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DISORDER OF CELLULAR IMMUNITY IN PEMPHIGUS VEGETANS

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Abstract. In an untreated 26-year-old female patient suffering from Neumann's pemphigus vegetans for 8 months (with neither preceding thymoma nor myasthenia gravis), several in vivo and in vitro phenomena of immunodeficiency involving both T and B cell system were disclosed. A diagnosis of defective immune state was established on the basis of the low IgG-serum level (though pemphigus antibodies were present), reduced T cell count in blood, weak PHA stimulation of lymphocytes, lack of skin reactivity to recall antigens and to most other bacterial antigens tested. Impaired chemotaxis and a deficient intracellular killing of *Candida albicans* by PMNL were also found. The conclusion is drawn that a combined disorder of both the B and T cell system is involved in the etiology of pemphigus vegetans, even when thymoma is ruled out.

Key words: Pemphigus vegetans; B- and T-cell system; Combined cellular immunodeficiency; Microphage dysfunction

The occurrence of auto-antibodies to intercellular substances of the stratified epithelium in diseases of pemphigus type reflects an increased B cell activity (3, 6, 9, 10). The modern conception of immunology, however, is based on the hypothesis of every immune response being preceded by a complex interaction of T and B cells (7). Hence, malfunctioning of the cellular immune system should be considered in cases of pemphigus (1). This view is supported by some reports on pemphigus vulgaris being associated with or preceded by myasthenia gravis and thymoma (11, 13). However, in the present case of pemphigus vegetans with some signs of immunodeficiency, neither thymoma nor myasthenic symptoms have occurred so far.

CASE REPORT

C. J., female, 26 yr. (Doc. No. 2132/78).

History. The patient felt healthy until 8 months before admission to hospital, denying any history of increased susceptibility to infectious diseases. In March 1978, painful oral 'ulcers' developed. Local treatment with antimycotics was ineffective. After 8 months, oozing lesions in the genital region and on the scalp also appeared.

Physical examination. Rather good general condition. No abnormalities of the internal organs or nervous system. Oral mucosa dark-reddened, swollen and studded with multiple, tender, fibrin-covered erosions. Marked lesions on tongue, soft palate, buccal mucosa and both lips. Elevated granulations in some lesions. No remnants of blisters. Hypersalivation. Genital labia maiora covered by coin-sized erosions. Hemispheric, cherry-sized, dull red, centrally ulcerated tumours in both genito-crural folds (Fig. 1). Malodorous vulvar discharge, though no lesions of vagina and cervix uteri. Oozing and crusted erosions also present on scalp. Bulbar conjunctiva reddened, glassy and swollen.

Laboratory data. ESR 4/12 mm, 7% eosinophils in hemogram. TPHA not reactive. Most data, apart from LDH (207.6 U/l), serum protein (5.8 g/dl), reduced thrombin time (9.6 min, 9.8 min) and partial thromboplastin time (33 min, 29 min), proved normal.

Candida species were isolated from vaginal smear and stool. *Staph. aureus*, Streptococci, *E. coli* and Enterococci were cultured from genital lesions.

Tzanck test (oral mucosa): Acantholytic cells.

Histology (genital lesion). Typical *Pemphigus vegetans* with digitiform acanthosis, suprabasal acantholysis, in-

Table I. *Humoral immune status and HLA typing*

Investigations	Results
Serology (ASL, AStaL, CRP, TPHA)	No abnormalities
Immuno-electrophoresis	Reactive dysproteinemia, no paraproteinemia
Immunglobulins	
IgG	600 mg/100 ml (↓)
IgM	110 mg/100 ml
IgA	200 mg/100 ml
Pemphigus antibodies	+ (Nov. '78, titre 1 : 64) + (May '79, titre 1 : 128)
HLA typing	HLA – A 3 HLA – AW 32 HLA – B 7 HLA – B 14

