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A CLINICOPATHOLOGICAL STUDY OF PEDIATRIC LUPUS NEPHRITIS IN TERITARY HOSPITAL OF BANGALORE

Seema H.S.

Department of Pathology, St.John's Medical College, Bangalore, KA, India.

ABSTRACT

Background: To study the clinical behavior of lupus nephritis in children from Southern India, and to report the differences in disease pattern.

Objectives:

1. To study histopathological changes and outcome in paediatric lupus nephritis.
2. To study the clinical and immunological spectrum of lupus nephritis.

Methodology: Laboratory received renal biopsy specimens with a clinical diagnosis of SLE by ARA criteria over a period of 6 years were included in the study and were classified according to the 1982 WHO Classification and reclassified ISN classification.

Results: Of the 16 cases studied, 12 patients were females (75%). ANA was the most frequently positive parameter occurring in 91% of cases. ds- DNA was positive in 9 cases. Anaemia was present in 10 cases (63%). In our study WHO Class IV lupus nephritis was most the common 63% (n=63). Acute renal failure was seen in 18% of paediatric cases and doubling serum creatinine was noted in 20% of paediatric patients.

Interpretation and conclusion: The incidence of disease was 3 times more common in females. WHO class IV was the commonest class, seen in 63% of cases. The percentage of patients having doubling serum creatinine was noted in 20% paediatric age group indicating poor renal outcome and prognosis in children.

Key Words: Paediatric, Systemic lupus erythematosus, Clinical profile, Serum creatinine, Lupus nephritis

INTRODUCTION

Systemic lupus erythematosus (SLE) is a prototype multi-system disease of autoimmune origin that accounts for significant mortality and morbidity

Lupus nephritis is an important complication occurring in up to 60% of patients with systemic lupus erythematosus (SLE) [1]. The clinical spectrum of lupus nephritis ranges from asymptomatic low grade proteinuria to rapidly progressive course with hypertension, oedema and leading to renal insufficiency within days[2]. Unlike adults, the clinical picture of SLE is often less characteristic in paediatric patients and a significant proportion of children present with severe renal disease at onset, but lack a sufficient number of criteria to be clearly diagnosed as SLE[3]. Nephritis in children may manifest with no symptoms, mild abnormalities, or may present with symptoms of diffuse proliferative disease[4]. Patients with severe histological forms of nephritis have more severe renal manifestations. The World Health Organization (WHO) has defined five histological types of lupus nephritis. Patients with pure mesangial nephropathy generally have good prognosis, whereas proliferative glomerulopathy especially diffused variant require aggressive therapy[2]. The factors affecting outcome are controversial and include male sex, black race, onset before puberty, persistent hypertension, impaired renal function, nephrotic syndrome, anaemia, class IV nephritis and increased histological index scores [5].

With this in the background, in this study we have emphasizes histopathological changes in paediatric lupus nephritis. We also studied clinical and immunological spectrum of paediatric lupus nephritis.

Corresponding Author:
Dr. Seema H.S., Department of Pathology, St.John's Medical College, Bangalore, KA, India.
Email: drseemapath28@gmail.com

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MATERIALS AND METHODS

In this study patients case records of children who were diagnosed to have SLE by American rheumatism association(ARA) criteria, and in whom renal biopsies was done in, St. John's Medical College, Bangalore for six years were retrieved and classified according to WHO classification. The study was both retrospective (January 1999 to January 2003) and prospective (February 2003 to December 2004). The clinical data and laboratory parameters like haemoglobin, hematuria, hypertension, low complement, doubling of serum creatinine, Antinuclear antibody(ANA) and Anti (double stranded) ds-DNA were retrieved from medical records department of St. John's Medical College Hospital in all cases. For this study, all the slides for light microscopy were examined.

The study complied with the guidelines of the local ethics committee.

Exclusion Criteria: Renal biopsies with a clinical diagnosis of discoid lupus, neonatal lupus and drug-induced lupus nephritis.

