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Henoch-Schonlein Purpura in Northeast India: Peculiarities in Presentation

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Abstract

Background and Aim: Henoch-Schönlein purpura (HSP) is the most common childhood vasculitis characterized by leukocytoclastic vasculitis. This study was done to describe the presentation and immediate outcome of children admitted to HSP at our Institute.

Methods: This retrospective study was conducted on children with HSP admitted to our department over a period of 7 years (January 2010 until December 2016).

Results: Twenty-three children with a diagnosis of HSP were identified during the study period. The mean age was 9.4 years (4 years to 16 years). There were 15 girls and 8 boys with a male: female ratio of 1:1.9. The youngest child was 4 years old and most of the children (73.9%) were in the age group 5-12 years. Forty percent of the children presented between January and March. Major manifestations were rash (100%), joint pain (52%), renal involvement (52%), and abdominal pain (47.8%). Three (13.0%) children presented with systemic manifestations before the appearance of the rash. One child had MPGN 2 years before the onset of rash. There was no mortality. Most of the children recovered well; six (26%) had persistent hypertension and three (13%) had persistent proteinuria. Hypertensive emergency was seen in two children. One child had intussusception that resolved spontaneously.

Conclusion: This study is the first study of Henoch Schonlein purpura from northeast India documenting certain peculiarities in the presentation. The results indicate a wide spectrum of presentations in HSP.

Keywords: Henoch Schonlein Purpura; IGA Vasculitis; Nephritis.

Conflict of interest: The authors declare no conflict of interest.
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Introduction

Henoch-Schönlein purpura (HSP) or IgA vasculitis is the most common childhood vasculitis characterized by leukocytoclastic vasculitis and immunoglobulin (Ig) A deposition in the small vessels in the skin, joints, gastrointestinal tract, and kidneys. Willium Heberden was the first to report, beginning in 1802, the observation of one child presenting with petechial hemorrhages on lower limbs and joint, abdominal pain, bloody stool, and gross hematuria.

The syndrome was named after 'Schonlein' who described the clinical entity characterized by purpura and joint pain as well as 'Henoch' who described its frequent association with gastrointestinal symptoms and kidney involvement (1). Overall, the prognosis of childhood HSP is excellent, and most children experience an acute, self-limited course. However, complications like acutely serious gastrointestinal involvement may cause significant morbidity and mortality (2). Although progression to end-stage renal disease is rare, it may occur in 1-2 % of the HSP cases (1, 2). This study was conducted to describe the presentation and immediate outcome of children presenting to our institute with Henoch Sconlein purpura.

Methods

This retrospective study was conducted on children admitted with HSP to our department over a period of 7 years (January 2010 until December 2016). Children who were admitted with a diagnosis of HSP were included in the study if they fulfilled either of the American College of Rheumatology (ACR) or European League Against Rheumatism (EULAR) criteria (2). Hematuria was defined as >5 RBCs/HPF of centrifuged urine or a positive urinary dipstick reading. Proteinuria was defined as a positive dipstick testing (≥30 mg/dL) or a spot urine protein to creatinine ratio of >0.2. Nephrotic range proteinuria was defined as a dipstick test of >2+ or a spot urine protein creatinine ratio of >2. Acute glomerulonephritis, hypertension, and acute kidney injury (AKI) were diagnosed as per the standard definitions. The definitions of hematological and serological parameters used were as follows: leucocytosis >15000/cumm; thrombocytosis >500,000/cumm; elevated ESR >40mm/1st hour; low C3< 88mg/dl.

This study was performed in accordance with the relevant guidelines and regulations and was approved by the Institute Ethics Committee of NEIGRIHMS, Shillong.

Results

Twenty-three children with HSP were identified during the study period. The mean age was 9.4 years (4 years to 16 years). There were 15 girls and 8 boys with a male: female ratio of 1:1.9. The youngest child was 4 years old and most of the children were in the age group 5-12 years (Figure 1). There tended to be a seasonal trend with about 40% of children presenting in the months of January to March (Figure 2). Major manifestations were rash, joint pain, renal involvement, and abdominal pain as detailed in Table 1. Five (21.7%) children had both renal and joint involvement. Three children (13%) had both abdominal and joint symptoms with renal involvement, and 2 (8.7%) children had renal involvement along with abdominal symptoms.

