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Clinical Presentation and Management Outcome of Childhood-Onset Systemic Lupus Erythamatosus in Baghdad

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Abstract

Introduction: Systemic lupus erythematosus (SLE) is an unpredictable autoimmune systemic disorder that often involves the kidney. In this study, we aimed to assess the clinical characteristics, pathological findings, and therapeutic response ofchildren presenting with lupus nephritis (LN).

Methods: We retrospectivelystudied 50 children with SLE admitted to the pediatric nephrology departments of four teaching hospitals in Baghdad between December 2009 and December 2011.

Results: The female to male ratio was 5:3. The median age was 11 years with a range of 5 -17 years. The commonest presenting features were weight loss (92%), fever (90%), edema (88%), arthritis (70%), hair loss (70%) and malar rash (60%). Examination revealed hepatosplenomegaly/ lymphadenopathy in 20% of patients. Anti-dsDNA was positive in 92% of patients.

Pathological examination revealed LN class I in 4%, class II (10%), class III (8%), class IV (74%) and class V (4%). All patients in class I, II and III achieved full remission after treatment with prednisolone. Thirty-one patients in class IV and V received induction treatment with cyclophosphamide followed by maintenance with cyclophosphamide (16 patients), mycophenolatemofetil (13 patients) or azathioprine (2 patients). Twenty-four of those patients achieved remission, four patients developed chronic kidney disease and three patients died. Five patients in class IV/V were treated with mycophenolate mofetil and three of them achieved remission, whilst three patients were treated with azathioprine and all of them achieved remission.

Conclusion: Diffuse proliferative glomerulonephritis (class IV) was the most common pattern of LN encountered in our study.

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Introduction

Systemic lupus erythematosus (SLE) is an unpredictable, episodic, multisystem, autoimmune disorder, with a higher rate and more severe organ involvement in children compared to adults [1]. Twenty percent of SLE cases begin in childhood [2].

Lupus as a diagnosis requires the combination of characteristic clinical and laboratory findings. In children, the prevalence is 1 in 100,000 with girls more frequently affected than boys. Renal disease is a common complication of SLE and can manifest as glomerulonephritis (GN), tubulointerstitial nephritis and antiphospholipid antibody syndrome (APS). Glomerulonephritis, usually synonymous with the term "lupus nephritis", is the most common and best-studied form of kidney involvement [3]. Proteinuria is the most frequent laboratory findingand up to 50% of children with lupus nephritis have a decreased glomerular filtration rate.

Double stranded DNA antibodies (anti-dsDNA) are specific for SLE and therefore very useful for diagnosis. Hypocomplementemia is observed in 75% of cases at presentation, particularly in patients with nephritis.

Treatment of lupus with or without nephritis is based on evaluation of the severity of the disease. In all cases with suspected renal involvement, the histopathological grading of renal biopsy is very helpful in deciding further treatment. Other potentially life-threatening symptoms, such as cerebral lupus, should also be taken into consideration when deciding on the initial treatment. The mainstay of treatment at the present time is based on corticosteroids and cyclophosphamide. For children with the worst disease spectrum, plasma exchange

and B-lymphocyte depletion therapy with intravenous rituximab may be added [4].

Methods

We retrospectively studied 50 patients with SLE admitted to the pediatric nephrology departments in the four teaching hospitals in Baghdad between December 2009 and December 2011. Patients were recruited from Al-KaramaTeaching Hospital (10 patients), Children Welfare Teaching Hospital (15 patients), Baghdad Teaching Hospital (18 patients) and the Central Children Teaching Hospital (7 patients). Data regarding clinical presentation, laboratory results and histological diagnosis were collected from patients'and their hospital records.

All patients aged 17 years or less and satisfying the revised American College of Rheumatology criteria (1982) for SLE were included in the study. Investigations included complete blood count, urinalysis, 24 hour urine protein excretion, serum creatinine, antinuclear antibody (ANA) and anti-dsDNA.

Nephrotic-range proteinuria was defined as proteinuria more than or equal to 1 g/m2/day. Hypertension was defined as systolic and diastolic blood pressure above 95th percentile for age, height and gender on 3 consecutive measurements.

