ORIGINAL CONTRIBUTIONS

CORRELATION OF CIRCULATING ANTIBODY TITRES WITH ACTIVITY OF DISEASE IN PEMPHIGUS

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Correlation of antibody titres with the clinical severity of the disease was done in 58 patients having pemphigus. Serial determinations of the antibody titres were done in 40 patients ranging from two to eight follow-up samples. Titre of the antibody correlated with the disease activity in 70% of the cases. In 6 patients with mild disease, the antibody titre was persistently high, while in 11 patients with moderate to severe disease activity, antibody was nil or present in low titres. While the former group may indicate better prognosis and prolonged remissions, the latter situation could be as a result of immune failure either due to fulminant disease or due to the immunosuppressive effect of the high doses of the drugs used to control the disease.

Key words : Pemphigus, Antibody titres, Correlation.

Circulating autoantibodies are present in the serum of pemphigus patients and titre of the antibodies have been stated to correlate with the clinical course of the disease [1-3] although results at variance have also been reported.[1] Most of the studies have been done in the west and there is paucity of information on this subject in our country. Therefore, the present study was undertaken to find out the immunological response of patients having pemphigus and to correlate the disease severity with the antibody titre.

Materials and Methods

Fifty eight patients having pemphigus were followed-up for a period of upto two and a half years. Fifty one of them were pemphigus vulgaris (PV) and 7 pemphigus foliaceous (PF). In all the cases, the clinical diagnosis was confirmed by histopathology. Circulating antibodies were detected by using human oesophagus as substrate. In 40 patients, serial estimations at periodic intervals for a period ranging from 3 months to 2½ years, were also undertaken.

Three ml of blood was collected from the patient. Serum was separated and stored at--70°C until used. Frozen sections from human oesophagus were cut, fixed in cold acetone and stored at -70°C. Staining was done by the indirect immunofluorescent technique using monospecific FITC labelled anti-human IgG, IgA, IgM and C_3 antibodies (Dakopatts, Denmark) and examined under Olympus epifluorescence microscope using HBO 50 lamp, primary filter of 450-490 nm and barrier filter of 520 nm.[5] In positive cases, the antibody titres were determined by the double dilution method. Antibody titres upto 1:20 were considered low, 1:40-1:80 as moderrate and more than 1:80 as high. Clinical severity of the disease was assessed according to the severity of the lesions and the area of the body involved. The grading was also done according to the dose of corticosteroids required to control the disease; patients requiring more than 60 mg of prednisolone or equivalent for

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control of the disease activity were graded as severe, those requiring 30-60 mg were labelled moderate and ones requiring below 30 mg were considered as mild. Patients in inactive phase did not have any lesions and were with or without the maintenance therapy.

Results

IgG was the predominant antibody. IgM and C_3 were demonstrated in only one case. Results of antibody titres and the disease activity are shown in Table I. There were a total of 156 samples. The disease activity was mild in 88, moderate in 41 and severe in 11 cases. Sixteen samples were collected when the patients had no lesions.

Four types of clinico-immunological responses were obesrved. First group had 26 patients where the clinical disease was severe to moderate and the titres were also high or moderate, which decreased with clinical improvement and rose again during exacerbation. In the second group of 15 patients, the clinical disease was mild and in some cases there were no active lesions, and correspondingly the titres were also low or nil but rose again along with exacerbation of the disease. In the third group of 6 patients, the clinical activity of the disease was low or nil but antibody titres were moderate or high. In the fourth group of 11 patients, the disease was severe or moderate but the titres were low or nil, and remained so during the course of the disease. Two patients in this group had fulminant fatal course of the disease, while one patient was a debilitated 82-year-old lady. Three patients had antinuclear antibodies also. One patient could not be controlled on corticosteroids and was put on cyclophosphamide therapy with a good response.

Comments

Forty one, out of 58 cases belonged to the first 2 groups with a good correlaiton between the antibody titres and the disease activity. Antibody titres were found to be higher in patients with moderate disease rather than the ones having very severe disease activity. 45% of those with severe disease showed high titres while 65.8% with moderate disease had high titres. It had been the experience of other workers also that there is an over-lap in the middle range of antibodies. Heavy doses of corticosteroids in patients with severe disease may also have a relationship with this observation as discussed later.

Table I. Correlation of the severity of the disease and reciprocal antibody titres.

Clinical state	Number of cases	Antibody titres			
		Negative	Low (1 : 20)	Moderate (1 : 40-80)	High (1 : 160 or above)
Severe	11	2 (18%)	4 (36%)	2 (18%)	3 (27%)
Moderate	41	8 (19.5%)	6 (14.6%)	14 (34.1%)	13 (31.7%)
Mild	88	45 (51%)	25 (28.4%)	16 (18.1%)	2 (2.2%)
No lesions	16	13 (81.2%)	1 (6.25%)	—	2 (12.5%)

Six patients of the third group were in an inactive phase for periods ranging from 2 to 10 years with or without a maintenance dose of corticosteroids. This group had prognostically better disease. Here, the antibodies could be detected even after 1-2 years of clinical remission. High titres in patients with low activity of the disease have been stated to be indicative of better prognosis and prolonged remissions.[6]

Eleven patients belonging to 4th group had low or absent antibody titres. Negative results in these patients may be due to many factors like poor antibody affinity to substrate, presence of interfering substances like antinuclear antibodies (ANA), immune failure or immune suppression. It is well known that pemphigus antigen present in the intercellular substance is a heterogenous group of antigens with varying affinity for the substrates.[7,8] Varied results have been reported using various substrates ranging from human skin, guinea pig lip mucosa and oesophagus, rabbit oesophagus, monkey oesophagus and human oesophagus.[1,3,9] In our own laboratory (unpublished data), affinity of human skin was compared with human oesophagus, and the results with the latter were found to be superior and more consistent. Therefore, it is felt that substrate affinity is not the reason of negative results in this group. Prozone phenomenon was ruled out by doing further dilution of the antibodies. In 3 patients, ANA were present and may be responsible for false negativity. But the more plausible explanation for the absence of antibodies seems to be immune failure or immunosuppression. It is well known that patients with fulminant disease or in an old debilitated state may have a failure of the immune response. Possibility of immunosuppression by the high doses of corticosteroids in this group of patients being responsible for negative results is strong.

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