Original Article

Iran J Pediatr
Jun 2008; Vol 18 (No 2), Pp:143-148

Acute Glomerulonephritis in Southern Iran

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Received: 23/09/07; Revised: 27/12/07; Accepted: 17/04/08

Abstract

Objective: Acute post streptococcal glomerulonephritis (APSGN) is the most common type of in-patient glomerulonephritis (GN) in childhood. It has not been studied well in this region yet. Here, we report our experience with APSGN in a tertiary referral center during a five-year period.

Material & Methods: Hospital records of all 137 children who had been admitted to Nemazee hospital, between 2001 and 2006, with diagnosis of acute glomerulonephritis (AGN) were reviewed. All demographic, clinical, paraclinical data and consumed medications were obtained.

Findings: Among 137 children diagnosed as AGN, 122 (89%) had APSGN. Other 15 (11%) children had membranoproliferative glomerulonephritis (n=4), mesangioproliferative glomerulonephritis (n=4), IgA nephropathy (n=2), lupus nephritis (n=2), rapidly progressive glomerulonephritis (n=2), and focal segmental glomerulosclerosis (n=1). Mean (SD) age in children with APSGN was 8.5 (3.5) (range, 3.5-13) years**,** 117 (96%) children developed APSGN following a sore throat and 5 (4%) following an impetigo, with 95 (78%) during the cold seasons of the year. Periorbital edema was found in 97.5%, hypertension 75%, gross hematuria 72%, oliguria 37%, generalized edema 19%, azotemia (BUN>20) 80%, and nephrotic-range proteinuria 24.5%. A high anti streptolysin–O (ASO) titer and a low C_3 level was detected in 84% and 86%, respectively. There was dilutional anemia in 51.5%, hyponatremia in 27%, and hyperkalemia 14%. With regard to medications, 19 patients received only furosemide, 73 cases furosemide and nifidipine, and 10 patients furosemide, nifidipine, and another antihypertensive medication. Hypertensive encephalopathy occurred in 3 cases, but no mortality was reported during the study period.

Conclusion: APSGN is the most common type of glomerulonephritis in this region. It follows sore throat in the majority of cases. It usually has an uneventful course.

Key Words: APSGN; Glomerulonephritis; Hypertension; Edema; Iran

Introduction

Acute glomerulonephritis (AGN) is heralded by acute onset of edema, hematuria, and hypertension, which is usually associated with oliguria and azotemia[1,2]. Acute post streptococcal glomerulonephritis (APSGN) is the most common type of in-patient

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glomerulonephritis (GN) in childhood[3,4]. APSGN usually occurs after streptococcal pharyngitis or streptococcal skin infection. Despite a well-known association between streptococcal infection and APSGN for more than hundred years, the exact cause and effect relationship, and also the reason that only certain strains are nephritogenic are not known yet[5-7]. In a recent study from Egypt, children with APSGN had a higher frequency of HLA-DRB_1 alleles than control group[8]. In another report from our region, during a seven-year period, 23% of all admissions to a renal unit were allocated to GN, with 9.4% being APSGN[4].

The present study was conducted to report the epidemiological data of children with admission diagnosis of AGN, in a referral center in southern Iran, during a five-year period, and describe their clinical and paraclinical features in detail.

Material & Methods

A retrospective chart review was done for all children who had been admitted to Nemazee Hospital (affiliated to Shiraz University of Medical Sciences, Iran) with impression of AGN, from March 2001 to March 2006. All children aged less than 15 years, with AGN as admission diagnosis and at least 3 months of follow up were included in the study.

Hospital records on admission, during hospital stay, and follow-up records were thoroughly scrutinized. Information on demographic, clinical, paraclinical data, and consumed medications was obtained. Paraclinical parameters included urinalysis on admission, 24-hour urine protein and creatinine, complete blood count, erythrocyte sedimentation rate, BUN, creatinine, serum Na^+ and K^+, C_3 level, anti-strptolysin O (ASD) titer, and kidney biopsy findings (if taken). Records of 137 children with diagnosis of AGN on admission were complete for the purpose of the study. Those with incomplete records were excluded from the study.

Diagnosis of PSAGN was made by clinical features and the course of the disease, rise in ASO titer, low C_3 at presentation, and also normalization of C_3 two to three months after presentation.

