SYSTEMIC LUPUS ERYTHEMATOSUS IN ORIENTAL MALES A CLINICAL PROFILE

M L Boey
P H Feng

SYNOPSIS

Few studies have characterized the clinical profile of male patients with systemic lupus erythematosus (SLE). The spectrum of organ involvement in 32 males with the disease were reviewed retrospectively. Presenting symptoms resembled other large combine series of males and females. Diffuse lymphadenopathy however was more common (38%). The commonest decade was between 10—19 years compared to 20—29 years in the feamles. Of the 32 patients reviewed 12 were alive and 12 had died. The fate of the remainder 8 were unknown. Infection and renal failure were the major causes of death. The survival rate for our male patients was 66% at 5 years and 61% at 10 years. This is marginally less than for all our SLE patients (70% at 5 years and 60% at 10 years). The relatively poorer survival of our patients compared to Western series may reflect poorer nutritional and educational status, ignorance and a more advanced disease state at presentation.

INTRODUCTION

Systemic lupus erythematosus (SLE) is characterized by a female to male ratio of 9:1. This sex differentiation is an outstanding genetic factor associated with the disease. Recent reports have also suggested that male patients have a decreased survival compared to female patients (1—4). We retrospectively studied 32 males with SLE to determine whether there are differences in the manifestations and severity of the disease between the sexes. The clinical features, course and prognosis of these patients are described below.

MATERIALS AND METHOD

32 males with SLE were seen at 4 general hospitals in Singapore between 1960 and 1981. 31 were orientals. They comprised 23 Chinese, 5 Indians and 3 Malays. All met the preliminary American Rheumatism Association criteria for the disease (5). Buccal smear and Karyo-type were performed in one male who had scanty axillary and public hair and small testes. These confirmed the 47 XXY chromosomal complement.

Salient clinical features in these patients were ascertained by retrospective review and included (a) age at diagnosis, (b) initial manifestations of the disease, (c) evidence of renal involvement as manifested by abnormal urine sediment, proteinuria $>$ 1 gm/24 hours or elevation of serum creatinine $>$ 1.4 ug/dl.

**Department of Medicine IV
Tan Tock Seng Hospital
Moulmein Road
Singapore 1130**

M L Boey, M Med (Int Med)
Senior Registrar

P H Feng, FRCPG, AM
Head and Senior Physician

Other significant recorded laboratory findings included (1) occurrence of thrombocytopenia or haemolytic anaemia (2) antibodies to double stranded DNA (3) reduced levels of serum complement. Percutaneous renal biopsy was carried out in 15 patients. Hormonal assays were not performed.

None of the patients gave a family history of lupus. Family studies were not pursued.

RESULTS

Age

78% of male patients were below 30 years of age at diagnosis. The commonest decade was between 10-19 years. Both these results are significantly different from the age distribution of female oriental SLE patients in our populations (Fig 1).

Initial manifestations

The initial manifestations of our patients are summarised in Table 1 and compared to a Grigor et al who studied 50 SLE patients (male and female) (6) and a Singapore study of 176 female SLE patients (7). Major initial manifestations were fever and malaise (47%), skin and mucus membrane involvement (69%) and arthritis (38%). There was a significant increase in involvement of the reticulo-endothelial system in the form of diffuse lymphadenopathy and hepatosplenomegaly in the male (38%). Lymph node biopsy in one patient showed a non-specific adenitis. Neuropsychiatric manifestation although rare in the 2 groups were observed in 9% of the male patients.

Laboratory investigations

Evidence of clinical renal involvement was higher among our male patients. 45% had abnormal urinary sediment and 35% had raised serum creatinine at diagnosis — Table 2. 15 patients consented to percutaneous renal biopsy. The renal tissue was studies by light microscopy, electron microscopy and immunoflorescent antibody technique. The histologicasl type of the 15 biopsies are shown in Table 3. During the period of study in this subset of patients 2 died of renal failure and 3 from non-renal causes. 7 were alive and the outcome of 3 remain unknown.

