MEDICAL PRACTICE

Occasional Survey

Criteria for Classification of S.L.E.

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Summary

Of 38 patients with systemic lupus erythematosus (S.L.E.) followed in this clinic during the past two years raised levels of anti-DNA antibodies were found in 36. The recently proposed criteria for the classification of S.L.E. were met in 33 of these 36 patients. Three patients with raised DNA antibody titres and some of the features of S.L.E. did not meet the criteria for a classification of S.L.E.

Introduction

Epidemiological and therapeutic studies in systemic lupus erythematosus (S.L.E.) are limited by a lack of a precise definition of the disease. The American Rheumatism Association (A.R.A.) have recently published criteria for the classification of the disease[1] based on a multicentre analysis. Out of 57 features analysed from a total of 696 cases 14 criteria were selected as being of significance. The presence of four or more was considered to be compatible with S.L.E. (table I). The introduction of an immunoassay for the measurement of anti-DNA antibodies provided a sensitive and highly specific aid to the diagnosis of S.L.E.[2 3 4] Current experience suggests that the test gives a negative response in conditions other than S.L.E. in which antinuclear factor is present.[4 5]

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In this study an evaluation of the A.R.A. criteria was made in our own S.L.E. patients, with particular reference to patients in whom raised anti-DNA antibody titres were found.

TABLE I—*A.R.A. Criteria for Classification of S.L.E.*

(1)	Facial erythema
(2)	Discoid lupus
(3)	Raynaud's phenomenon
(4)	Alopecia
(5)	Photosensivity
(6)	Oral or nasal ulceration
(7)	Arthritis without deformity
(8)	L.E. cells (2 or more)
(9)	Chronic false positive serological tests for syphilis (longer than 6/12)
(10)	Proteinurea (>3·5 g/day
(11)	Cellular casts
(12)	Pleuritis or pericarditis
(13)	Psychosis or convulsions
(14)	Haemolytic anaemia or leucopenia (<4,000/mm³) or thrombocytopenia (<100,000/mm³)

Patients and Methods

Thirty-eight patients in whom a diagnosis of S.L.E. had been made and in whom DNA antibody status is known have been seen in our clinics during the past two years. Of these patients 36 had DNA binding values greater than 30%. In two patients values remained normal throughout the period of observation and were excluded from the analysis. DNA binding activity measurements were performed as previously described[6] using ^{14}C-labelled DNA (supplied by Radiochemical Centre, Amersham, Bucks). The clinical and laboratory features were analysed for the A.R.A. criteria.

Results

In 33 (91·7%) of the 36 patients the diagnosis of S.L.E. met the A.R.A. criteria. The mean number of positive criteria in our series was 5·44. The incidence of each of the manifestations in the 36 DNA antibody positive patients is shown in table II and is compared with the distribution in the A.R.A. study. Of particular interest are the three patients diagnosed as having S.L.E. who had raised DNA antibody titres but did not meet the A.R.A. criteria.

Case 1.—A 34-year-old Canadian woman first presented in March 1971 with acute pericarditis. She also complained of a two-year history of mild arthritis of the small joints of hands and feet. Examination showed pericarditis with a local friction rub, left-sided pleural effusion, and synovitis of small joints. Investigation showed E.S.R. 97 mm in one hour. Positive L.E. cells and A.N.F. (1/250), negative rheumatoid factor. DNA binding 89%. The arthritis has continued without development of erosions.

Case 2.—A 20-year-old American woman presented in September 1971 with haemolytic anaemia. Investigation showed a positive Coombs test and the red cells were coated with IgG, IgM, and complement. E.S.R. 67 mm in one hour. L.E. cells and A.N.F. positive (1/1,250). Complement (C_3) 40%, DNA binding 63%. The haemolytic anaemia improved with corticosteroid therapy but the serum complement (C_3) remained low.