Statistical analyses were performed using SPSS 11 (SPSS, Chicago, IL) package. Unless otherwise stated, values are Mean± SD. Chi-square was used to test the significance. Statistical significance was defined as $P<.05$.

Findings

Among one hundred and thirty seven children with AGN, 122 (89%) had APSGN. Three children with APSGN presented with rapidly progressive glomerulonephritis (RPGN). The other 15 (11%) children were diagnosed as follows: Membranoproliferative glomerulonephritis (MPGN) (n=4), mesangioproliferative glomerulonephritis (MESPGN) (n=4), IgA nephropathy (n=2), lupus nephritis (n=2), RPGN with causes other than APSGN (n=2), and focal segmental glomerulosclerosis (FSGS) (n=1).

The average age (SD) was 10.36 (3.16) (range 2-14) years for the whole children population and 8.5 (3.2) (rang 3.5-13) years in APSGN cases. Male to female ratio was 3.03 (103/34) for the whole population and 2.93 (91/31) for APSGN children.

The number of APSGN cases per year was 34, 30, 24, 20, and 14 from 2001 to 2006, respectively. The mean (SD) hospital stay was 5.4 (2.6) (range 2-26) days for children with APSGN. The mean (SD) duration of follow up was 30 (26) (range 5-58) months.

One-hundred and seventeen (96%) children had a history of preceding sore throat or upper respiratory tract infection 9.0 (3.5) (range 7-16) days before admission. Five (4%) children had skin manifestations of impetigo 16 (7) (range 14-24) days before hospitalization. Clinical findings of children with APSGN are depicted in table 1. The most frequent clinical findings were periorbital edema, gross hematuria, and hypertension.

Table 1 - Clinical findings of 122 children with APSGN

Clinical findings	Frequency
Periorbital edema	119 (97.5)
Hypertension	92 (75%)
Gross hematuria	88 (72%)
Oliguria	45 (37%)
Fever	24 (20%)
Abdominal pain	24 (20%)
Generalized edema	23 (19%)
Flank pain	7 (6%)

Convulsion with very high blood pressure was reported in three children. It was controlled with lowering of blood pressure. Transient blindness lasting for a few hours was found only in one child. In regards to the seasonal variation, 96 (78.7%) children had onset of their disease during the cold months of the year (from November to the end of April). Among them, 44 (36%) children had APSGN during winter (22nd December to 19th March). The remaining 26 patients (21.3%) experienced APSGN in the other months of the year (P<0.05).

The major laboratory findings of the 122 APSGN children are summarized in table 2. Serum creatinine equal or more than three times of normal age-related values was present only in 21 (17.2%) children. It was normalized in 16 of them during the first week of hospital stay, and in 2 cases, during the second week. The remaining 3 children developed RPGN following APSGN, which took more than three weeks for their renal function to normalize. They received methyl-prednisolone pulses and also underwent several sessions of hemodialysis (HD).

Seventeen (14%) children had hyper-kalemia sometime during their disease (serum K^+≥5.5 mEq/l); For 14 (82%) of them, serum potassium was corrected by conservative therapy, and the remaining three were RPGN cases, for whom HD was performed.

Table 2 - Paraclinical findings in children with APSGN

Laboratory findings	Frequency
Microscopic hematuria ≥5RBC/HPF	122 (100%)
Proteinuria≥1+	122 (100%)
Leukocyturia WBC≥5//HPF	117 (96%)
BUN<20mg/dl	24 (20%)
BUN>20mg/dl	98 (80%)
Normal Serum Creatinine*	52 (42.6%)
Serum Creatinine*3times Nl*	21 (17.2%)
Hyponatremia (Na^+<135 mEq/l)	34 (27%)
Hyperkalemia (K^+≥5.5mEq/l)	17 (14%)
Triglycerides >95th percentile	51 (56%)
Cholestrol >95th percentile	24 (26%)
ESR† (20-40mm/hr)	63 (70%)
ESR>40mm/hr	27 (30%)
Hemoglobin <12gm/dl	63 (51.6%)
Proteinuria>40mg/m^2/hr	30 (24.5%)
Low serum C_3	105 (86%)

**Normal age-related value*
† Erytrocyte Sedimantasion Rate

Hemoglobin (Hb) level was less than 12 mg/dl in 63 (51.6%) children. For 10 children, a Hb level less than 10 mg/dl was found, among whom, 3 children were known cases of minor thalassemia and 3 others were the cases that developed RPGN.

