

Systemic Lupus Erythematosus: Initial Manifestations and Clinical Features After 10 Years of Disease

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Abstract

We studied the initial manifestations and late features in our lupus patients. The clinical data of patients fulfilling the American College of Rheumatology criteria for systemic lupus erythematosus (SLE) were entered prospectively for newly diagnosed patients and cumulatively for those with at least 10 years of disease duration. Ninety-seven Group A (newly diagnosed; 86 females and 11 males; mean age 31 years; 83 Chinese, 11 Malays, and 3 Indians) and 58 Group B (more than 10 years disease duration; 56 females and 2 males; mean age 41 years; 50 Chinese, 5 Malays, and 3 Indians) lupus patients were studied. The commonest clinical features in Group A were: haematological (73%), arthritis (57%), malar rash (43%), renal disorder (31%) and photosensitivity (30%). Group B patients had haematological (78%), malar rash (73%), arthritis (69%), renal disorder (59%) and photosensitivity (33%). Renal disorder was significantly increased over the years ($P < 0.001$). Hypertension was present in 18% (Group A) and 59% (Group B) ($P < 0.00001$), diabetes mellitus in 5% (Group A) and 10% (Group B) ($P = ns$), atherosclerosis in 2% (Group A) and 7% (Group B) ($P = ns$). Cataract formation was not present in Group A patients but was present in 10% of Group B patients. Renal disorders and morbidity factors like hypertension and cataracts increased significantly over the years. Optimum treatment of lupus patients should therefore include close attention to these factors.

Ann Acad Med Singapore 1997; 26:278-81

Key words: Atherosclerosis, Cataract, Diabetes mellitus, Hypertension, Renal disorder

Introduction

Systemic lupus erythematosus (SLE) is a chronic rheumatic condition that present with protean manifestations. The initial manifestations can vary from patient to patient and new clinical features can develop as the disease progresses. Corticosteroids are used frequently to control major organ involvement and many patients are on them for a long time. Potentially serious and significant morbidity can arise from chronic steroid ingestion. As part of a comprehensive epidemiological study on SLE, data on lupus patients were entered into a customised database. The data captured were analysed with regards to initial manifestations and clinical features in patients with more than 10 years of disease. The aims of this study were characterisation of the initial

manifestations and features in newly diagnosed lupus patients, and comparing these to patients with more than 10 years of disease. In addition we also attempt to identify the potential morbidity features which may result from chronic steroid ingestion. Identification of these allow for early and effective intervention in therapy.

Materials and Methods

Patients

Patients who were on follow-up in the Department of Rheumatology and Immunology and who satisfied the American College of Rheumatology (ACR) criteria for classification of SLE¹ were entered into the study. Two groups of lupus patients were studied: Group A-those with disease duration of less than 1 year, and Group B-

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those with disease duration of more than 10 years. Patients were identified with an alphanumeric code for confidentiality reasons and the master list was only available to the investigators for study purposes.

Data Collection

The data were recorded into a standard protocol by rheumatologists and then entered into a customised database. Standard definitions were provided for each item of data and a booklet on "definitions of terms" was attached to each protocol for easy reference. Each rheumatologist was also given a personal copy of the booklet on "definitions of terms". Data which showed errors in internal consistency were rechecked by going back to the source documents. Random checks on completed protocols by comparing with the source documents were also performed to ensure data accuracy.

Definitions of Terms

Renal disorder: Persistent proteinuria greater than 0.5 gm per day or greater than 3+ if quantitation not performed or cellular casts present (may be red cell, haemoglobin, granular, tubular or mixed).

Nephrotic syndrome: proteinuria >3.0 gm/day with peripheral oedema and serum albumin <30gm/dl.

Nephritic syndrome: microscopic haematuria [>5 red blood cell per high-powered field (RBC/hpf)], proteinuria, elevated serum creatinine with or without hypertension.

Rapidly progressive glomerulonephritis: deterioration of renal function over days to weeks in the absence of any other cause.

Hypertension: blood pressure of >160/90 mmHg on 3 separate occasions.

Diabetes mellitus: A random blood glucose level of >11 mmol/L or a fasting blood glucose level of >7 mmol/L with symptoms of polyuria and polydipsia, or an asymptomatic patient with 2 blood glucose levels greater than the value stated.

Atherosclerosis: detected by generalised bruits on clinical examination (in the absence of large vessel vasculitis), ultrasound examination of the carotid arteries, calcifications of blood vessels on plain radiographs or angiography.

Cataract: opacification of the lens, preferably with fundoscopic confirmation.

Statistical Analysis

Chi-squared analysis was used to detect significant differences between the groups. A *P* value of less than 0.05 was considered significant.

Results

A total of 155 lupus patients were entered into the

study. Group A comprised of 97 patients while Group B had 58 patients with a mean age of 31 years and 41 years, respectively. Table I shows the sex ratio and ethnic composition. The 5 commonest initial clinical manifestations were haematological involvement, arthritis, malar rash, renal disorder and photosensitivity (Table II). The cumulative prevalence rate of arthritis, malar rash and renal disorder increased in Group B patients. However, only renal disorder showed a statistically significant increase (*P* <0.001). Table III characterises the mean age, sex ratio and types of renal disorder in both groups. The prevalence of nephrotic syndrome was significantly increased in Group B patients with renal disorder (*P* <0.04) and represented about 20.7% of all Group B patients. This cumulative percentage is comparable to those reported among black (28.9%) and white (19.5%) lupus patients by Ward and Studenski.² Four potential morbidity conditions (hypertension, diabetes mellitus, atherosclerosis and cataract) that are related to chronic steroid ingestion were analysed in the 2 groups. Table IV shows the prevalence

