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IMMUNOFLUORESCENT FOLLOW-UP STUDIES IN PATIENTS WITH BULLOUS DERMATOSES

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Abstract. Basement zone antibody titres were studied in two patients with bullous pemphigoid over a period of 1½ and 3½ years. Titres remained almost constantly even after a complete healing of all lesions, without any treatment. Direct immunofluorescence revealed basement zone antibodies in one of these two patients when examined after healing had occurred. Three patients with bullous dermatoses showed pemphigus antibodies at the inception of the disease. Basement zone antibodies were present simultaneously in one patient. In the subsequent course of observation in the two other patients, pemphigus antibodies were replaced by basement zone antibodies and in one case by nuclear antibodies too. These findings make the pathogenetic import of these "auto-antibodies" difficult to understand.

Key words: Basement zone antibody titer; Bullous pemphigoid; Bullous dermatoses; Pemphigus antibodies; Nuclear antibodies

The detection of autoantibodies in bullous dermatoses (1, 9) has raised several questions concerning their etiological and pathogenetic importance. In pemphigus vulgaris the level of antibody titre is related to the clinical condition (2, 11), whereas in pemphigoid, such definite correlation is missing (11). Using direct immunofluorescence, no antibodies could be found at the basement zone in any patient after healing (3). The indirect method, however, showed one-third of the patients as having circulating antibodies (3).

The present study was designed to conduct longer immunofluorescent follow-up studies in patients with pemphigoid and who showed a complete clearing of all lesions. Furthermore, we studied the change of pemphigus antibody specificity in patients with bullous dermatoses during the course of the disease.

MATERIALS AND METHODS

Basement zone antibody titres in 2 female patients with bullous pemphigoid were studied over a period of nearly 1½ years (patient I, 84 years old; Fig. 1) and 3½ years (patient II, 72 years old; Fig. 2).

In a group of 3 other patients with bullous dermatoses (patients III, IV and V, aged 69, 58 and 74 years) we could trace pemphigus antibodies at the inception of the disease. Table I contains a tabulation of this study.

Immunofluorescence methods and materials were used as described elsewhere (6, 7).

RESULTS

Patient I (Fig. 1) has been free of disease for 1½ years, patient II (Fig. 2) for 1¼ years, since therapy was terminated. The antibody titre remained relatively constant. At the beginning of therapy, antibodies bound to the basement zone could be shown by direct immunofluorescence to be present in both patients. At the most recent examination, however, we could reproduce this result in patient II (Fig. 2) only. Patient I showed no direct immunofluorescence although her basement zone antibody titre was higher (Fig. 1). At the second examination, biopsies were taken from the same area as at the onset of the disease. The so-obtained epidermis of patient I was incubated with patient's II serum. In this way, we achieved antibody binding to the basement zone.

In patient III, the clinical, histological and immunofluorescent findings confirmed the diagnosis of pemphigus vulgaris (Table I). Pemphigus antibodies were verifiable in December 1971; three examinations during the last two years merely showed basement zone antibodies to be present, though the patient had a complete clearing of all skin lesions.

Patient IV was admitted to our clinic in 1966 with a pemphigus vulgaris that had been histologically verified (Table I). Immunofluorescent examinations in September 1971 revealed equal titre values of pemphigus antibodies and basement zone antibodies. The most recent immunological test showed basement zone antibodies in addition to a high titre of

