Predictive Factor of Severe Renal Involvement in Children with Henoch-Schoenlein Purpura

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Objective: *To find out which of the clinical manifestations or laboratory findings is the predictive factor of severe renal involvement in children with Henoch-Schoenlein purpura (HSP).*
Material and Method: *Data of clinical manifestations and laboratory findings in children with HSP at Queen Sirikit National Institute of Child Health between January 2003-December2007 were prospectively collected and analyzed.*
Results: *There were 168 cases, 86 boys and 82 girls (M:F ratio= 1.05:1), the age ranged from 2 to 15 years (mean $\pm$ SD = 6.9 $\pm$ 2.6 years, mode = 6.8 years). Development of severe renal involvement was identified in 11 cases (6.6 %). Abnormal urinalysis (microscopic hematuria or proteinuria) on the day of diagnosis was statistically significant ($p < 0.001$) as a predictive factor of severe renal involvement during follow-up. Early systemic corticosteroid administration due to severe abdominal pain was not statistically significantly different between the patients with or without severe renal involvement.*
Conclusion: *Abnormal urinalysis on the day of diagnosis was the only predictive factor of severe renal involvement in children with Henoch-Schoenlein purpura. Early systemic corticosteroid administration due to severe abdominal pain did not prevent severe renal involvement.*

Keywords: *Henoch-Schoenlein purpura, Severe renal involvement*

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Henoch-Schoenlein purpura (HSP) is a small-vessel vasculitis that occurs primarily in childhood. It is characterized by non-thrombocytopenic palpable purpura in dependent areas, arthritis, abdominal pain, and renal involvement. Although the exact etiology remains largely unclear, its several potential etiologic agents include group A beta-hemolytic streptococci (GABHS), other bacterial or viral organisms, immunizations, and drugs[1]. The prognosis for most patients with HSP is excellent with full recovery and no permanent residua[2]. Severity of renal disease is the most important indicator of long-term prognosis[3,4]. Renal involvement may manifest with transient hematuria or proteinuria, nephritic or nephrotic syndrome or renal failure[5,6]. If the risk of renal involvement could be predicted by any initial clinical manifestations or laboratory findings at diagnosis, that evidence could be used to identify which children with HSP will need follow-up with close attention.

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Material and Method

The 1990 criteria of the American College of Rheumatology[7] were used to diagnose Henoch-Schoenlein purpura (HSP). The data of children with HSP at the first visit was prospectively collected using a structured clinical record form. The clinical manifestations included vital signs, palpable purpura, ecchymosis, hemorrhagic bullous lesion, subcutaneous edema, arthritis/arthralgia, and abdominal pain. The laboratory investigations included complete blood count (CBC), urinalysis (UA), erythrocyte sedimentation rate (ESR), BUN, creatinine, antistreptolysin O (ASO) titer and Mycoplasma titer. Abnormal urinalysis was defined as presence of either proteinuria $\geq$ 1+ or RBC $\geq$ 5 cells/field. The clinical features and urinalysis of all patients were followed-up

and monitored for severe renal involvement. Corticosteroid was administered to the patients with severe abdominal pain, severe skin lesions, evidence of bleeding at any organ, or severe renal involvement. Severe renal involvement defined as cases that developed massive proteinuria or nephrotic syndrome or hypertension or renal insufficiency. Each case was followed-up at 1, 2, 3, 6 and 12 months after the diagnosis.

Statistical Analysis

The statistical analysis in the present study were performed with SPSS (version 11.5 for Windows). The subjects' age was expressed as mean $\pm$ SD and mode. Comparative analysis of categorical variables to evaluate the predictive factor of severe renal involvement was performed using Fisher's exact test and the p-value < 0.05 was considered to indicate statistical significance.