Palpable purpura was the most common symptom that was universally present at some point in time. Four children (17.3%) presented with systemic manifestations before the appearance of the rash. In these 4 children, 2 presented with abdominal pain and then developed the typical purpuric rash 1 to 2 weeks later. The other child initially presented with renal manifestations followed by the appearance of purpuric rash after 2 weeks. Another child had membranoproliferative glomerulonephritis (MPGN) on biopsy 2 years prior to presentation with a typical HSP rash.

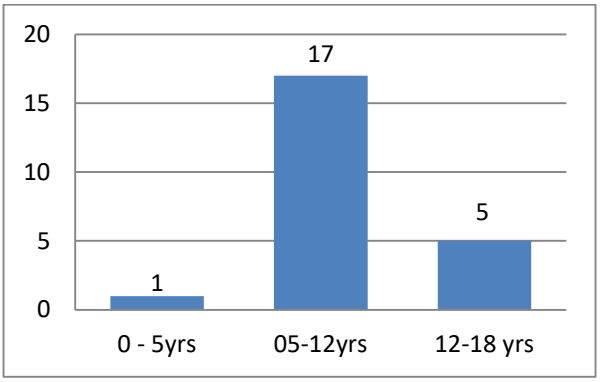

Figure 1. Frequency distribution as per age group

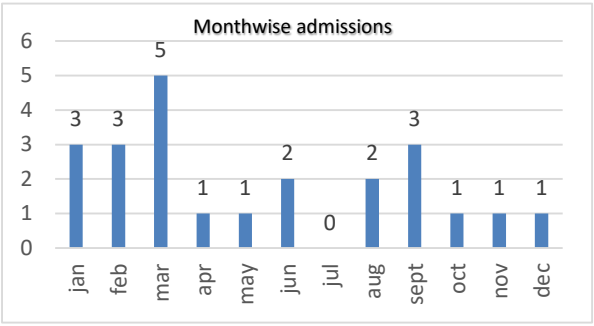

Figure 2. Monthly trend in admission of children with HSP

Palpable Purpura

The distribution of the rash was predominantly in the lower limbs as a typical palpable purpura. The pattern of the rash included – 'lower limbs and buttocks', 'lower limb, buttocks and upper limbs', 'lower limbs, buttocks and trunk' and 'all over the body' in 14 (60.9%), 4 (17.4%), 3 (13.0%) and 2 (8.7%) children, respectively. One of the children with a rash all over the body also had a purpuric rash in the face including the malar area whereas the face was spared in others. Systemic lupus erythematosus (SLE) was ruled out in this child.

Renal manifestations

Eleven (47.8%) children with HSP had renal manifestations in the present series. The children with renal manifestation tended to be older than those without renal manifestation (10.4 + 4.6 vs 8.5 + 2.3 P=0.033). The most common feature was

pedal and periorbital edema that was observed in 10 (90.9%) children with HSP nephritis (HSPN).

Table 1. Summary of clinical features

No.	Observations	Number (n=23)	Percentage (%)
1	Rash	23	100 %
2	Large Joint pain	12	52 %
	Monoarticular large joint	1	4.5%
	Polyarticular joint pain	11	47.8 %
3	Renal involvement	12	52 %
	Proteinuria	3	13 %
	Hematuria	2	8.7 %
	Proteinuria + Hematuria	7	30.4%
	Generalized edema	11	47.8 %
4	Abdominal pain	11	47.8 %
5	Persistent hypertension	6	26 %
6	Positive Stool for occult blood	5	21.7 %
7	Persistent proteinuria	3	13.4%
8	HTN emergency	2	8.7 %
9	Oliguria	2	8.7 %
9	Renal + Joint involvement	5	21.7 %
10	Renal + joint + Abdominal involvement	3	13 %
11	Renal + Abdominal involvement	2	8.7 %

Hematuria was noted in nine (69.2%). Proteinuria was present in 10 (76.9 %) children with HSPN 6 of whom (54.5%) had nephrotic range proteinuria. Acute nephritic syndrome was seen in five (45.5%) children with HSPN. Two children developed hypertensive encephalopathy (18.2%). Three (27.3%) continued to have persistent proteinuria and four (36.4%) had persistent hypertension. Three (27.3%) children had isolated proteinuria and hematuria without hypertension or edema. Apart from these 11 children with HSPN, three (13.0%) had soft tissue edema of the legs without any features of nephritis like proteinuria, hematuria, or hypertension. Three children (13%) had AKI, which touched baseline at the time of discharge from the hospital. Eight (72.7%) children had either severe nephritic syndrome or nephrotic range proteinuria and thus met the indication for biopsy. One child refused consent and hence seven children underwent biopsy.

