Lupus nephritis and lupus band test

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Summary

Twenty-seven patients with histologically confirmed lupus nephritis were studied to identify the incidence of lupus band and its significance to histological patterns of nephritis and complement levels. It was found that the kidney involvement is 2.5 times more frequent in lupus band positive patients. The association of a positive lupus band and low C_3 level signifies the presence of diffuse proliferative glomerulonephritis rather than membranous glomerulonephritis. The results, together with earlier reports, are discussed.

Introduction

Since the identification of immunoglobulins and complement components at the basement membrane zone of non-exposed clinically normal skin of patients with systemic lupus erythematosus (SLE), known as the lupus band test (LBT) (Burnham and Fine, 1971), the relationship of the band to renal damage has been the subject of few reports with controversial conclusions (Caperton, Bean and Dick, 1972; Gilliam *et al.*, 1974; Dantzig *et al.*, 1975; Wertheimer and Barland, 1976). In these reports, the significance of the band test in patients with and without renal damage, not all of whom had renal biopsy were assessed. In the present study, the authors selected 27 patients with lupus nephritis, confirmed by histology, to study the incidence of LBT and identify the band's relation, if any, to the histological patterns of nephritis and the complement levels.

Materials and methods

Twenty-seven patients, who met the preliminary criteria of the American Rheumatism Association for SLE (Cohen *et al.*, 1971), were included in this study. There were 25 females and 2 males with their ages ranging from 11 to 48 years. The racial distribution, reflecting the attendance at the SLE clinic, were 21 Chinese, 5 Malays and one Indian. All

patients had laboratory evidence of renal damage. Renal and skin biopsies were done either simultaneously or within one week of each other. The renal specimen was divided into 2 portions, one half for light microscopic study and the other half for direct immunofluorescent test. The renal histological changes were classified according to the criteria of Baldwin *et al.* (1970). A 4-mm punch biopsy from uninvolved skin of the flexor aspect of the upper arm was obtained for direct immunofluorescence. Serum for C_3 concentration was obtained a day or two before the renal biopsy. The complement was measured by using the single radial diffusion method.

Direct immunofluorescence: a 4- μ cryostat section of the specimen was air dried, washed with phosphate-buffered saline and incubated with fluorescein-conjugated anti-human immunoglobulins (IgG, IgA and IgM) and anti-human complement C_3 (Behringwerke AG, Germany). The slides were viewed with a Leitz Wetzler fluorescence microscope equipped for epi-illumination.

Results

Twenty-one patients had diffuse proliferative glomerulonephritis (DPGN), 5 had membranous glomerulonephritis (MGN) and one had focal proliferative glomerulonephritis (Table 1). There was insufficient renal tissue for immunofluorescence in 11 patients. Of the remaining 16 patients, all except one had IgG and C_3 in the renal glomeruli. All the classes of immunoglobulins and C_3 were found with almost equal frequency. C_3 was found 3 times more frequently in the kidney than in the skin.

The LBT was positive in 19 (70%) of the 27 patients. Both IgG and IgM were found with equal incidence although in some patients both did not occur together. In 2 patients without IgG at the skin basement membrane zone, IgM alone was found. Both these patients had DPGN. IgA occurred with

TABLE 1. Immunofluorescence of skin and kidney in relation to renal histology, the LBT and serum C₃ concentration (normal C₃ concentration=65-130 mg/dl)

Patient	Renal glomerular pathology	LBT	Skin basement membrane/glomerular fluorescent deposits				Serum C ₃ (mg/dl)
			IgG	IgA	IgM	C ₃	
1	DPGN	-	-/ND	-/ND	-/ND	-/ND	71
2	DPGN	+	+/+	-/-	+/+	-/+	7
3	MGN	+	+/ND	-/ND	+/ND	-/ND	76
4	DPGN	+	+/+	+/+	+/+	-/-	41
5	DPGN	+	+/ND	+/ND	+/ND	-/ND	56
6	MGN	-	-/ND	-/ND	-/ND	-/ND	111
7	DPGN	+	+/+	-/-	+/+	+/+	33
8	DPGN	+	+/ND	-/ND	+/ND	-/ND	3
9	DPGN	+	+/+	-/-	-/+	-/+	86
10	DPGN	+	+/ND	-/ND	+/ND	-/ND	72
11	DPGN	+	+/+	+/+	+/+	-/+	48
12	DPGN	+	+/+	+/+	+/+	-/+	28
13	DPGN	+	+/ND	-/ND	-/ND	-/ND	59
14	DPGN	+	+/ND	+/ND	+/ND	-/ND	40
15	DPGN	+	+/ND	-/ND	-/ND	-/ND	72
16	DPGN	+	+/+	+/+	+/+	+/+	40
17	DPGN	-	-/+	-/+	-/+	-/+	100
18	MGN	-	-/+	-/+	-/+	-/+	50
19	DPGN	+	+/ND	+/ND	+/ND	-/ND	22
20	DPGN	-	-/+	-/+	-/+	-/+	0
21	MGN	-	-/+	-/+	-/+	-/+	60
22	DPGN	+	-/+	-/+	+/+	+/+	38
23	DPGN	-	-/+	-/+	-/+	-/+	34
24	DPGN	+	-/ND	-/ND	+/ND	-/ND	43
25	FPGN	+	+/+	-/+	+/+	+/+	49
26	MGN	+	+/+	-/+	+/+	-/+	70
27	DPGN	-	-/+	-/+	-/+	-/+	72

