

antigenic moiety, gave rise to the pemphigus antigen during evolution. Another possibility is that the precursor of pemphigus antigen is distinct from the pemphigus antigen detected in mammalian and avian skin and shows no reactivity with our antiserum by indirect IF.

Further studies with other species and antisera will help to elucidate this question. In either case, however, it is clear that the pemphigoid antigen has been preserved during evolution, thus indicating that it may have an important function.

ACKNOWLEDGEMENTS

This work has been supported by NIH Biomedical Research Support Grant no. RR-05383.

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Distribution of Complement and Immunoglobulin in Oral Pemphigus Lesions

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Received March 4, 1978

Abstract. The present report describes four cases of oral pemphigus vulgaris lesions in which complement, in contrast to the situation as reported for skin, was found only in the basal and parabasal layer, whereas IgG was present in all layers of the epithelium.

Key words: Pemphigus vulgaris; Complement; Oral mucosa

Pemphigus is a bullous disease affecting skin and oral mucosa. It is characterized histopathologically by intra-epithelial bullae with loss of cohesion of the epithelial cells (7). Immunopathological circulating antibodies to the cell surfaces of stratified squamous epithelium are found in patients with disease in the active stage and, furthermore, studies on biopsy specimens from affected areas have demonstrated *in vivo* localization of immunoglobulin and complement at the periphery of the epithelial cells (1, 6).

Biopsies from pemphigus skin lesions are reported to show a similar distribution of immunoglobulin and complement, with deposits in both basal and spinous cell layers (2, 4, 5, 6, 10). The present report describes 4 cases of oral pemphigus vulgaris lesions in which complement was found only in the basal and parabasal layer, whereas immunoglobulin was present in all layers of the epithelium.

MATERIAL AND METHODS

The clinical and histological data of the patients are given in Table I. All patients were investigated for *in vivo* bound antibodies and complement in lesions and surrounding normal mucosa and for the presence of circulating antibodies to the cell periphery of stratified squamous epithelium.

Biopsy specimens were taken under local anesthesia, immediately frozen and stored at -70°C . Specimens were processed for detection of *in vivo* deposits of IgG, IgM, IgA and C_3 using conjugates and immunofluorescence staining methods previously described (4, 11). The conju-