Histopathological details are given in Table 2. An immunofluorescence study was done in four cases. All the cases showed dominant IgA deposition in mesangial distribution. As per the International Study for Kidney Diseases in Children (ISKDC) classification, four cases were in class II, one case was in class IIIa, one case was in class IIIb, and one case was in class VI. (Table 2)

Joint involvement

Arthritis or arthralgia was documented in 12 (52 %) children.

The large joints like knees, ankles, hips, and elbows were involved. One child (8.3%) had a single large joint involvement (knee joint) whereas the rest had multiple joint involvements (91.7%).

In all the children, the onset of the rash preceded joint symptoms.

Although a temporal relationship was variable, it usually occurred within 3 weeks of the onset of rash (in 66.7% of the cases). A striking female preponderance was seen in children with joint pain as compared to those without (M: F: 1:5 vs 1.2: 1; P = 0.04). All of the children with joint pain had a typical presentation of HSP.

Gastrointestinal symptoms

Abdominal pain was seen in 11 (47.8%) children. Abdominal pain preceded the rash by 2 weeks in 2 children. One child had a frank lower gastrointestinal bleeding. The stool was tested for occult blood in seven children, and the results were positive in five cases. Radio imaging was only done in 8 children. An abdominal ultrasound showed mild ascites in three children (13%) and features of bowel ischemia and intussusception in one child (4.4%), which was also confirmed on the CECT abdomen. However, intussusception was transient and resolved spontaneously. The other four children had normal ultrasound results.

Table 2. Summary of renal lesions on biopsy

Serial no.	Renal Histopathology	Immunofluorescence	ISKDC classification
1.	Pure mesangio-proliferative glomerulonephritis	Not done	Class II
2.	First biopsy- Membrano-proliferative glomerulonephritis	Not done	Class VI
	Repeat biopsy 2 years later- Diffuse mesangio-proliferative glomerulonephritis with less than 50% crescentic glomerulonephritis and 30% slcerosed glomeruli	Not done	Class IIIb
3.	Focal segmental necrotizing glomerulonephritis	Not done	Class IIIa
4.	Pure mesangio-proliferative glomerulonephritis	IgA- Mesangial positivity IgG & C3- Glomerular capillary wall positivity IgM- Negative	Class II
5.	Pure mesangio-proliferative glomerulonephritis	IgA- Mesangial positivity IgG & C3- Glomerular capillary wall IgM-Glomerular capillary wall positivity	Class II
6.	Diffuse mesangio-proliferative glomerulonephritis with less than 50% crescentic glomerulonephritis	IgA- Mesangial positivity and capillary positivity IgG & C3- Glomerular capillary wall positivity IgM- Negative	Class IIIb
7.	Pure mesangio-proliferative glomerulonephritis	IgA- Mesangial and capillary positivity IgG & C3- Negative IgM-Glomerular capillary wall positivity	Class II

Central nervous system manifestations

The only CNS manifestation was hypertensive encephalopathy in two children with nephritis who presented with seizure and altered sensorium. There was no focal deficit, and magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) analysis were normal in both of the children.

Hematological and serological findings

The mean hemoglobin was 11.29 ± 1.86 gm/dl and the mean leukocyte count was 13670 ± 6417/cumm in these children. Neutrophilia was seen in 19 (82.6%) children. The mean platelet count was 3.9 ± 1.58 lacs/cumm in these children.

There was no thrombocytopenia in any of the cases. The erythrocyte sedimentation rate (ESR) was variable with an average of 37.85± 23 mm at the end of the first hour. Seven children had raised ESR more than 40mm in the first hour. There was no associated coagulopathy in any of the children. Other investigations were done as and when indicated.