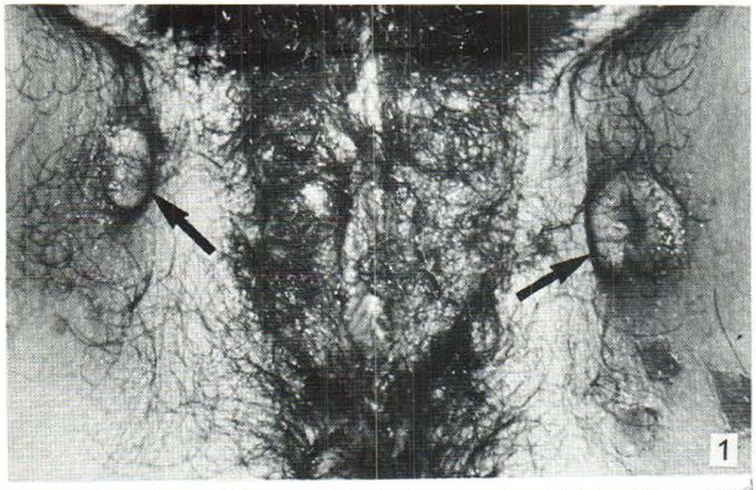

Fig. 1. Erosive and vegetating lesions (↑) in genital area.

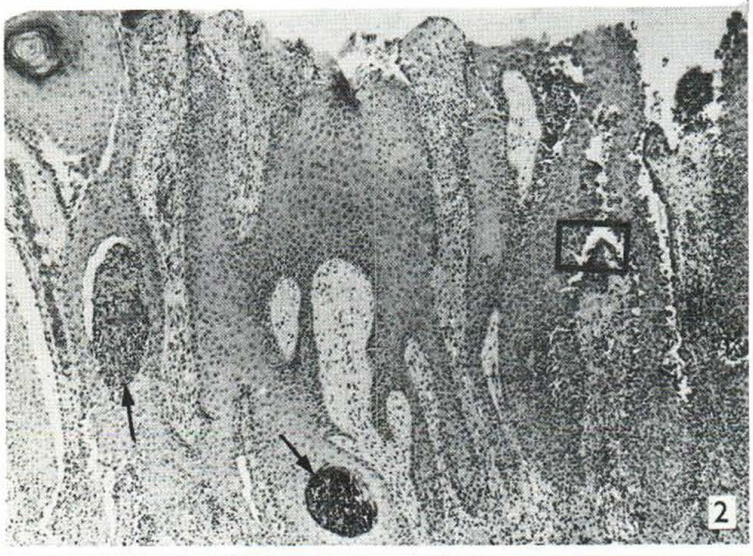

Fig. 2. Histology of genitocrural lesion. Eosinophilic pustules (↑).

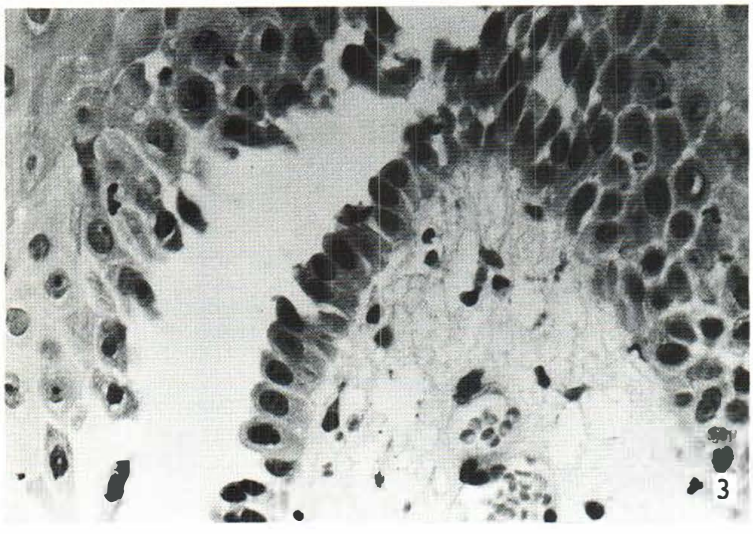

Fig. 3. Detail of Fig. 2.