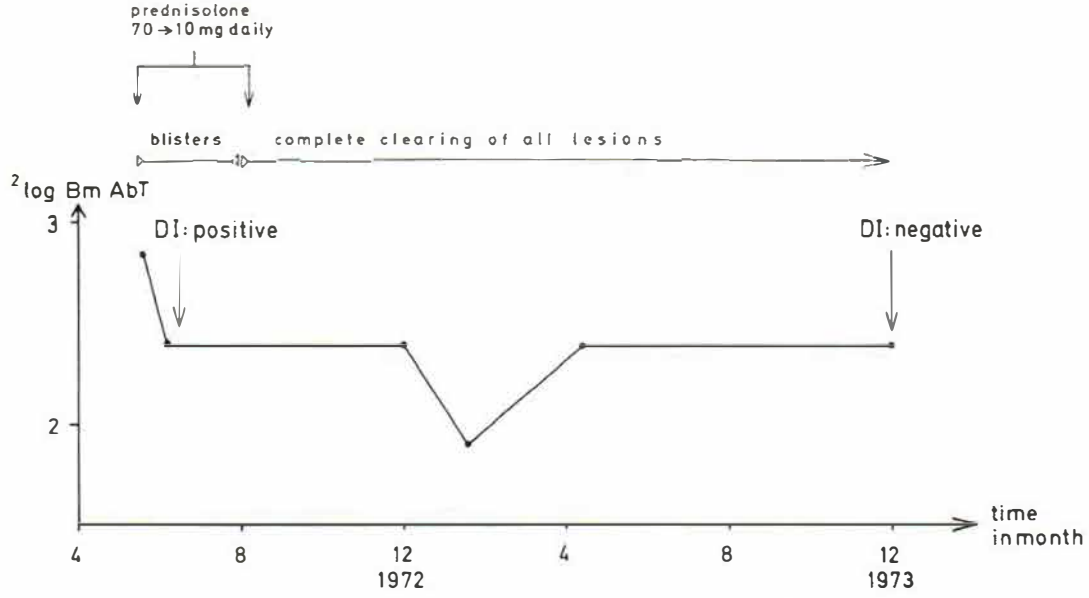

Fig. 1. Follow-up study on titres over 1½ years in a patient (I) with bullous pemphigoid. *Ordinate:* ²log basement zone antibody titre. *Abscissa:* time in months. Clinical condition and therapy are briefly stated above the graph. *DI* = direct immunofluorescence.

nuclear antibodies. Since July 1973 this patient has shown a complete clearing of all lesions, without any treatment.

In patient V (Table I), histological examination verified a bullous pemphigoid. Immunofluorescent studies initially showed almost equal titres of pemphigus and basement zone antibodies. Two years later we obtained the same result.

