued. During the first 2-3 weeks of this therapy, the skin lesions resolved. The circulating antibodies disappeared and the ESR was stable within normal limits. The prednisone therapy was then gradually reduced over a period of 5 weeks to 45 mg daily, at which point dapsone (100 mg daily) was added.

The patient was discharged on 9th June 1978 with completely resolved skin lesions and was kept in remission on daily oral doses of 15 mg prednisone and 50 mg Dapsone, supplemented with 300 mg nicotinic acid and diet.

INVESTIGATION OF THE LABILE ESR

Sufficient blood for 10 ESR tests was collected by venepuncture and the 10 tests were performed simultaneously at room temperature by the Sedimat® system (disposable PVC tubes) (2). All the tests gave different results, varying from 4 to 72 mm/h (Fig. 1). Another series of 10 ESR tests was carried out by the Westergren method (9) (glass tubes), but the results varied similarly. Tests performed at 37°C showed the same lability (range: 11-70 mm/h). However, at a temperature of 4°C, lability of the ESR did not occur; 10 tests at this temperature were within the range 2-4 mm/h. A control series of 10 tests with blood from a healthy donor was carried out (both by the Westergren and the Sedimat system), in order to exclude possible errors in method and technique. No lability could be detected.

In order to study whether the labile ESR was caused by factors in the plasma or on the erythrocytes, the following