The levels of antinuclear antibody (ANA), serum amylase, and lipase were measured only in four patients, which were unremarkable. The C3 level was measured only in one patient that was within the normal range.

Treatment and outcome

Only non-steroidal anti-inflammatory drugs were used for joint pain. A short course of steroid was used in case of abdominal pain, occult blood in the stool, and renal involvement. Nineteen (82%) required steroid therapy. Three children with severe histology (ISKDC class IIIa, IIIb, and VI) continued to have persistent proteinuria. A boy with an MPGN like histology was treated with pulse cyclophosphamide followed by a long-term alternate day steroid regimen. The other two children with persistent proteinuria received a longer-term alternate day steroid regimen (up to 3 months). Enalapril as an antiproteinuric agent was given to all three children with persistent proteinuria.

Discussion

The present series included 23 children with HSP with a mean age of 9.4 years (range: 4-16 years) and a male: female ratio of 1:1.9. Most of the children (95%) were in the age group 5-12 years. Major manifestations were rash, joint pain, renal involvement, and abdominal pain as detailed in Table 1. They usually had multiple system involvement. Most of the children with HSP tend to be in the age group 4-6 years (3). However, the mean age of the children ranges from 3.5 to 8.5 years in different series (4-10). Our series had an even higher mean age at presentation of 9.4 years although it was not markedly different from the findings of Bagga et al and Kumar et al (7, 8). Most authors included children up to 12-13 years as seen in Table 3.

Our unit sees children up to 18 years of age and we had 5 (21.7%) children in the age group 12-18 years, which explains the higher mean age.

There were more girls with HSP in this series (M: F: 1: 1.9) as compared to the male preponderance found in most series (4-9). However, the M: F ratio ranges from an almost equal gender ratio of 1.2:1 to a striking male preponderance of 2.6: 1 in the literature (8, 9). The female preponderance seen in our series is in contrast to what is already known and might be because of the small sample size or regional/ ethnic factors. A large series from Spain also found a female preponderance (11, 12). HSP cases are known to occur more commonly in the winter and spring (1, 6). Our cases were seen throughout the year with the majority of the cases occurring from January to March (winter-spring). The seasonal distribution supports the hypothesis that infection might be a trigger for this condition (1, 6). However, in our series, only three children had a history of preceding respiratory tract infection.

As seen in most series, a typical purpuric rash was found to be a universal feature (4-10). However, only 20 (87.0%) children had the rash as the presenting symptom, which is similar to the findings of Cheng et al (6). In the remaining three (13%) children, the symptoms preceded the rash thereby making the diagnosis illusive at presentation. Two (9%) children had abdominal pain before the appearance of the rash, a finding also described by Kawasaki Y et al (13). Only one child presented with renal manifestation before the rash, which is an extremely rare finding.

Gastrointestinal manifestations can precede the rash by 2 weeks in up to 20% of the cases. The rash may also occur up to months after the initial presentation (1). In our series, rashes occurred within weeks of presentation. One child was diagnosed as biopsy showing MPGN 2 years before the appearance of the rash. Although an MPGN-like picture is known in HSPN, whether this association is coincidental or part of the same disease process is not clear. Moreover, such a long gap between the initial presentation and onset of rash has been described earlier (8).

Renal involvement at presentation (HSPN) was seen in 11 children (47.8%), which is comparable to the high proportion of HSPN in other in-patient series (6, 8, 10). In population-based studies, the proportion of HSPN is expected to be 20% (14). Kumar et al also documented a lower proportion of HSPN in their series as it was a rheumatology clinic-based data in contrast to most in-patient hospital-based data (7). Renal manifestation is the major prognostic factor and a higher severity of renal involvement is associated with a worse prognosis (1, 2, 8). Severe presentation in terms of either nephritic syndrome or nephrotic range proteinuria was seen in eight children (72.7% of HSPN). Isolated hematuria with or without proteinuria was seen in three (27.3%) children. This is in contrast to values of 33% and 67% respectively in a population-based study by Stewart et al, which is obviously due to the selection bias of an inpatient-based study as ours (14).