Microscopic examination: The types of samples that were obtained were:

i. Formalin fixed renal core biopsies which were stained with 1. Haematoxylin and Eosin (H&E) 2. Periodic acid-Schiff (PAS) 3. Periodic acid methenamine silver stain (PAS-M)
ii. Data collected was analyzed based on following observations after classifying the renal biopsies according to the 1982 WHO classification, reclassified according to (International society of nephrology) ISN classification.

RESULTS

Our study comprised of 16 cases belonging to paediatric age group (Age less than 16years). In our study out of 16 paediatric patients, 12 were females and 4 male. ANA was positive in 13 of 14 cases tested. (See in Table 1). Anti ds-DNA was positive in 9 of the 11 patients tested. (See in Table 2). Anaemia was present in 10 cases of 13 patients whose data was available (See in Table 3). Hypertension was noted in 9 out 12 cases whose data was available. Low complement was noted in 4 cases. Hematuria was seen in 9 of the 15 children whose data was available. In our study out of 16 cases, 10(63%) cases belonged to class IV, 5 cases belonged to class III and one case belonged to class II (See table 4). We reclassified the biopsies according to ISN2003 classification and results are given in Table5. Nine cases had high urine proteinuria(3+) and 8 of these belonged to Class IV. Eight of the 9 children who had hematuria belonged to class IV. Out of 16 cases 6 cases had no follow up. In these 10 cases, 2 cases that are 20% of childhood lupus nephritis showed doubling of serum creatinine. Out of 16 cases 3 children developed acute renal failure, 2 of them belonged to class IV and one belonged to class III.

DISCUSSION

Demographic data

In our study 14% of cases belonged to the paediatric age group (<16years). In this group the male to female ratio was 1:3 and there was no child of less than 5 years. The youngest child was 8 years old. All these data are comparable with other Indian studies done by Gupta[6] et al, and Chandrasekaran [7]et al.

Clinical, laboratory and immunological data

ANA was positive in 92% of cases whereas Indian studies by singh [8]et al, and Ali[9] et al showed ANA positivity in 100% of cases .Prior drug therapy, which is a common phenomenon in Indian set up could account for it. Anti-ds DNA was positive in 81%of cases (9out of 11 tested), in concordance with other studies singh [8]et al and Ali[9] et al. Anaemia was present in 77 of cases in contrast to the adults who had anaemia in only 49% of the cases. Hypertension was present in 75% of the cases tested where as in study done by Ali[9] et al and Hari [10]et al and it was seen only in 45-55% of cases.

Histopathology

In children also class IV lupus nephritis was the most common lesion, which is in 63% of cases. A pointed to be noted here is that there was no case of Class V lupus nephritis, which is in line with the studies done by Gupta[6] et al and Chandrasekaran [7] et al. 1 case belonged to class II and 5 cases belonged to class III. Recategorisation of biopsies with ISN 2003 classification showed no significant difference in the class that could have affected the treatment and prognosis. In our study we have noticed 88% of cases who had urine proteinuria(3+) and hematuria belonged to class IV, reconfirming that class IV lupus nephritis has the worse prognosis.

Complications

- Acute renal failure was seen in 18% of paediatric cases, whereas study done by Yang[11] et al showed only 7% of his cases to have renal failure, which probably reflect on better treatment and follow up available there.
- Doubling serum creatinine was noted in 20% of paediatric patients which when compared to adults (7%) is high and probably warrants us to be more diligent in management and follow up.
- Hematuria and proteinuria which indicate severe renal involvement was more common in Class IV

lupus nephritis which is in concordance with other studies like Agwaral[5] et al indicating bad prognosis and again reminding the need of aggressive therapy.

CONCLUSION

Lupus nephritis in children is said to have poor prognosis is getting ratified in our study, that to children with class IV lupus nephritis having higher incidence of hematuria, proteinuria and doubling of serum creatinine which indicates severe renal involvement and graded prognosis. Hence we conclude that renal biopsy, early diagnosis and strict aggressive treatment regime is a must especially in Indian settings to prevent further complications and mortality in pediatric age group.

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Conflicts of interests: The authors declare that they have no conflicts of interests.

