Lupus nephritis

Collaborative study by the French Society of Paediatric Nephrology

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SUMMARY Sixty two children were included in a collaborative study to determine the prognosis for lupus nephritis. Renal involvement was confirmed by histologic study of renal biopsy specimens which were classified into five categories: minimal lesions (11 cases, 18%); focal segmental glomerulonephritis (15, 24%); diffuse proliferative glomerulonephritis (30, 48%); membranous nephropathy (5, 8%); and glomerular sclerosis (1, 2%). That the predictive value of the early biopsy is limited was indicated by the most recent status of 37 patients five years after onset—total remission (13, 35%); urinary abnormalities or nephrotic syndrome (7, 19%); moderate renal failure (4, 11%); chronic renal failure (7, 19%); and hypertension (6, 16%). Treatment did not always prevent the development of severe renal failure; in particular, plasmapheresis failed to avert the death of one patient and the development of chronic renal failure in two others.

There are conflicting views on the prognosis for childhood systemic lupus erythematosus, which is related to the degree of renal involvement. In a recent study the 10 year survival rate of children without nephropathy approached 100%.¹ The results of a collaborative study to evaluate the prognosis of lupus nephritis carried out by the French Society of Paediatric Nephrology are reported here.

Patients and methods

The patients were selected from paediatric hospitals in Amiens, Clermont-Ferrand, Lille, Marseille, Montpellier, Nancy, Nantes, Paris, Reims, Toulouse, Tours, and Hanover (Germany).

All were 15 years of age or younger. Serologic confirmation of the clinical illness was required (a positive lupus erythematosus test or positive antibody to DNA (anti-DNA) titre of any dilution). Renal disease in these patients was confirmed by the presence of one or more of the following:

(1) Proteinuria, defined as greater than 200 mg/24 hours.

(2) Haematuria, defined as greater than 10 000 red blood cells/ml urine.

(3) Nephrotic syndrome, defined as massive proteinuria—greater than 50 mg/kg/24h. (Early

nephrotic syndrome is that which began during the first three months of the disease).

(4) Moderate renal failure, defined as creatinine clearance between 50 and 10 ml/minute/1.73 m².

(5) Severe renal failure, defined as creatinine clearance under 10 ml/minute/1.73 m².

(6) Early acute renal failure, defined as one that began during the first three months of the disease and later regressed or resolved.

Renal involvement in all patients was confirmed by histologic study of renal biopsy.

Descriptive terminology for renal histology. Renal biopsies, evaluated by light microscopy, were classified into the following categories:

(1) Minimal lesions—glomeruli seemed normal.

(2) Focal segmental glomerulonephritis—involvement consisted of local or segmental necrosis or proliferation.

(3) Diffuse proliferative glomerulonephritis—a widespread glomerular involvement with proliferation and a variable degree of capillary wall thickening and leucocyte infiltration.

(4) Membranous nephropathy—diffuse thickening of the capillary wall.

(5) Glomerular sclerosis.

Fresh renal tissue was incubated with fluorescein isothiocyanate labelled anti-human IgG, IgM, C3, and anti-IgA for immunofluorescent study.

Table 1 Major clinical features in 62 children with systemic lupus erythematosus

Fever	75%
Rash	72%
Arthritis or arthralgia	64%
Hypertension	39%
Pericarditis or myocarditis	26%
Neurological	19%
Pleurisy	10%

Results

Forty seven of the 62 patients were girls and 15 were boys. In 10 patients the onset of disease was before 10 years of age. Clinical features are shown in Table 1.

Haematological manifestations. Anaemia was present in 33 (54%) patients, leucopenia in 28 (45%), and thrombocytopenia in 13 (21%) patients.

Laboratory findings. Antinuclear antibodies were detected in all 62 cases at the time of diagnosis. Anti-DNA antibodies were found in 88% of the patients tested: hypocomplementaemia (low CH50) was present in 95% of the patients tested.