Therapy and its complications

Treatment of our patients were along standard

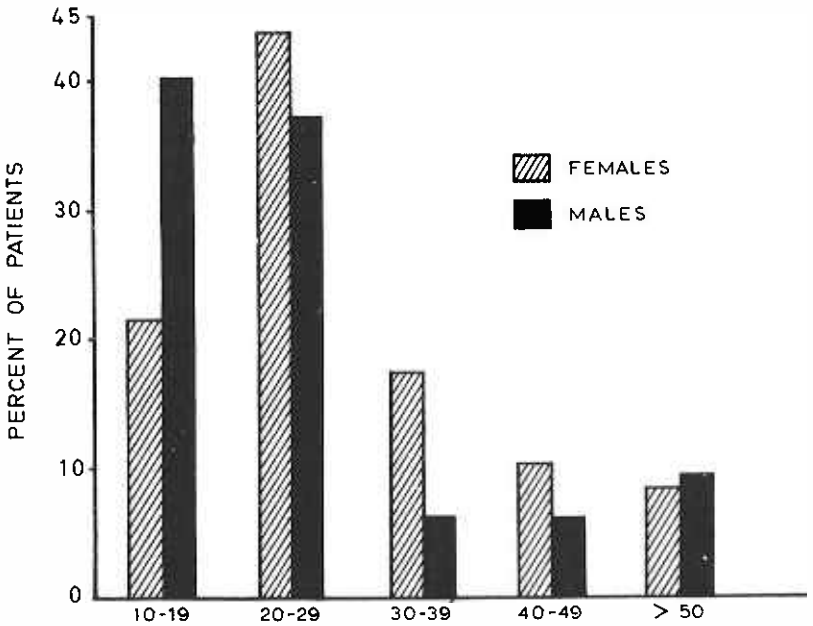

FIG 1 AGE AT DIAGNOSIS (YEARS)

TABLE 1
INITIAL MANIFESTATIONS OF SLE

Manifestations	London group (Grigor)	Singapore group (Feng)	Male SLE
Arthritis/arthralgia	62%	44%	38%
Skin and mucus membrane	20	52	69
Fever, malaise	4	48	47
Thrombocytopenic purpra	4	4	13
Haemolytic anaemia	4	3	9
Neuropsychiatric	4	4	9
Swelling of face/leg		36	13
Lymphadenopathy		8	38
Respiratory		7	6
Cardiovascular		3	6

TABLE 2
INITIAL LABORATORY FINDINGS

Laboratory test	London group (Grigor)	Singapore group (Feng)	Males
Anaemia	52% (Hb < 11 gm)	39%	43%
Haemolytic anaemia	12	8	9
Leucopenia	46	45	19
Thrombocytopenia	26	33	32
Anti-nuclear antibody	100	98	81
Anti-DNA antibody	100	100	80
Hypocomplementemia	56	75	79
Urine RBC > 5/HPF	30	34	45
TUP > 1 GM/24 HRS	26	33	37
Raised serum creatinine	10	26	35

TABLE 3
RENAL BIOPSY AND OUTCOME IN 15 MALE PATIENTS

Histological type	Number	Outcome
Minimal change	2	2 Alive
Mesangial	3	1 Dead (N-R) 2 Unknown
Focal proliferative	3	1 Alive 2 Dead (1 RF)
Diffuse proliferative	3	1 Alive 2 Dead (1 RF)
Membranous	2	2 Alive
Membrano-proliferative	2	1 Alive 1 Unknown
	15	7 Alive (3 N-R) 5 Dead (2 RF) 3 Unknown

N-R = non-renal
RF = renal failure

lines. Low dose steroids and anti-inflammatory drugs were used in mild patients. High dose steroids (prednisolone 45 mgm/day or more) and immunosuppressive agents (cyclophosphamide and azathioprine) were used in severe cases or those who develop intolerable side effects to steroid therapy.

DISCUSSION

This study of 32 male patients, mainly orientals, reveal a number of interesting findings. Male patients with SLE were diagnosed at an earlier age compared to our other female SLE patients. This infers an earlier onset of the disease. Most of the clinical features tended to be similar to the female group except for a four fold increase in diffuse lymphadenopathy. The reason for this is unclear but diffuse lymph gland enlargement varying from 36-59% has been described (11, 12, 13). With regard to renal involvement, males seem to have a slight increase of nephritis (> 10%) as judged by urine microscopy and serum creatinine levels.

In a prospective study of 30 men with SLE, Miller et al (14) reported that the clinical, laboratory and serological features tended to be similar to those of 155 females followed in the same clinic. In our patients, central nervous involvement was more common. Arthritis was less frequent than females.