TABLE I: PATIENTS' CHARACTERISTICS

	Group A	Group B
Sex ratio (Female:Male)	86:11	56:2
Mean age (y)	31	41
Range(y)	18 to 63	25 to 61
Race: Chinese	86%	86%
Malay	11%	9%
Indians	3%	5%

TABLE II: THE 5 COMMONEST CLINICAL FEATURES IN THE STUDY GROUPS

	Group A	Group B	<i>P</i> value
Haematological	73%	78%	ns
Arthritis	57%	69%	ns
Malar rash	43%	73%	ns
Renal disorder	31%	59%	0.001
Photosensitivity	30%	33%	ns

ns: not significant

TABLE III: TYPES OF RENAL DISORDERS IN PATIENTS WITH RENAL INVOLVEMENT

	Group A	Group B	<i>P</i> value
Mean age (y)	29	41	
Sex ratio (Female:Male)	26:4	33:1	
Renal disorder			
Persistent proteinuria	81%	82%	ns
Cellular casts	48%	44%	ns
Nephrotic syndrome	10%	35%	0.04
Nephritic syndrome	33%	23%	ns
RPGN	5%	3%	ns

ns: not significant; RPGN: rapidly progressive glomerulonephritis

TABLE IV: PREVALENCE OF MORBIDITY FACTORS IN THE STUDY GROUPS

	Group A	Group B	P value
Hypertension	18%	59%	0.001
Diabetes mellitus	5%	10%	ns
Atherosclerosis	2%	7%	ns
Cataract	0%	10%	

ns: not significant

of these 4 conditions in the 2 study groups. Hypertension was noted to be significantly elevated in Group B lupus patients ($P < 0.001$) and 10% of the Group B patients also developed lens opacification. Seventeen Group A patients (12 females and 5 males) and thirty-four Group B patients (32 females and 2 males) had hypertension. In these hypertensive patients, 60% of the Group A patients had an associated renal disorder while only 42% of Group B patients had an associated renal disorder. The Group B patients who developed cataracts have a mean age of 37 years and they all had chronic corticosteroid ingestion of more than 5 years duration with total cumulative dosage exceeding 5 gm.

Discussion

Prospective cohort study is the ideal way to fully and accurately document the development of clinical features and risk factors in a defined population of lupus patients.³ The present study had the limitation of capturing mainly retrospective data and may not fully reflect the actual development of these features due to the possibility of incomplete data documentation in the case notes. Analysis of the initial manifestations of Group B patients will not yield a representative picture as many of the original data are not available or not properly documented. Moreover, many of the patients were diagnosed prior to the 1982 publication of the ACR revised criteria for classification of SLE. However, since the population in Singapore was relatively stable over the last 10 years, with no major migration into or out of the country and no major therapeutic advances that may change manifestations in the first year of disease have occurred during this period, it is valid to presume that Group A patients' clinical features are reflective of the local lupus population. Comparison of prevalence of clinical features between the groups revealed significant morbidity factors and aided us in the design of future studies.

The renal disorder prevalence rate doubled from 31% in newly diagnosed patients to 59% in patients with more than 10 years of disease, indicating its importance in the clinical course of patients. These prevalence rates were higher than those of 1000 patients analysed in the Euro-lupus study.⁴ Their patients had a prevalence rate of 16% at initial presentation and this increased to 39%

later (the mean disease duration was 9 years). The higher prevalence rates in our patients may have a genetic basis. The Group B patients were also noted to have a significantly increased prevalence rate of hypertension (59%). Although the prevalence rate of hypertension in individuals between 40 and 50 years old is not available in the local population, results of a health screening survey of 1224 individuals above the age of 55 years, showed a prevalence rate of only 24.8%,⁵ less than half the prevalence rate in our Group B patients. Hypertension has been noted to be associated with lupus nephritis⁶ but in our Group B patients, only 42% had an associated renal disorder, suggesting that factors like chronic corticosteroid ingestion is likely to be the major contributor to the development of hypertension in the majority of patients. Age did not seem to play a major role as the mean age of these patients was 41 years old. Regular measurements of blood pressure is mandatory for early detection of hypertension because treatment can reduce hypertensive complications.

Diabetes mellitus⁷ and atherosclerosis⁸ are usually thought to be associated with chronic corticosteroid ingestion. However, the prevalence rates of these 2 conditions are not higher than the general population. The prevalence rate of diabetes mellitus among Singaporeans aged 30 to 69 years is 12%⁹ and Group B patients had a prevalence of 10%. Similarly, the prevalence rate of atherosclerosis is comparable (7% versus 6.2%) to those senior citizens screened in a healthy survey.⁵ Ten per cent of Group B patients developed cataract while none of the patients had cataract noted at initial presentation. This prevalence rate is high since only 3.9% of individuals aged 55 years and above had cataract.⁵ Moreover, these patients displayed a mean age of only 37 years and the cataract formation is probably related to chronic ingestion of corticosteroids.^{10,11}

In our lupus patients, renal disorders were common. Morbidity factors like hypertension and cataract formation were related to chronic corticosteroids ingestion. Optimum treatment of our lupus patients should include paying close attention to these factors by judiciously reducing the dosage of corticosteroids and substituting other therapeutic agents as a steroid sparer.

Acknowledgement

We would like to thank Staff Nurse Wong Mew Hong for her help in data entry and management.

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