Serum C_3 level was low in 105 (86%) patients which normalized after three months in all of them. ASO titer was elevated in 103 (88%) of 117 children with APSGN following an upper respiratory infection. Nephrotic-range proteinuria (24hr urine protein>40mg/m^2 /hr) was present in 30 (24.5%) children, in majority of whom, it was transient (lasting <2weeks).

In regards to diuretic and antihypertensive therapy, 20 patients had not received any medication, 19 children had only furosemide, 73 furosemide and nifidipine, and the remaining 10 cases had received more than two medications.

Among all 137 children with AGN, kidney biopsy was only performed in 24 children. The indications for kidney biopsy included a rapidly progressive course, persistent proteinuria for longer than 2 weeks, normal C_3 at presentation or any other atypical features, and features in favor of lupus nephritis. Biopsy findings were as follows: exudative glomerulonephritis (n=6), MPGN (n=4), exudative and crescentic glomerulonephritis (n=3), crescentic glomerulonephritis with negative immunoflorsent (IF) findings (n=2), IgA nephropathy (n=2), class-IV lupus nephritis (n=2), FSGS (n=1), and mesangioproliferative glomerulonephritis without specific cause (n=4).

Recovery of renal function 3 months after presentation was complete in all cases including the three cases with RPGN. However, microscopic hematuria was still present in 113 (92.5%) children and non-significant proteinuria was found in 71 (59%) of them. No mortality or no progression to chronic renal failure was found in any of children with APSGN during the study period. However, in two children, recurrence of APSGN occurred 3 and 4 years after the initial attack.

Discussion

One hundred and thirty-seven children with diagnosis of AGN on admission were studied. Eventually by considering all available data, 122 children were diagnosed as APSGN. The age range in children with APSGN was 3.5 to 13 years with a mean of 8.5±3.2 years. These are in accordance with findings of other studies[1-3].

In the majority of children in this study (96%) symptoms of glomerulonephritis had appeared 9±3.5 days following a sore throat or upper respiratory infection while only in a minority (4%), it developed 16±7.0 days after a skin infection. This latent period is also in agreement with other studies[1]. Roy et al also found a prodromal throat infection in the majority of children with APSGN in their study[9]. In contrast, in a study by Berríos et al[10], only a minority of children were found to have a prodromal throat infection before APSGN.

Male/female ratio in our study population was 2.93 which was higher than in other studies. The majority (79%) of them developed APSGN during the cold months of the year with 36% presenting in winter which is in accordance with other studies[1,2].

The major clinical features (hematuria, proteinuria, edema, hypertension, oliguria, and azotemia) are similar to other studies. Also hyperkalemia and hyponatremia were observed with the same frequency as in other studies. However, gross hematuria (72%) and nephrotic-range proteinuria (24.5%) was more prevalent in our study comparing to others[1-3]. In addition, the prevalence of hypertriglyceridemia (56%) and hyper-cholesterolemia (26%) was also slightly more than in other studies[11]. The high prevalence of these findings might be related to the tertiary referral nature of our center in which we deal with some complicated patients referring from medical centers, all over the southern Iran.

As in other studies, ASO titers and serum C_3 levels decreased in 88% and 86% of the children with APSGN, respectively[1-3].

Antibody titers such as anti-DNAse B are not checked in this center. Also as in other studies, we found dilutional anemia in 51.5% of children and a high ESR (≥20mm/hr) in the records of all children that have been checked[12].

As in other surveys[4,13], short-term prognosis among our children with APSGN was quite excellent. Although non-significant proteinuria and microscopic hematuria were still present in majority of children, all APSGN cases (even those presenting with RPGN) had a normal renal function at their 3rd monthly visit. Persistence of nephrotic range proteinuria and hypertension during the follow-up visits was found to be important predictors of renal dysfunction in another study[14]. No mortality was reported in this study.

Convulsion with very high blood pressure was seen in three children, and Recurrent APSGN occurred in two children. Previous studies have reported these events after APSGN[2,15-17]. However, transient blindness which occurred in one of these cases has not been reported by other studies.

We should clarify that since our study was a retrospective one, it is possible that we have missed some data or some patients in this study.

Conclusion

By what we have observed, APSGN is the most common type of glomerulonephritis in our in-patient units and it usually has an uneventful course.

Acknowledgement

The authors wish to thank Dr. Hamed Jalaeian for his editorial assistance.

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