Comparing survival data, we found a marginally decreased survival in male patients compared to our general SLE population. This does not detract from the fact that survival of our patients i.e. orientals, as a whole is lower compared to Caucasian patients. Such a phenomenon has been reported by Kaslow (15). We believe that one reason for this is environmental and due to less than optimal socio-economic conditions of our patients. Poorer living conditions, ignorance and reliance on traditional herbal remedies lead to faulty medication, a greater risk of infection and a more advanced disease presentation. In contrast, Wallace et al (1) reported better female survival. This was independent of nephritis. Seemingly worse prognosis in males, especially those with nephritis have been reported (2, 3, 4).

The association of SLE and Klinefelter's Syndrome in one of our patient is note worthy. Elevated oestriol levels in SLE patients with Klinefelter's syndrome, suggest chronic oestrogenic stimulation (16). Hormonal levels were not assayed in our patient. Studies in murine models of SLE implicate sex hormone in the origin of autoantibodies (17) and overall morbidity (18, 19).

Study of immunogenetics, racial and hormonal factors in our patients are in progress.

ACKNOWLEDGEMENTS

We thank the directors, physicians and medical record officers of Singapore General Hospital, Tan Tock Seng Hospital, Toa Payoh Hospital and Alexandra Hospital.

REFERENCES

1. Wallace DJ, Podell T, Weiner J, Klineberg Jr, Forouzesh S, Doubois EL: Systemic lupus erythematosus — survival patterns. JAMA 1981; 245:934-8.
2. Appel GB, Silva FG, Piram CL et al: Renal involvement in systemic lupus erythematosus. Medicine 1978; 57:371-410.
3. Cade R, Spooner G, Schlein et al: Comparison of azathioprine, prednisolone and heparin alone or combined in treating lupus nephritis. Nephron 1973; 10:27-56.
4. Hayslett JP, Kashganan M, Cook CD et al: The effect of azathioprine on lupus glomerulonephritis. Medicine 1972; 51:393-412.
5. Cohen AS, Reynolds WE, Franklin EC et al: Preliminary criteria for the classification of systemic lupus erythematosus. Bull Rheum Dis 1971; 21:643-8.
6. Grigor R, Edmonds J, Lewkonia R, Bresnihan B, Hughes GRV: Systemic lupus erythematosus — a prospective analysis. Ann Rheum Dis 1978; 37:121-8.
7. Feng PH: Unpublished data.
8. Feng PH, Tan TH: Tuberculosis in patient with systemic lupus erythematosus. Ann Rheum Dis 1982; 41:11-4.
9. Gordon MF, Stolley PD, Schinnar R: Trends in recent systemic lupus mortality rates. Arthritis Rheum 1981; 24:762-9.
10. Lee P, Urowitz MB, Bookman AAM et al: Systemic lupus erythematosus — a review of 110 cases with reference to nephritis, the nervous system, infections, aseptic necrosis and prognosis. Quart J Med 1977; 46:1-32.
11. Harvey AM, Schulman LE, Tumulty PA et at: Systemic lupus erythematosus; review of the literature and clinical analysis of 138 cases. Medicine 1954; 33:291-437.
12. Dubois EL, Tuffanelli DL: Clinical manifestations of systemic lupus erythematosus: computer analsysis of 520 cases. JAMA 1964; 190:104-11.
13. Estes D, Christian CL: The natural history of systemic lupus erythematosus by prospective analysis. Medicine 1971; 50:85-95.
14. Miller M, Urowitz M, Gladman D, Killinger D: Male SLE. Arthritis Rheum 1982; S58 (Abstract 329).
15. Kaslow RA: High rate of death caused by systemic lupus erythematosus among U.S. residents of Asian descent. Arthritis Rheum 1982; 25;414-8.
16. Stern R, Fisherman J, Brusman H, Kunnel HG: Systemic lupus erythematosus associated with Klinefelter's syndrome. Arthritis Rheum 1977; 20:18-22.
17. Roubinian JR, Talal N, Greenspan JS, Goodman JR, Siiteri PK: Effect of castration and sex hormone treatment on survival, anti-nuclei acid antibodies, and glomerulonephritis in NZB/NZWF1 mice. J Exp Med 1978; 147:1568-83.
18. Roubinian JR, Papoian R, Talal N: Androgenic hormones modulate autoantibody responses and improve survival in murine lupus. J Clin Invest 1977; 59:1066-70.
19. Melez KA, Reeves JP, Steinberg AD: Regulation of the expression of autoimmunity in NZB/NZWF1 mice by sex hormones. J Immunopharm 1978; 1:27-42.