TABLE II—*Incidence of Positive Criteria in 36 Cases of S.L.E.*

Criteria	No. (%) of	% in Preliminary Criteria
(1) Facial erythema	23 (63·9)	63·7
(2) Discoid lupus	11 (30·6)	17·1
(3) Raynaud's phenomenon	7 (19·4)	20·0
(4) Alopecia	23 (63·9)	43·3
(5) Photosensitivity	6 (16·7)	36·7
(6) Oral or nasal ulceration	8 (22·2)	15·1
(7) Arthritis	32 (88·9)	89·8
(8) L.E. cells	27 (75·0)	91·8
(9) Chronic false positive serological tests for syphilis	3 (8·3)	11·8
(10) Profuse proteinurea	9* (25·0)	19·6
(11) Cellular casts	6 (16·7)	47·8
(12) Pleuritis	11 (30·6)	60·4
Pericarditis	7 (19·4)	18·8
(13) Psychosis/convulsions	7† (19·4)	19·2
(14) Haemolytic anaemia	5‡ (13·9)	16·3
Leucopenia	17§ (47·2)	39·6
Thrombocytopenia	5 (13·9)	11·4

*An additional 9 patients had proteinuria <3·5 g (range 0·2 g-2·8 g/24 hours).
†An additional 4 patients had other C.N.S. manifestations attributed to their disease.
‡An additional 13 patients had W.B.C. >4,000/mm³ but had absolute lymphopenia.
§An additional 3 patients gave positive response to Coombs test.

The two patients suffering from S.L.E. in whom antibody titres remained normal throughout the period of observation, and who were therefore excluded from the study, both satisfied the A.R.A. criteria with nine and six features respectively. In both cases the positive features had been present before the start of the study, the patients remaining clinically quiescent throughout the two-year study period.

Discussion

With the increasing resort to multicentre trials on S.L.E. patients there is a need for widely accepted criteria for its classification. The 91·7 correlation between our 36 cases of S.L.E. and the A.R.A. criteria is encouraging and similar to the series reported by Lie and Rothfield.[7] The aim of the A.R.A.'s committee on diagnostic and therapeutic criteria was to evaluate those clinical manifestations and laboratory investigations which were of most use in classifying the disease for population surveys and studies on natural history and therapeutic trials. The 14 criteria reported by the committee were arrived at after analysis of the information provided on 696 cases by 52 North American rheumatology centres.

There was good correlation between the percentage distribution of most individual criteria in our cases and those in the A.R.A. study. Only in the incidence of alopecia, photosensitivity, cellular casts, and pleuritis were there any major discrepancies. Alopecia proved to be a frequent and recurring feature of our S.L.E. cases, and its comparatively low incidence in other series is surprising. Our low incidence of the other three criteria is at present unexplained.

Good correlation was obtained in the patients with profuse proteinuria, but the high level (>3·5 g/day) recommended in the A.R.A. criteria excluded 50% of our patients with increased 24-hour urine protein output. This point was examined in the A.R.A. study, and levels of proteinuria below 3·5 g/day were not found to have sufficient specificity when compared with levels found in other conditions. Five of our cases had renal damage demonstrable on renal biopsy without fulfilling either of the A.R.A. criteria referable to renal disease. Biopsy in these cases was performed partly because of persistently lowered serum complement levels. Measurements of serum complement may prove valuable as a criterion in future assessments.

The neuropsychiatric manifestations in S.L.E. are frequent and may be variable in presentation[8] and difficult to diagnose.[9] These problems have recently been reviewed.[10] The correlation between psychosis and convulsions in the various series is good. A total incidence of 30·6% of neuropsychiatric symptoms was seen in our patients if all manifestations are included. These ranged from psychosis and convulsions to chorea, visual disturbances, and cranial nerve lesions. This high figure still falls short of the 59% incidence reported by Estes and Christian.[11] Leucopenia is a recognized feature of S.L.E. White counts below 4,000/mm³ were found in 47·2% of our cases. A further 36·1% of our patients with normal total white cell counts (range 4,000-13,700/mm³) had lymphopenia when absolute values were calculated.

The three cases in which fewer than four criteria were present highlight some of the difficulties involved in classification of diseases. The A.R.A. criteria were not intended primarily for diagnostic purposes but were particularly constructed to have high specificity against rheumatoid arthritis and other non-rheumatic diseases.

Fries and Siegel[12] criticized the criteria and suggested revisions based on more modern techniques of information handling. In their series "false-positive" results were seen in significant numbers of patients with rheumatoid arthritis, systemic sclerosis, discoid L.E., "lupoid hepatitis," and polyarthritis. Serum complement levels and anti-DNA antibody titres are usually normal in these conditions[4 5 13] and appear to merit inclusion in future classification studies.

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