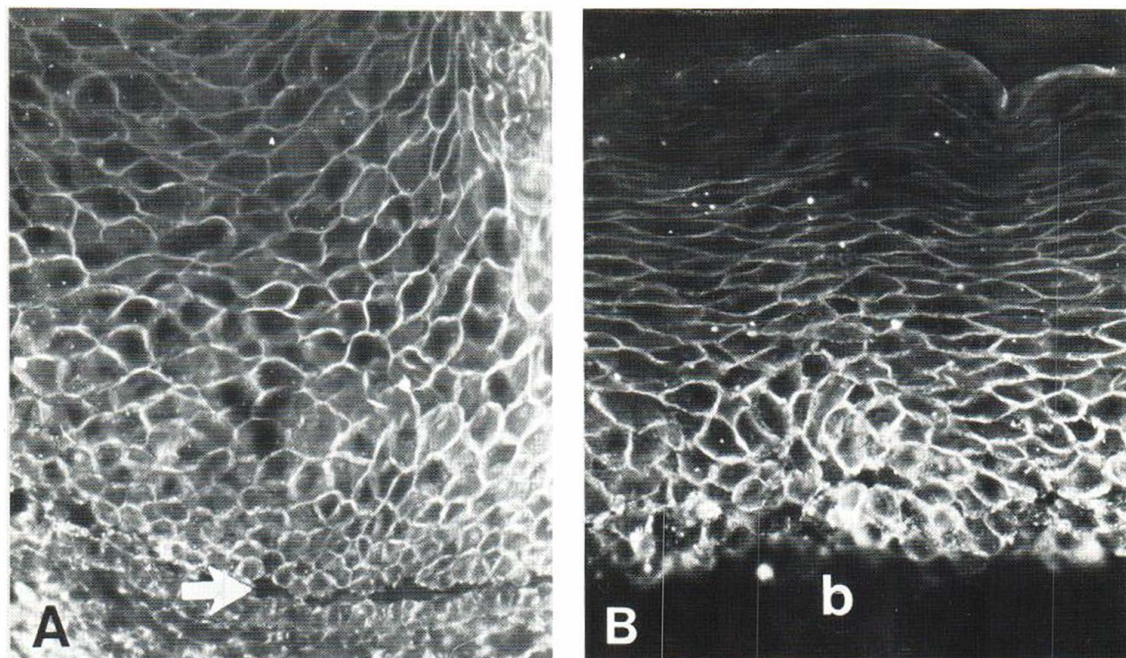


Fig. 1. Direct immunofluorescence staining of tissue from two different oral pemphigus lesions, staining for IgG. (A) Deeper layer of the epithelium with suprabasal splitting (arrow) $\times 165$. (B) Epithelium covering bulla, *b* indicating

bullae, $\times 245$. Positive staining is seen at the cell membranes in the basal and spinous cell layers. Only the surface of the epithelium reacts negatively.

gates were adjusted to the same antibody titre (3) and titrated by a two-fold serial dilution in order to detect possible quantitative differences in immunoglobulin and complement deposits. Patients' sera were examined for circulating antibodies to epithelial cell membranes, using guinea pig lower lip as antigen and rabbit antihuman IgG conjugated with FITC as conjugate. The conjugate, the staining method and the fluorescence microscope have been described previously (3, 11).

RESULTS AND DISCUSSION

A summary of the immunofluorescence stainings is presented in Table II. Immunoglobulin and complement were found in all four lesions and surrounding normal epithelium. IgG was found at the cell periphery of basal and spinous cells (Fig. 1 A+B), a finding consistent with many previous observations

Table 1. *Clinical and histological data of four patients with pemphigus vulgaris*

Patient	Age Sex	Duration of disease (months)	Oral in- volvement	Skin involvement at time of in- vestigation	Histology	Systemic steroids
Hj	52 ♂	3	+	—	Suprabasal splitting with acantho- lytic cells	None
SB	61 ♀	18	+	Appearing after 18 months	Ditto	None
MM	72 ♀	20	+	+	Ditto	+
AJ	49 ♀	6	+	—	Ditto	None

Table II. Immunofluorescence findings in four pemphigus patients with oral involvement

Patient	Direct immunofluorescence staining for immunoglobulin and complement in oral biopsies				Endpoint titres of IgG serum antibodies to stratified epithelium from guinea pig
	IgG	IgM	IgA	C ₃	
HJ	+	—	+	+	1:256
SB	+	+	—	+	1:8
MM	+	—	—	+	1:128
AJ	+	—	—	+	—

(2, 5, 10). Titrations have revealed a gradual decrease of immunoglobulin, from the basal cells to the surface of the epithelium. Only the 2–3 surface cell layers never stained positively for immunoglobulins. Interestingly, C₃ appeared, in all stainings, predominantly at the cell membranes in the basal and parabasal layer, with practically no staining of the superficial epithelium. Occasional staining of the basement membrane was noticed (Fig. 2).

Although it cannot be excluded that C₃ is present in subdetectable amounts in the superficial epithelium, there certainly seems to be a quantitative difference in the distribution of IgG and C₃ in the

investigated lesions. The fact that immunoglobulin and complement can only be detected simultaneously in the basal and parabasal cell layers supports the previous suggestion that acantholysis, the basic pathological process in pemphigus, may be mediated by the complement system (4, 5, 9). However, it cannot be ruled out that complement activation in the acantholytic areas is a result of the epidermal injury rather than its cause. The *in vitro* studies demonstrating that acantholysis can occur without the involvement of complement support the latter hypothesis (8).

Most previous studies on immunoglobulin and complement deposits in pemphigus lesions have been carried out on skin biopsies. In the present work there was no opportunity for immunological investigations on skin lesions. It would be of interest, however, to learn whether the difference in distribution of IgG and C₃ is limited to oral mucosa or is present in other stratified epithelia. Furthermore, in order to gain a better understanding of the pathogenesis in pemphigus lesions, future studies are needed in order to answer the question why C₃ appears only to be present in the lower part of the epithelium and whether this is a constant finding or whether it only appears in certain cases.

