LUPUS NEPHRITIS- A CRITICAL ANALYSIS OF 17 PATIENTS

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Abstract

Over a 3 year period from June 94 to June 97, out of 28 patients of systemic lupus, 17 were diagnosed as renal lupus. Demographic data showed 12 females and 5 males, mean age being 32.2 years (range 12 to 54 years). Mean time gap between presentation and definitive diagnosis was 32.4 days (7 days to 5 years). 2 patients (11.76%) presented renal lupus, one (5.88%) with acute interstitial lung disease and the remaining had the usual systemic manifestations of lupus. Anti dsDNA antibodies were positive in all patients while ANA was negative in 3 cases. Renal involvement consisted of rapidly progressive glomerulonephritis in 2 patients (11.76%), nephrotic syndrome in 4 (23.52%) and non nephrotic range proteinuria in 11 (64.70%) patients. Mean serum creatinine at presentation was 2.4mg/dl (0.8mg/dl to 8.9 mg/dl). Three patients were dialysis dependent. Renal histology on light microscopy comprised of class II lesions in one (5.88%), class III in 4 (23.52%), class IV in 11 (64.70%-including one with crescents) and class V in one (5.88%) patient. All patients with advanced class III/IV lesions were treated with corticosteroids and cyclophosphamide pulses. Except one patient who died of pyopericardium all others improved and their serum creatinine stabilised around 2.3 mg/dl (0.8 to 4.6 mg/dl). The study highlights the importance of early diagnosis and aggressive management in this potentially treatable disease.

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Key words: Lupus nephritis; Pulse cyclophosphamide.

Introduction

Although, multiple immunologic abnormalities of lupus can affect virtually any organ system, involvement of kidney is often a major source of patient morbidity and mortality. Renal involvement in lupus is extremely diverse ranging from asymptomatic urinary findings to fulminant renal failure or florid nephrotic syndrome. Pathologic alterations can affect the glomerular, tubulointerstitial and vascular compartments of the kidney [1].

The diagnosis of SLE can often be established by the presence of certain clinical and laboratory features defined by the modified American Rheumatism Association (ARA) criteria; the development of any four or more criteria during the course of illness confers a 96% sensitivity and specificity. However, at presentation the diagnosis of SLE may be difficult to establish as a patient may display fewer than four of the criteria. There may be a considerable time lag between the initial presentation and establishment of diagnosis [1-3].

The incidence and prevalence of SLE and of lupus nephritis vary considerably among different studies and a large number of factors are known to influence

renal manifestations. The course of lupus nephritis is quite variable and the response to treatment depends upon a number of factors [4-6]. This communication deals with a critical analysis of cases of lupus nephritis seen and treated at this center.

Material and Methods

All the patients of SLE presenting to this centre between June 94 to June 97 formed the material for study. The diagnosis of SLE was established based upon the ARA criteria. All the manifestations of the disease in each patient were recorded. Anti-nuclear antibodies (ANA) and anti-ds DNA antibodies were estimated in all cases. The interval between the initial presentation and establishment of diagnosis was noted.

All the patients were investigated for any renal involvement by urinalysis (biochemical and microscopic), 24 hour urinary protein, blood urea and serum creatinine values. Kidney biopsy was done in all patients who had evidence of renal involvement. The renal lesions were classified according to the WHO classification. The patients with class III and class IV lesions were treated with corticosteroids (1.0 mg/kg/day for 8-12 weeks and tapered to 10-15 mg/day) and intravenous cyclophosphamide pulses of 15 mg/kg each every month for six months and then three monthly for two years. The maintenance therapy at the end of two years consisted of corticosteroids only. The response to therapy was evaluated clinically and by laboratory parameters. Any side effects were carefully recorded. The patients were followed up for a mean duration of 2.6 years (range 1.8 years to 3.7 years).

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TABLE
Histological lesions and other features (n=17)

Histological lesion	No of patients	Proteinuria		Haematuria	S creatinine mg/dl	
		Nonnephrotic	Nephrotic		<1.5	> 1.5
Class II	1	1	—	1	1	1
Class III	4	3	1	3	2	1
Class IV	11	8	3	8	4	8
Class V	1	—	1	—	1	—

Observations

28 patients were diagnosed as SLE between June 94 to June 97. 17 of these were found to have evidence of renal involvement on the basis of urinary abnormalities and/or elevation of blood urea and serum creatinine values. 12 patients with lupus nephritis were females and 5 were males. The mean age was 32.2 years (range 12 to 45 years). Mean time gap between onset of symptoms and definitive diagnosis of SLE was 32.4 days (range 7 days to 5 years). Microscopic hematuria was seen in 12 patients (70.6%) and hypertension was observed in 10 patients (58.8%) with renal involvement. Kidney size was normal by ultrasonography in all the patients.