Table1: Pediatric cases- ANA

ANA	Number of cases
Positive	13
Negative	1
Not done	2

Table 2: Pediatric cases- ds DNA

ds DNA	Number of cases
Positive	9
Negative	2
Not done	5

Table 3: Pediatric cases- Anemia

Anemia (Hemoglobin <10gram/dl)	Number of cases
Present	10
Absent	3
Data not available	3

Table 4: Distribution of cases according to 1982 WHO classification:

1982 WHO Class	Number of cases
Class I	0
Class II	1
Class III	5
Class IV	10
Class V	0
Class VI	0

Table 5: Case distribution-ISN 2003 classification

Class	Number
Normal by LM, IF, EM	0
Class 1	0
Class 2	2
Class 3A	3
Class 3A/C	2
Class 4SA	2
Class 4GA	5
Class 4GA/C	2
Class 5	0
Class 5 with 2	0
Class 5 with 3	0
Class 5 with 4	0
Class 6	0

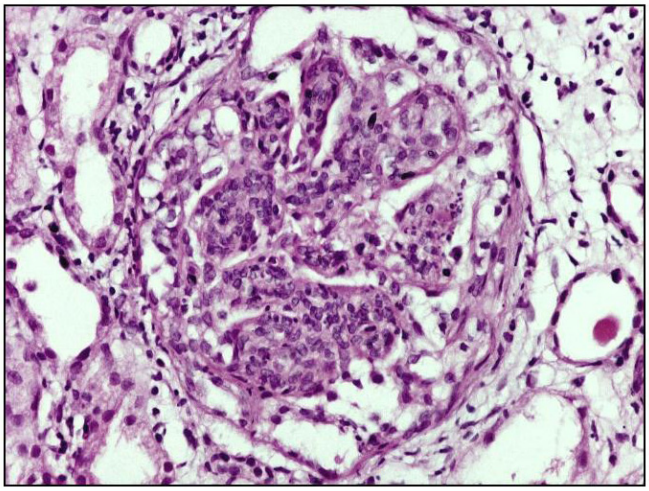

Figure 1: Glomerulus from class IV lupus nephritis showing diffuse endocapillary proliferation.

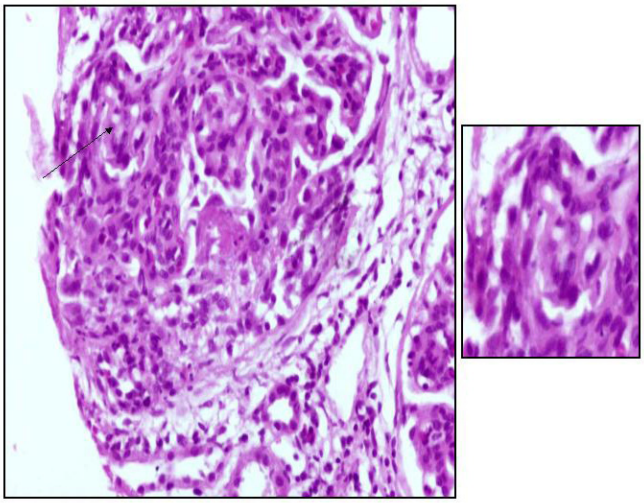

Figure 2: Glomerulus showing diffuse proliferative glomerulonephritis with wire loops.

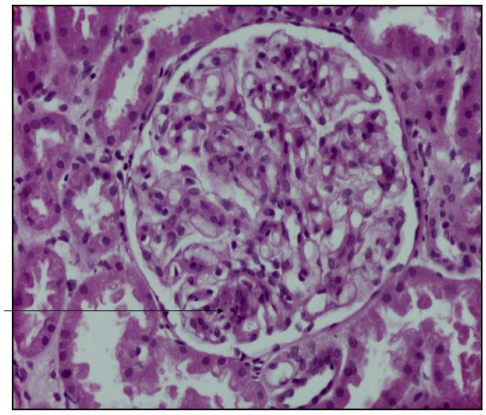

Figure 3: Glomerulus showing segmental proliferation with fibrinoid necrosis

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