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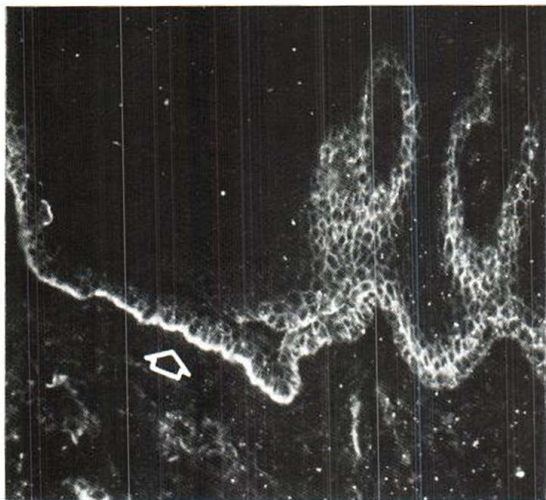


Fig. 2. Direct immunofluorescence staining of tissue from an oral pemphigus lesion, staining for C₃. Positive staining is seen at the cell membranes in the basal and parabasal layers and in some areas of the basement membrane zone (arrow), $\times 85$.

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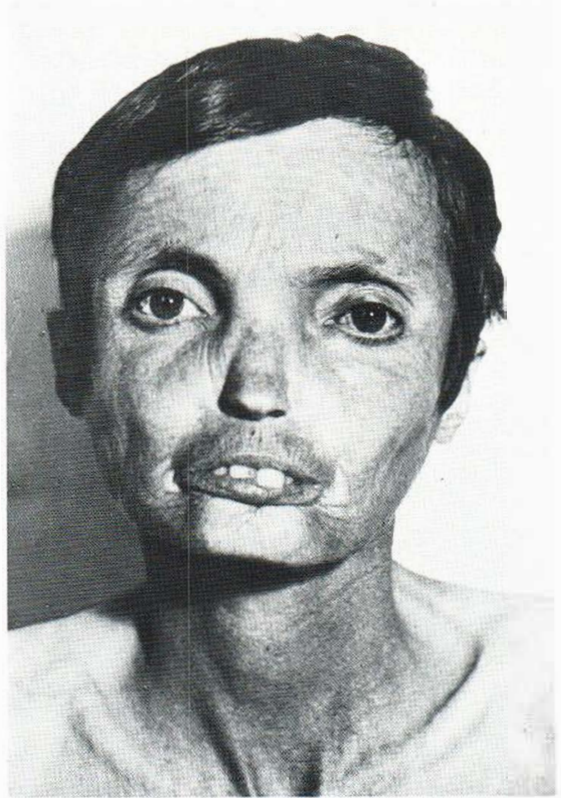


Fig. 1.

Werner's Syndrome and the Cellular Immune Reactions

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Abstract. A case of Werner's syndrome in a 39-year-old man is described. PPD and trichophyton intradermally proved negative; the percentage of T-lymphocytes and the lymphocyte response to PHA were reduced. Cellular immune reactions seem to have been impaired in this case.

We describe here a case of Werner's syndrome in a 39-year-old man. 14 members of the family were examined but no other instance was found.

CASE REPORT

The patient was 156 cm high and his weight was 38 kg. The limbs were thin. The voice was high-pitched and raspy. The radix nasi was depressed and he had

hypertelorism. Severe cutaneous changes had emerged after the age of 20. The skin was atrophic with circumoral furrows (Fig. 1). The teeth were protruding and he had a recessive chin. He had both hyper- and hypopigmented spots on the extremities and pronounced teleangiectasies on the back and the nates, which gave the appearance of poikiloderma. The subcutaneous fat was reduced (Fig. 2). Ulnar deviation of fingers II-V of both hands was prominent. Contractures of the metacarpo-phalangeal joints of the same fingers were present (Fig. 3). He had keratotic plaques on the pressure points of the soles and an ulcer on the right big toe. Hair and nails were normal, but he had no axillary or pubic hair. Histological examination of a skin lesion on the back was compatible with usual findings in Werner's syndrome.

X-ray examination of the skeleton showed osteoporosis. Ophthalmological examination revealed teleangiectasies and aneurysms of the blood vessels of the sclerae, subcapsular cataracts, vitreous opacities and degenerative macular changes. Leukokeratosis of the vocal cords was found. The patient was not mentally retarded. The velocity of the conductivity of the peripheral nerves was decreased. Hypogonadism with low excretion of androgens in the urine was found. Heart and lungs were normal.