Renal manifestations. The mode of presentation and the histological findings are shown in Table 2. Immunofluorescent studies were carried out in 43 patients. Immunoglobulin and complement deposition were present in the mesangial areas (92%), along capillary walls (78%), or along tubular basement membranes (13%). The predominant immunoglobulins were IgG (88%), IgM (36%), C3 (31%), and IgA (28%). In 10 patients, normal kidney immunoglobulins were always present, predominantly in the mesangial areas.

Follow up data. The causes of death of six patients are given in Table 3, and the histological evolution of the disease is shown in Table 4. Repeat biopsies were performed on 25 children: in eight there was

Table 3 Causes of death in six cases

Myocarditis, acute stage	3
Pneumonitis, acute stage	1
Chronic renal failure	2
Unknown	1

no appreciable change in the severity or pattern of the renal lesion; in 11 the glomerular changes ameliorated; in six glomerular changes progressed; and glomerular sclerosis developed in four. Sixty one of the 62 patients (98%) were given prednisolone or its equivalent and 19 received immunosuppressive drugs during the first three months. After this time 58 of the 62 patients (93%) were given prednisolone and 34 (55%) received immunosuppressive drugs. The seven patients with chronic renal failure have been treated by prednisolone (2); prednisolone and immunosuppressive drugs (3); and prednisolone, immunosuppressive drugs, and plasmapheresis (2).

Eight patients have undergone plasmapheresis: one died, two progressed to terminal renal failure, and five were cured.

Discussion

The prognosis for systemic lupus erythematosus in childhood is similar to that in adults, and a striking observation is that when there is no nephropathy the survival rate 10 years from onset is 100%¹. Prognosis is affected considerably by the early development of nephritis. In our patients the mode of presentation and the renal histology were similar to those in adults, mode of presentation providing a reliable indication of renal lesions. For example, acute renal failure seems frequent in diffuse proliferative glomerulonephritis. Repeat biopsies, however, showed that minimal lesions or focal and segmental glomerulonephritis may progress to more severe disease such as sclerosis of the glomeruli or diffuse proliferative glomerulonephritis. On the other hand

Table 2 Initial presentation in relation to renal histology findings

	Haematuria ± proteinuria	Early nephrotic syndrome	Early acute renal failure
Minimal lesions (11)	8	0	0
Focal segmental glomerulonephritis (15)	15	3	4
Diffuse proliferative glomerulonephritis (30)	30	13	11
Membranous nephropathy (5)	5	2	0
Glomerular sclerosis (1)			1

Table 4 Clinical state at least five years after disease onset in relation to renal histology

	Minimal lesions	Focal segmental glomerulonephritis	Diffuse proliferative glomerulonephritis	Membranous nephropathy
Complete remission (13)	5	4	4	0
Urinary abnormalities (7)	0	0	5	2
Moderate renal failure (4)	0	0	4	0
Chronic renal failure (7)	0	2	5	0
Death (6)	1	1	4	0

improvement of renal lesions may be observed, and the cellular proliferation of the diffuse proliferative glomerulonephritis may resolve. Consequently, the predictive value of the early renal biopsy is limited. Of 172 cases in the published reports, 26 (15%) patients died and 21 (12%) progressed to chronic renal failure.¹⁻⁵ We have observed similar results.

The influence of treatment is difficult to define in our patients: no treatment seemed to prevent completely the onset of severe renal failure. In particular, plasmapheresis did not avert the death of one patient and the development of chronic renal failure in two others. It would be difficult to specify the best method of treatment from our clinical experience. Corticosteroids seem logical treatment in diffuse proliferative glomerulonephritis and immunosuppressive drugs would seem best reserved for those in whom the former fails. Treatment for less severe cases—that is, minimal lesions, focal and

segmental glomerulonephritis, and membranous nephropathy—is uncertain.

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Received 12 November 1984