Results

During January 2003 to December 2007, 168 cases of HSP were diagnosed at Queen Sirikit National Institute of Child Health. There were 86 boys and 82 girls (M:F ratio = 1.05: 1), the age ranged from 2 to 15 years (mean $\pm$ SD = 6.9 $\pm$ 2.6 years, mode = 6.8 years). One hundred and fifty-four cases (92%) were 2-10 years old with the peak at 4-8 years old (Fig. 1). There was a seasonal trend in rainy (July and August) and winter (December and January) seasons (Fig. 2). Palpable purpura was found in 100 % of the cases and the locations of palpable purpura were at legs, arms, buttocks and ears in 166 (98.8%), 62 (36.9%), 53 (31.6%) and 15 (8.9%) cases respectively. Ecchymosis, hemorrhagic bullous lesion and subcutaneous edema were detected in 20 (11.9%), 11 (6.6%) and 27 (16.1%) cases respectively. Severe abdominal pain and arthritis/arthralgia were presented in 90 (53.6%) and 78 (46.4%) cases respectively. The locations of arthritis/arthralgia were at ankle, knee and wrist in 70 (41.7%), 26 (15.5%), and 9 (5.4%) cases respectively.

Leucocytosis (WBC > 10,000 cells/cu mm) was found in 116 cases (69.1%). The ESR more than 20 mm/hr was found in 101 of 146 (69.7%) evaluated cases. The ASO titer was elevated in 70 cases (41.7%) and four-fold rising of Mycoplasma titer was detected in 9 cases (5.4%). Abnormal urinalysis (microscopic hematuria or proteinuria) on the day of diagnosis was found in 31 cases (18.5%).

One case was excluded from the present analysis due to severe renal involvement on the day of diagnosis. From the remaining 167 cases, severe renal involvement was identified in 11 cases (6.6%). Detailed clinical features on the day of diagnosis, onset of severe renal involvement, and renal manifestation of these 11 cases are presented in Table 1. The baseline clinical manifestations and laboratory tests of the patients to predict severe renal involvement are shown in Table 2. Abnormal urinalysis on the day of diagnosis was statistically significant ($p < 0.001$) as a predictive factor of severe renal involvement during follow-up. Ecchymosis, hemorrhagic bullous lesion, abdominal pain, arthritis/arthralgia, and ASO titer elevation were all not associated with the incidence of severe renal involvement. Early systemic corticosteroid was administered due to severe abdominal pain in 9 of 11 cases (81.8%) who developed severe renal involvement.

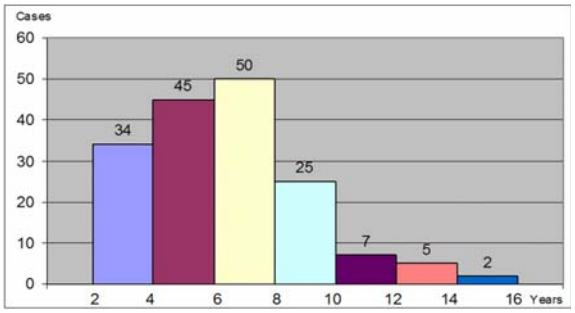

Fig. 1 Age distribution

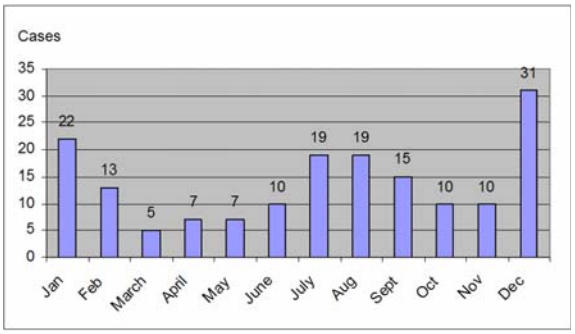

Fig. 2 Monthly distribution

Discussion

Abnormal urinalysis (microscopic hematuria or proteinuria) on the day of diagnosis was found in 18.5% of the 168 HSP patients. The authors found 11 cases (6.6%) developing severe renal involvement which is in accordance with other report[8]. Outi et al[9] reported the occurrence of nephritis in 46% of HSP

Table 1. Clinical features on the day of diagnosis of 11 patients with severe renal involvement