Two of the 28 patients (7.14%) presented with renal involvement only, one (3.57%) patient presented with interstitial lung disease and in the remaining the presentation was with usual skin and systemic manifestations of SLE. Anti ds DNA antibody was positive in all patients with renal involvement whereas ANA was negative in three (17.6%) cases. The titres of anti ds DNA antibodies did not have any correlation with the clinical severity of the disease.

Out of the 17 patients with lupus nephritis, two patients (11.76%) presented as rapidly progressive glomerulonephritis (RPGN). Four patient (23.52%) had nephrotic syndrome and the remaining 11 patients (64.7%) had non-nephrotic range proteinuria. Mean serum creatinine at presentation was 2.4 mg/dl (range 0.8 mg/dl to 8.9 mg/dl). Three cases were dialysis dependent.

Histologically renal lesions comprised of class II lesions in one (5.88%), class III lesions in 4 (23.52%), class IV in 11 (64.77%) including one with crescents, and class V in one (5.88%).

All patients with advanced class III and class IV lesions were treated with corticosteroids and pulse cyclophosphamide therapy whereas patients with class II and mild class III lesions were treated with steroids alone. All the patients showed good response to therapy within 3-4 weeks. The serum creatinine levels decreased in all the patients who had elevated levels initially. In the others with normal levels at onset, there was no worsening. Three patients (17.64%) who were dialysis dependent at the onset, became dialysis independent after the treatment was initiated. The response to treatment was maintained in all the patients throughout the period of follow up. The complications of cyclophosphamide therapy noticed were haemorrhagic cystitis in one case, neutropenia in one case and serious systemic infections in two cases out of which one died due to pyopericardium. *Staphylococcus aureus* (coagulase positive) was isolated in the patient who died of pyopericardium, while no organisms could be isolated in the other two cases.

Discussion

SLE involves almost every system in the body but renal involvement accounts for most of the morbidity and mortality. The diagnosis of SLE may be easy if

the characteristic skin and systemic manifestations are present but in a large number of cases the disease evolves slowly and the diagnosis is not suspected for a long time. As a result there may be a considerable time lag between the first symptom and the establishment of diagnosis [1-3]. We have observed a mean time lag of 32.4 days (range 7 days to 5 years) between the first symptom and the establishment of diagnosis. The results are comparable with other studies.

Clinical renal involvement in SLE occurs in 60-70% of the cases, however with electron microscopic studies, renal involvement is seen in almost 100% cases. In our series clinical renal involvement was seen in 60.7% patients of SLE. Patients with renal involvement usually have other skin and systemic manifestations of SLE preceding the renal involvement. However, in about 20% cases renal involvement may be the first manifestation of the illness [1] as was seen in 2 of our patients.

The severity of the renal involvement in SLE is variable and the histological lesions have been classified depending upon the severity [7]. Histological lesions may not always correlate well with the clinical severity, hence kidney biopsy should be performed in every patient with clinical/laboratory evidence of renal involvement [8-10]. We found class III/class IV lesions in 88.22% of the cases. Our results correlate well with other studies [7-9].

In the last few years it has been shown that aggressive immunosuppressive treatment with corticosteroids and pulse cyclophosphamide therapy in class III/IV lesions can halt the progression of the disease to end stage renal failure [11-13]. We treated all our patients with class III/IV lesions with aggressive immunosuppression and observed a good response. All the three patients who were dialysis dependent initially could be taken off dialysis and in the others, the serum creatinine settled at a lower level.

A number of studies have reported better survival and improvement in renal function in patients treated with cyclophosphamide pulses and steroids than with steroid therapy alone [14-15]. In patients resistant to

corticosteroids and cyclophosphamide, cyclosporin and gamma globulins have been tried with variable success rates [16-17]. We did not use any of these drugs in our patients.

One of our patients who presented with rapidly progressive glomerulonephritis, was treated with plasmapheresis along with pulse methyl prednisolone and cyclophosphamide therapy. The patient showed good response and became dialysis independent. Plasmapheresis has been shown to bring about a quick control of the disease in severe cases [18].

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