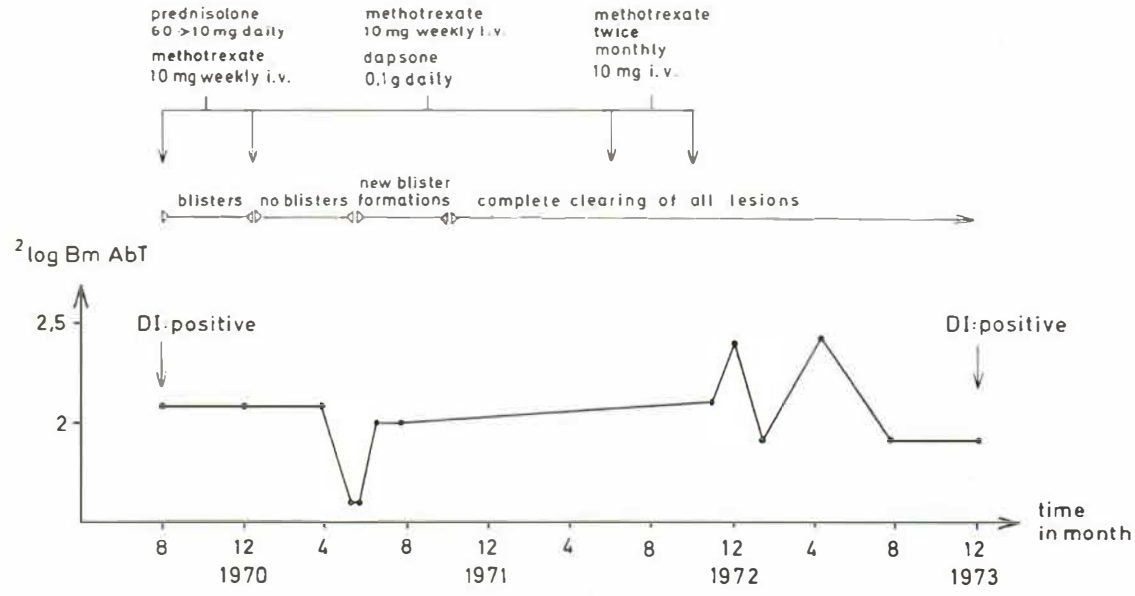

Fig. 2. Follow-up study on titres over 3½ years in patient II with bullous pemphigoid. *Ordinate:* ²log basement zone antibody titre. *Abscissa:* time in months. Clinical condition and therapy are briefly stated above the graph. *DI* = direct immunofluorescence.

Table I. *Summary of findings in 3 patients with bullous dermatoses*

Several antibodies of different specificity were simultaneously present or occurred in the course of the disease in all 3 patients
+, positive; −, negative

Pat. no.	Date of examination	Indirect immunofluorescent staining: Intercellular areas	Indirect immunofluorescent staining: Basement zone	Indirect immunofluorescent staining: Nuclear	Histological diagnosis	Clinical findings	Therapy (daily dose)
III	May 1968	Not examined			Pemphigus vulgaris	Blisters on skin and mucus membranes	Prednisone, 100–20 mg
	Dec. 1971	+	−	−		Skin free. Recurring blisters on mucus membrane of mouth	Prednisone, 20 mg and imurek, 100 mg
	Nov. 1972	−	+	−		Skin free. Recurring blisters on mucus membrane of mouth	Prednisone, 20 mg and imurek, 100 mg
	April 1973	−	+	−		Skin free. Recurring blisters on mucus membrane of mouth	Prednisone, 20 mg and imurek, 100 mg
	Oct. 1973	−	+	−		Skin free. Recurring blisters on mucus membrane of mouth	Prednisone, 20 mg and imurek, 100 mg
IV	Aug. 1966	Not examined			Pemphigus vulgaris	Blisters on skin and mucus membranes.	Prednisone, 150–20 mg
	Sept. 1971	+	+	−		Skin free. Recurring blisters on mucus membrane of mouth.	Prednisone, 20 mg
	Dec. 1973	−	+	+		Skin and mucus membranes free since July 1973	None, since July 1973
V	Aug. 1971	+	+	−	Bullous pemphigoid	Blisters on entire skin. Mucus membranes free	Prednisone, 60–10 mg and imurek, 50 mg
	Oct. 1971	+	+	−		Blisters on entire skin. Mucus membranes free	Prednisone, 60–10 mg and inmurek, 50 mg
	Dec. 1971	+	+	−		Blisters on entire skin. Mucus membranes free	Prednisone, 60–10 mg and imurek, 50 mg
	May 1973	+	+	−		Single blisters on the back	Prednisone, 10 mg

DISCUSSION

Earlier studies (5) point to a correlation between the basement zone antibody titre and pemphigoid activity. More recent investigations (11) reported high antibody titres even after healing had occurred. Our sequential study confirms this result. With the direct method of immunofluorescence we found antibodies at the basement zone in patient II after healing. This contradicts the assumption that secondary inflammatory reactions caused the loss of antigen—"antigene Narbe"—(4). In agreement with Beutner (3) we could not demonstrate antibody binding at the basement zone by direct immunofluorescence in patient I, although a high serum antibody titre was present. When employing the indirect method, however, we succeeded in binding antibodies of patient II to the basement membrane of the skin of patient I. Jordon (9) has reported similarly.

During the course of the disease in patient III (pemphigus vulgaris) we observed basement zone antibodies instead of pemphigus antibodies. Patient IV showed the same phenomenon.

In a third patient (patient V) we observed the immunofluorescent patterns of both pemphigus vulgaris and bullous pemphigoid, using the same antigenic substrate. Similar findings have been reported previously by Misgeld (10), though using different antigenic substrates. Chorzelski & Jablonska (8) attribute the variable results of these reactions to errors in the applied technique.

The results of our findings do not help to elucidate the pathogenetic significance of these "auto-antibodies".

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