HERPES ZOSTER IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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SYNOPSIS

Out of 184 systemic lupus erythematosus (SLE) patients in Malaysia, 24 patients developed herpes zoster (HZ). The incidence is compared with that described elsewhere. The distribution of HZ tended to be extensive but complications were very infrequent. The treatment for SLE was not affected.

INTRODUCTION

Patients with SLE have increased susceptibility to bacterial and fungal infections(1). Several authors(2, 3, 4, 5) have suggested that there is an increased incidence of HZ amongst selected groups of SLE patients. This paper reports the incidence and characteristics of HZ in an unselected group of SLE patients.

MATERIAL AND METHOD

From 1975, all SLE patients were followed in a central SLE clinic of the University Hospital, Malaysia. SLE was diagnosed when patients fulfil the preliminary criteria of the American Rheumatological Association (ARA) for it and have low complement levels in the active phase of the disease. Patients came from all parts of the country. Most of the patients had moderate to severe SLE as determined by a previously defined set of criteria(6). All patients (except those with mild arthralgia and rash) were treated according to the following regimen: (i) Prednisolone 60 mg daily for 2-4 weeks, then 120 mg alternate days for 2 weeks. The dose of prednisolone was reduced by 20 mg every 2 or 4 weeks. Higher initial dose (100 mg daily) of prednisolone was used for the very ill patients when initial response to 60 mg prednisolone was poor. (ii) Cyclophosphamide at 2 mg/kgm/ day was added when patients failed to respond to prednisolone. (iii) Chlorambucil 0.1-0.2 mg/kg when patients could not tolerate cyclophosphamide. (iv) Azathioprine 100 mg/day was used in a few patients previously given this drug.

Patients were followed at the SLE clinic biweekly, then monthly and 3 monthly. Most patients complied with this schedule. In between visits they saw their own physicians but continued with the medication prescribed at the SLE clinic. At each visit the clinical and laboratory aspects of SLE were assessed and intercurrent illness or complications looked for.

HZ was diagnosed when patients had typical vesicles, pustules, scab or scar that distinctly followed characteristic dermatomes. One patient with scanty vesicles along a dermatome and another who started with a characteristic lesion but eventually disseminated had the zoster virus confirmed by electron microscopy.

RESULTS

A total of 184 sequentially registered SLE patients were followed for a period of 6 months to 5 years. Of these 168 (91.3%) were females and 16 (8.7%) males. The racial origin of the groups was as follows: 142 Chinese (77.3%); 30 Malays (16.3%); 10 Indians (5.4%). Their ages ranged from 11 to 67 (mean 26.6) years. Twenty four out of this group of patients (11.3%) developed HZ over this period. Twenty-two (92%) were females, 2 (8%) were males; 20 (83.5%) Chinese and 4 (16.5%) Malays. Their ages ranged from 13-45 (mean 34.6) years (Table I).

TABLE I

CHARACTERISTICS OF STUDY POPULATION

Patients	Total	HZ
No.	184	24
Age range (Mean) (years)	11-67 (26.6)	14-35 (34.6)
Sex: Female (%)	168 (91.3)	22 (92)
Male (%)	16 (8.7)	2 (8)
Race: Malays (%)	30 (16.3)	4 (16.5)
Chinese (%)	142 (77.2)	20 (83.5)
Indians (%)	10 (5.4)	0
Others (%)	2 (1.1)	0

Characteristics of SLE (Table II).

Three patients had mild SLE prior to developing HZ. One patient whose main complaint was arthralgia had 2 episodes of HZ along 2 different dermatomes. A second patient developed HZ when she had idiopathic thrombocytopenic purpura (ITP). Seven years later she fulfilled the ARA preliminary criteria for SLE. A third patient had confirmed SLE 10 years after she had ITP. The HZ appeared soon after SLE was confirmed.

All the other 21 patients had moderate to severe SLE (6) prior to having HZ. Twelve of these had severe manifestations such as confusion or coma; one patient had cerebellar signs. Twenty-one patients had diffuse proliferative glomerulonephritis diagnosed by percutaneous renal biopsy. Eighteen had the nephrotic syndrome, one died in acute renal failure, 2 had persistent renal insufficiency (S. Creatinine 2-5 mg/100 ml — 0.18-0.44 mmol/l).

The SLE of 23 patients had improved by the time of appearance of HZ. Three were still moderately active. Eight were inactive while 12 had only residual face or trunk rash or had mild urinary changes.