Acute renal insufficiency is generally rare and is seen in 1-2% of the cases (1, 15, 16). However, the AKI rate was as high as 13% in this study, which was similar to the results of study by Bagga et al (8). Three children had renal sequelae in form of persistent hypertension and proteinuria.

The renal lesions associated with HSPN are different ranging from pure mesangio-proliferative glomerulonephritis to a focal segmental necrotizing glomerulonephritis to diffuse crescentic glomerulonephritis and a pattern similar to that of membranoproliferative glomerulonephritis. (17, 18).

The lesions observed in kidney biopsy samples from patients with HSPN are strongly dependent on the timing of renal biopsy in relation to the onset of clinical symptoms and detection of urinary abnormalities (17, 18).

Table 3. Comparison of findings with other studies

	O Chen (6) (n=120)	Bagga (8) (n=47)	Kumar (7) (n=45)	Trapani S (10) (n=150)	Our study (n=23)
Setting	Pediatric Inpatient	Pediatric Inpatient	Rheumatology clinic	Pediatric Inpatient	Pediatric inpatient
Mean age (years)	6.6	8.5	7.6	6.1	9.4
Age range (years)	1-12	3-12	2.5-13	-	4-16
M:F ratio	1.9:1	2.6:1	2:1	1.8:1	1:1.9
Abdominal pain (%)	56.7	63.8	78	51	47.8
HSP nephritis (%)	54.5	51.1	31	54	47.8
Purupra (%)	100	95.6	100	100	100
Joint Pain (%)	65	46.8	60	15	52
Intussception (%)	0.8	2.1	2.2	-	4.3
No rash at presentation (%)	12.5	-	-	-	13

Early acute clinical phases of HSPN are characterized by mesangial and endocapillary hypercellularity, often with fibrinoid necrosis and small cellular crescents, whereas segmental sclerosis, mostly associated with fibrous crescents, is seen in advanced stages (17). The histologic lesions have been classified by the ISKDC into five classes (I, II, III, IV, and V) according to the presence and number of glomeruli involved with crescents being a pivotal feature. (17, 18) A membranoproliferative-like pattern is assigned to class VI. The risk of the development of chronic kidney disease (CKD) increases with the severity of the histologic lesions at presentation. (17) In the present series, 4 out of 7 cases with renal biopsy were in class II with one case each in class IIIa, IIIb, and VI. On immunofluorescence, the most characteristic finding includes predominant glomerular deposits of IgA. (17, 18) The typical immunofluorescence pattern is diffuse, granular mesangial staining with associated capillary wall staining in patients with endocapillary proliferation. IgG and/or IgM and fibrin-related antigens are also found in 65–75% of renal biopsy samples of HSPN. Complement components co-exist with immunoglobulins. (18) There is a strong association between histological parameters of increased severity of HSPN with extensive capillary IgA and complements deposits (18). In the present series, four cases had immunofluorescence done, which showed IgA deposits in mesangial distribution in all cases. Two out of 4 cases also had a capillary distribution of IgA due to the presence of endocapillary proliferation and crescent formation.

Abdominal pain was seen in 11 (47.6%) and joint pain in 12 (52%) children in the cases, which is consistent with most series. There was one case of intussusceptions that resolved spontaneously and did not require surgical intervention. The child was on prednisolone. Joint pain was usually polyarticular involving large joints of the upper and lower limbs. Joint involvement subsided with no residual injury.

Laboratory investigations showed a normal hemoglobin concentration with neutrophilic leucocytosis and a variable value of ESR, which were similar to findings described by Kawasaki et al (13). The platelket count was normal in all children. Other laboratory tests like ANA, C3, and anti-streptolysin-O (ASLO) are needed to rule out differential diagnoses on a case-by-case basis.

Conclusion

This is the first series from the northeastern part of India that documents certain peculiarities in the presentation. The main characteristics of the present series was a higher mean age at presentation, a female preponderance, intussusception resolving

spontaneously, the presence of a hypertensive emergency, and a high AKI rate, indicating wide spectrum of presentations in HSP. There was no mortality in the series but three (13%) children developed chronic residual renal disease.

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Conflict of Interest
The author declares no conflicts of interest.

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Ethics
Not declared.

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