ND=not done; DPGN=diffuse proliferative glomerulonephritis; MGN=membranous glomerulonephritis; LBT=lupus band test; FPGN=focal proliferative glomerulonephritis.

less frequency compared to other classes of immunoglobulins and in all the patients with this immunoglobulin DPGN was present. C₃ was found in only 4 patients. Sixteen patients (76%) of the 21 with DPGN had a positive LBT and 2 (40%) of the 5 with MGN had a positive LBT (Table 2). Fourteen (74%) of the 19 patients with a positive LBT had a low C₃ concentration, all of whom had DPGN and 5 (26%) had normal C₃ concentration (Table 3). Eighteen of the 27 patients with renal damage had a low C₃ concentration.

Discussion

As the identification of the presence and severity of renal damage in SLE has prognostic value, the LBT as a marker for renal damage has assumed a significant role in the management of patients. The different conclusions as to the significance of the LBT to the renal lesion in earlier studies (Burnham and Fine, 1971; Caperton *et al.*, 1972; Dantzig *et al.*, 1975) are partly due to the choice of different site for skin biopsy, the assessment of renal damage by clinical and laboratory methods without histological confirmation and the varying temporal relationship between the renal and skin biopsy. Wertheimer and Barland (1976), taking into con-

sideration the above factors, could not find any significant correlation between the renal lesion and LBT, although Gilliam *et al.* (1974) reported the existence of such a correlation. In the present study, it was found that kidney involvement was 2.5 times more frequent in LBT positive patients than in those with a negative lupus band. It is difficult to explain the findings of Wertheimer and Barland (1976) but as the relationship between a positive LBT and the renal damage has been studied by 2 possible methods, Gilliam *et al.* (1974) studying the incidence of renal damage in LBT positive patients and the present authors studying the incidence of a positive LBT in patients with renal damage, with similar results, the conclusion reached is probably more accurate. Low C₃ concentrations were found in 74% of the 19 patients with a positive LBT and 67% of the 27 patients with renal damage. Although statistical analysis is not possible as patients without renal damage were not included in this study, the figures suggest that a positive LBT, low C₃ concentrations and renal lesion are closely related.

Similar classes of immunoglobulins were detected both in the kidney and the skin, as was also reported by Gilliam *et al.* (1974), who concluded that the kidney and the skin shared a common pathogenic

TABLE 2. Relationship between renal histology and the LBT

Renal histology	No. of patients	No. with positive band	Positive (%)	No. without a band	Negative (%)
DPGN	21	16	76	5	24
MGN	5	2	40	3	60

DPGN=diffuse proliferative glomerulonephritis; MGN=membranous glomerulonephritis; LBT=lupus band test.

TABLE 3. Relationship between serum C₃ concentration, the LBT and renal pathology. (Normal C₃ concentration = 65–130 mg/dl)

C ₃	No. of LBT-positive	No. of LBT-negative	No. of DPGN	No. of MGN	No. of focal
Low	14	4	15	2	1
Normal	5	4	6	3	

LBT=lupus band test; DPGN=diffuse proliferative glomerulonephritis; MGN=membranous glomerulonephritis.

mechanism. This was further confirmed by Pennebaker, Gilliam and Ziff (1977) who found that the immunoglobulin class of DNA binding activity in the serum and skin in SLE was similar. However, more of the present patients had C₃ in the kidney than in the skin. This is probably due to the fact that activated complement components, known mediators of inflammation (Ruddy, Cigli and Austen, 1972) are more likely to be present in the kidney which showed both clinical and microscopic damage than in the normal skin.

It is generally agreed that DPGN is more serious and has a worse prognosis than MGN. It was found in this study that patients with DPGN were more likely to have a positive LBT and low C₃ concentrations than those with MGN. Thus, the association of a positive LBT in the non-lesional skin and hypocomplementaemia not only signifies the presence of lupus nephritis but also a more serious form of renal pathology.

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