Correspondence

Lymphocyte subpopulations in essential mixed cryoglobulinaemia

SIR, Essential mixed cryoglobulinaemia (EMC) is an uncommon disease characterised by the formation of cryoprecipitable complexes involving IgM and IgG.¹ The IgM component can be monoclonal (type II cryoglobulinaemia) or polyclonal (type III cryoglobulinaemia) and displays an anti-Fc antibody activity comparable to rheumatoid factor. However, an idiotype-anti-idiotype reaction between IgM and IgG has been reported.² Although hepatitis B virus (HBV) has been implicated in the aetiology of some cases of the disease,^{3 4} little is known about its immunopathogenesis. The availability of monoclonal antibodies specifically directed against human lymphocytes and their subsets⁵ has provided a new tool for the analysis of T cell and B cell populations in human diseases. Recently, we investigated peripheral blood lymphocytes and the distribution of inducer-helper and suppressor-cytotoxic subsets in five patients with EMC.

Three men and two women, mean age 53 years (range 33-63), were investigated. All five patients had recurrent purpuric rash and two had arthralgia. Three patients had liver disease (Table 1, patients Nos 1, 2, and 3) and three had HBV serological markers in their serum (patients Nos 1, 3, and 4). At the time of the study none of the patients were receiving any treatment.

Lymphocytes were separated from heparinised whole blood by a density gradient technique (Ficoll-Hypaque). Monoclonal antibodies to all peripheral T cells (OKT3), to helper T cells (OKT4), to suppressor T cells (OKT8) (Ortho Diagnostics), and to B cells (B-1) (Coulter clone) were used, and cells numbers were assessed under fluorescence epi-illumination with a Dialux 20 EB Leitz microscope.

As shown in Table 1 the two patients with type II

cryoglobulinaemia had high percentages of peripheral T cells (OKT3⁺) and helper-inducer T cells (OKT4⁺), with nearly normal percentages of suppressor-cytotoxic T cells (OKT8⁺), and consequently a high ratio OKT4⁺/OKT8⁺; while the three patients with type III cryoglobulinaemia had normal percentages of OKT3⁺ OKT4⁺, and OKT8⁺ subsets of T lymphocytes. The percentage of B-1⁺ cells was normal in all patients.

Our results are in disagreement with those reported by Meroni *et al.*,⁶ which showed reduced percentages of OKT4⁺ cells with a low ratio OKT4⁺/OKT8⁺ in patients with EMC. Moreover, these investigators⁶⁻⁸ found evidence of in vitro abnormalities in the function of suppressor-cytotoxic T lymphocytes and B lymphocytes.

Our data are difficult to interpret, though they suggest the possibility that different immune derangements can occur in EMC according to the type (II to III) of the cryoglobulinaemia. Further studies are necessary on a greater number of patients.

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Table 1 Lymphocyte subpopulations in patients with essential mixed cryoglobulinaemia

Patient No	Sex	Age (years)	Cryoglobulinaemia type	Reactivity with monoclonal antibodies to:				
				OKT3 ⁺ (% of positive cells)	OKT4 ⁺	OKT8 ⁺	B-1 ⁺	OKT4 ⁺ /OKT8 ⁺ Ratio
1	F	60	Type II IgMk-IgG	90	68	15	6	4.5
2	F	57	Type II IgMk-IgG	92	65	20	8	3.2
3	M	33	Type III IgM-IgG	74	52	29	10	1.7
4	M	52	Type III IgM-IgG	65	48	20	11	2.4
5	M	63	Type III IgM-IgG	70	57	28	8	2
Normal values in 10 adults (range)				59-83	32-61	16-32	7-17	1.2-2.9

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Systemic lupus erythematosus without clinical renal abnormalities

SIR, We read with interest the study of O'Dell *et al*¹ showing a high incidence of mesangial changes in renal biopsies from patients with systemic lupus erythematosus (SLE) without clinical renal abnormalities. They found no cases of focal or diffuse proliferative glomerulonephritis. These results are different from those previously reported by other authors^{2 3} and question the relevance of renal biopsy in these patients.

Recently we have performed renal biopsy in 13 patients with SLE (fulfilling the American Rheumatism Association revised criteria⁴) who had no clinical signs of renal involvement (no urinary sediment abnormalities, absence of proteinuria, and serum creatinine below 1.3 mg/dl (115 µmol/l)). All renal biopsy specimens were examined by two pathologists and categorised according to the modified classification proposed by the World Health Organisation.⁵

Five cases (38%) showed no histological or immunofluorescence changes (type I), six (46%) patients had a mesangial nephropathy (three type IIa and three type IIb), and two (15%) had a focal proliferative glomerulonephritis (type III). None of the patients had previous evidence of neurological abnormalities. Patients with normal renal biopsies (type I) only had arthritis, skin lesions, and Raynaud's phenomenon. In contrast, six patients with histological renal involvement had serositis or haemolytic anaemia. All cases with silent nephropathy were treated with steroids and showed a benign clinical course with stable renal function and absence of urinary abnormalities during follow up (one to 76 months, mean 27 months).

On the basis of these results we agree with O'Dell *et al*¹ that, in the absence of clinical renal abnormalities, significant renal involvement is uncommon in SLE. However, as reported by Mahajan *et al*² and Lehey *et al*³

and confirmed in the present study, a few patients may have severe renal lesions requiring steroid therapy. Thus until more information becomes available we believe that a renal biopsy should be performed in those SLE patients presenting with clinical manifestations other than arthritis or cutaneous lesions since this policy may allow detection of silent nephritis lesions.

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SIR, We appreciated the letter of Font *et al* and the opportunity to respond to it. The findings of Font *et al* that none of the 13 lupus patients without clinical evidence of renal disease had diffuse proliferative glomerulonephritis are very similar to our findings but very different from the findings of Mahajan *et al*.¹ We were surprised that five of the 13 lupus patients in their study (Font *et al*) had completely normal renal biopsies. All of our patients, despite the absence of clinical renal abnormalities, had mesangial abnormalities as shown either by light microscopy or by immunofluorescence studies. Our findings are similar to those of most other studies published in the literature, which show that most patients, despite the absence of clinical renal disease, have abnormalities on renal biopsies.¹⁻⁴

We do not agree with the recommendation of Font *et al* that because they found focal proliferative glomerulonephritis in two of their patients they would advocate renal biopsies in lupus patients in the absence of clinical renal abnormalities. As stated in our paper there is no evidence in the literature to suggest that early treatment of histopathological abnormalities found on renal biopsy in the absence of clinical findings will in any way influence prognosis. In fact, all studies in lupus nephritis that have looked at the question have concluded that clinical parameters are a much stronger indication of prognosis than histological classification.