Table II. *Cellular immune status, including granulocyte functions*

Investigations	Results	
T and B cells in venous blood (E-rosette formation, membrane immune fluoresc. technique cf. 5)	B cells	26%
	T cells	30%
Lymphocyte response	To PHA	Reduced
	To Candidin	∅
Immediate and delayed skin reactivity	Bacterial antigens (Allergopharma)	∅ (pos. to *Klebsiella pneum., Pseudomon. aerug.* only)
	Candidin (Bencard)	∅
	Trichophytin sp. (Allergopharma)	∅
	Tuberculin GT 1.0 (Behringwerke)	∅
Granulocyte functions in vitro	Phagocytosis of viable *Cand. alb.*	Normal
	Phagocytosis of heat-inactivated *Cand. alb.*	Normal
	Intracellular killing of *Cand. alb.*	Impaired
	NBT test	Normal
	Chemotaxis	Impaired

tra-epidermal eosinophilic pustules, proliferating papillary layer with edema and diffuse inflammatory infiltrate consisting predominantly of neutro- and eosinophils (Figs. 2 and 3). Mucoid edema around subpapillary venules and sweat glands.

Immunofluorescence. Antiepithelial IgG-antibodies positive: IIF 1:64, DIF 1:64; C'3 1:32.

Follow-up and treatment. Both corticosteroids and nystatin were administered topically and systemically (initial daily dosage 80 mg 6-methyl prednisolone). Marked improvement after a few days. No immunosuppressive drugs. After 5 weeks' treatment, dismission of patient in fairly good condition (maintenance dose 20 mg 6-methyl prednisolone daily).

In May 1979, severe genital relapse after arbitrary reduction of recommended steroid dose. Pemphigus antibodies (IFF, IgG): 1:128. Short-term high dosage of corticosteroid cleared the lesions rapidly again.

DISCUSSION

Despite the prolonged illness, the patient's general condition and laboratory check-up were scarcely affected. Some minor disturbances of blood coagulation did not correspond to the clinical state. Interestingly, the slightly depressed serum level of IgG rose to normal again after a few weeks of treatment with corticosteroids.

There are few published reports on decreased IgG serum levels in pemphigus vulgaris (9). In most cases IgG levels were found to be elevated. Increased numbers of circulating B cells in patients with pemphigus vulgaris or bullous pemphigoid have also been observed (2).

In the present case, the impairment of both T cell and PMNL functions is striking. The impairment of some important T cell functions clearly indicates a state of cellular immunodeficiency, yet cannot account for either the origin or clinical significance of this abnormality. Likewise the question is open whether the immunodeficient state is primary to, or resulting from, or aggravated by, the pemphigus disease persisting for 8 months. Apart from recalcitrant oral and genital candidosis, there was no evidence of any inborn or acquired immunoparalysis. In particular, neither thymoma nor myasthenic symptoms were proven.

Safai et al. recently reported on a patient with thymoma and myasthenia gravis who developed intraoral pemphigus lesions in association with cellular immunodeficiency (13). B cells were lacking in venous blood, no circulating pemphigus antibodies could be demonstrated, and antinuclear, antithyroid, and antimuscular antibodies were absent. Lymphocyte responses to various mitogens as well as to common bacterial antigens were diminished. Skin reactivity to recall antigens was negative. The NBT test with PMNL was also impaired, yet T cell count was normal.

The immunological findings in our case partly differ from, and partly correspond to, those mentioned above. In addition, both chemotactic activity and intracellular killing of *C. a.* by PMNL were impaired. There was no evidence, however, of an NADH-dependent oxidase deficiency of PMNL.

Every immunological response in the human organism is assumed to depend on a complex interaction of T and B lymphocytes, and T cells with 'helper' or 'suppressor' functions are known to play an important part in the regulation of B cell activity by stimulating or suppressing antibody production (4, 5, 8, 12). It can be concluded from the present and other observations that disturbances in the cooperation between T and B cells may be fundamental for the pathogenesis of pemphigus, at least of vegetans type. In what way and to what extent the microphages are involved in injured immunoregulation remains to be cleared up. However, in case of pemphigus the main constituents of the cellular immune system, including PMNL, should be examined before treatment in order to trace any immunological imbalances which may be intrinsic for the genesis of autoimmune disorders such as pemphigus.

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