All patients were subjected to percutaneous renal biopsies. The slides were processed for light microscopy and immuno-staining. Grading was done according to the revised WHO criteria (1995) as follows: Class I (minimal mesangial GN), class II (mesangial proliferative lupus GN), class III (Focal proliferative GN), class IV (diffuse proliferative GN), class V (membranous GN) and class VI (glomeruloseclerosis).

Patients were treated according to the following regimens. For class I-III the mainstay of treatment was oral prednisolone. Class IV and V were treated with prednisolone and various combinations of cyclophosphamide, mycophenolatemofetil (MMF) and azathioprine. When used for induction, intermittent IV cyclophosphamide pulses were administered monthly for sixmonths. As maintenance therapy, cyclophosphamide was then administered every threemonths for a total period of 30 months. MMF was given at a dose of 15 mg/kg twice daily.

Criteria of remission included clinical stabilization of the patient, normalization of blood pressure, normalization of complement levels and urine protein to creatinine ratio < 0.5.

Results

The female to male ratio was 5:3. The median age was 11 years with a range of 5 -17 years. The commonest presenting features were weight loss (92%), fever (90%), edema (88%), arthritis (70%), hair loss (70%), malar rash (60%), neurological manifestations (44%) and oral ulcers (30%). Clinical examination revealed hypertension in 60% and hepatosplenomegaly/lymphadenopathy in 20%. Hematological abnormalities were found in 92% of patients.

The majority of patients had nephrotic syndrome (68%) while 32% had subnephrotic proteinuria. Fifty percent had microscopic hematuria and 8% had macroscopic hematuria. Seven patients had renal impairment at presentation (14%). ANA and anti-dsDNA were positive in 90% and 92% respectively. Low C3 and C4 were found in 78% and 86%, respectively.

Pathological examination revealed LN class I in 4%, class II (10%), class III (8%), class IV (74%) and class V (4%). All patients in class I, II and III achieved remission following treatment with prednisolone. Thirty-one patients in class IV and V received induction treatment with cyclophosphamide and prednisolone followed by maintenance with either cyclophosphamide (16 patients), MMF (13 patients) or azathioprine (2 patients). Twenty-four of those patients achieved remission, four developed chronic kidney disease and three died. Five patients in class IV and V were treated with MMFand prednisoloneand three of them achieved remission. Three patients in these classes were treated with azathioprine and prednisolone and all of them achieved remission.

Discussion

Renal disease is frequent in children with SLE. In the absence of aggressive treatment, the child may die or progress to renal failure [5]. However, there is still some controversy regarding the best treatment. In the study performed by National Institute of Health, the incidence of renal failure was significantly higher in patients treated with prednisolone alone compared with patients given IV cyclophosphamide. Also, there was a trend for a better outcome in patients who received IV cyclophosphamide alone or in combination with MMF or Azathioprine [6]. Our patients received various combinations of cyclophosphamide, MMF and azathioprine along with steroids.

Radhakrishnan and colleagues compared MMF and IV cyclophosphamide as induction therapies in patients with lupus nephritis. Both treatment groups manifested similar and significant reductions in proteinuria, and essentially stable renal function. There was one death in each group

and similar numbers of infections and gastrointestinal symptoms were observed on the two regimens [7]. Spetie and colleagues described 13consecutive SLE membranous nephritis patients who received MMF and predisolone.After a mean follow-up of 16 months, nine (96.2%) patients were in complete remission and two (15.4%) had partial remission [8]. Mok and colleagues evaluated the effect of azathioprine and prednisolone in 38 Chinese lupus nephritis patients; 12 months after starting treatment, 67% of the patients had achieved complete remission and 21% had partial remission [9, 10].

The higher proportion of females and common presenting features in this study are consistent with the literature and with similar studies in the region [11-13]. The high prevalence of class IV lupus nephritis in this study is also similar to reports from Iran [13].

Conclusion

Diffuse proliferative GN(class IV) was the most common pattern of lupus nephritis encountered in our study.

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