The serum complement 3 and 4 levels of all patients were low initially. By the time of appearance of HZ, the C3 C4 levels were normal in 9, and low in 8 (Normal C3 = 60-130mg/100 ml, C4 = 20-60 mg/ml).

At the time of appearance of the HZ, 3 patients were not on medication, eight were receiving a mean daily dose of 5-15 mg prednisolone and the rest were getting 15-60 mg prednisolone daily. Five patients were receiving immunosuppressive drugs. In all patients, treatment was not altered when HZ appeared.

After the appearance of HZ, the SLE did not become more severe. Six patients developed exacerbation of SLE 6 months later and the patient with cerebellar lesion died.

Characteristics of HZ

The HZ occurred 2 weeks to 6 years after confirmation of SLE. In 4 patients it recurred soon after steroid therapy was increased.

Twenty-two patients had one episode of HZ, 2 had two episodes of HZ each time when the SLE was under control. In 16 patients the HZ involved only one dermatome, in 2 patients it involved a division of the trigeminal nerve. In 6 patients it affected more than one dermatome simultaneously. Of these 6 patients 2 patients later had disseminated varicellar lesions. These 2 patients had recently had large doses of steroids.

Only 2 patients required mild analgescis: both had trigeminal nerve involvement. All patients had topical soothing and drying agent. No antiviral agent was used. The HZ lesions scabbed in 7-10 days without sequelae.

TABLE II

SEVERITY OF SLE IN HZ PATIENTS

Activity of SLE (Wang et al. 1980)	Severe	Moderate	Mild	None
Before HZ	15 (62.5%)	6 (75%)	3 (12.5%)	0
At onset of HZ	1	3	12	8
After 6 months of HZ	3 1 died	3	6	10
Of 184 patients (at maximal severity)	42 (22.8%)	120 (65.4%)	22 (12%)	

DISCUSSION

The true incidence of HZ in SLE may be difficult to determine since some patients may develop very mild lesions. The true incidence may be higher than the 11.3% reported here as only patients with definite evidence of involvement of dermatomes have been included. Other studies report an incidence of 5-43.3% (2,3,4,5). These studies concern SLE patients with selected complications and may not represent the true incidence. This study however confirms the higher incidence of HZ in SLE than in the general population where the incidence is said to be 0.25% (7). The incidence appears to be higher in SLE that in malignancies of all types (0.85%) but comparable to that in Hodgkin's lymphoma (9%) (8). There appears to be no age, sex or racial predilection when those affected were compared to the whole population of SLE patients.

HZ appears to occur in patients who have had severe SLE associated with severe drop in the complement levels. However at the time of appearance of HZ, the activity of SLE had subsided markedly (Table II).

The HZ of SLE patients is quite extensive. In 8 patients it involved more than one dermatome and in two it was disseminated. However most of the patients did not develop any complications: only 2 patients with trigeminal involvement required analgesics. The duration of lesions was not prolonged (7) and there was no infection or postherpetic neuralgia; the latter could be due to the beneficial effect of steroid therapy demonstrated by Keczkes et al (9)

Haralampos (4) suggested that the development of HZ was not affected by steroids or immunosuppressives. Five of the 24 patients were on immunosuppressives, the dose of which was not reduced when HZ appeared. The use of large dose steroid in patients with severe SLE rather than the severity of the SLE itself could have accounted for the higher incidence of HZ in these patients. However, as noted by Keczkes et al. (9), prednisolone did not cause dissemination or prevented healing.

Staples et. al. (1) noted that the incidence of HZ in SLE is higher than in rheumatoid arthritis or in the nephrotic syndrome. The reason is not clear but it is known that patients with SLE have depressed phagocytic functions (10) and cell medicated immunity (CMI) amongst other immunological abnormalities (2). Gershon et al. (11) found that patients with HZ are capable of vigorous recovery of CMI but may be unable to sustain this type of immunity.

This probably explains the normal recovery is our patients and the tendency to recur.

It is concluded that HZ in SLE patients is more frequent than in the general population. There is no age, sex or racial susceptibility to it. HZ usually appears as the activity of SLE subsides. The HZ may be extensive but recovers normally without sequelae. Corticosteroids may affect the distribution and incidence of HZ but it does not increase the severity and might reduce the incidence of neuralgia. The relationship of HZ to the immunological disturbances of SLE requires to be studied.

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