Case	Age (months)	Severe abdominal pain	Ecchymosis	Hemorrhagic bullous lesion	Abnormal Urinalysis*	Onset of severe renal involvement	Renal manifestation
1	36	+	-	-	-	1 month	- Massive proteinuria
2	40	+	+	-	Proteinuria 1+	1 month	- Massive proteinuria
3	52	+	-	-		1 month	- Massive proteinuria
4	57	+	+	-	Proteinuria 2+	3 days	- Massive hematuria - Hypertension
5	76	+	-	-	Proteinuria 2+ RBC 15-20	14 days	- Massive proteinuria - Massive hematuria
6	84	-	-	+	RBC 7-10	8 months	- Massive proteinuria
7	89	+	-	-	-	12 days	- Massive proteinuria
8	89	-	+	-	-	3 days	- Massive proteinuria
9	92	-	-	-	Proteinuria 2+	14 days	- Massive proteinuria
10	95	-	-	-	Proteinuria 1+	1 month	-Massive proteinuria - Massive hematuria
11	127	-	-	-	Proteinuria 1+	3 months	- Massive proteinuria - Hypertension

* Statistically significant ($p<0.001$) as a predictive factor of severe renal involvement

Table 2. Clinical manifestations ,laboratory tests , and corticosteroid treatment as predictive factors for the development of severe renal involvement

Predictive factors	Severe renal involvement (n = 11)	No severe renal involvement (n = 156)	p -value
Ecchymosis (n = 20)	3	17	0.10
Hemorrhagic bullous lesion (n = 11)	1	10	0.38
Severe abdominal pain (n = 90)	6	84	0.24
Arthritis/arthralgia (n = 78)	7	71	0.13
ASO titer elevation (n = 70)	4	66	0.23
Abnormal urinalysis (n = 31)	7	24	0.0001
Corticosteroid treatment (n = 102)	9	93	0.09

patients. Nachi[6] reported from systematic review that proteinuria and/or hematuria occurred in 34.2 % of these patients. Onset of severe renal involvement ranged from 3 days to 8 months, 5 cases (45.5%) within 2 weeks, 4 cases (36.4%) at 1 month, 1 case at 3 months and 1 case at 8 months.

There were various clinical manifestations in HSP patients. In the present study the authors found ecchymosis, hemorrhagic bullous lesion, subcutaneous edema, abdominal pain and arthritis/arthralgia in 11.9%, 6.6%, 16.1%, 53.6% and 46.4% respectively. Sticca et al[8] reported that the manifestations were palpable purpura (100%), articular (68%) and gastrointestinal involvement (32%).

HSP was often preceded by various bacterial, especially streptococcal and viral infections. We detected ASO elevation in 70 cases (41.7%) which was similar to another study[10]. Mycoplasma pneumonia infection was reported to be associated with HSP[11,12]. The authors detected four- fold rising of Mycoplasma titer in 9 cases (5.4%).

Other studies in the medical literature reported that the presence of severe abdominal pain at the start of the HSP clinical picture was associated with HSP nephritis[13-16]. In the present study the only prognostic factor predicting development of severe renal involvement in HSP according to Fisher's exact test was abnormal urinalysis at disease onset.

Nine of 11 cases (81.8%) who developed severe renal involvement had received systemic corticosteroid. This evidence demonstrated the trend that early corticosteroid administration did not prevent severe renal involvement which agreed with the previous reports[9,14,17].

Conclusion

Most HSP patients have excellent prognosis with full recovery and no permanent residue. Severity of renal disease is the most important indicator of long-term prognosis. In the present study the authors demonstrated that abnormal urinalysis at presentation is a predictive factor of severe renal involvement. The authors recommend to follow-up closely these patients especially in the first month after the onset of HSP and use urinalysis as a simple test to detect renal complication.

Potential conflicts of interest

None.

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ปัจจัยที่จะทำนายโรคไตชนิดรุนแรงในเด็กที่เป็น Henoch-Schoenlein purpura

วนิดา ลิ้มพงศานุรักษ์, ชูเกียรติ เกียรติขจรกุล, ศรีศุภลักษณ์ สิงคาลวณิช

วัตถุประสงค์*: เพื่อหาปัจจัยอาการทางคลินิกและผลการตรวจทางห้องปฏิบัติการเพื่อทำนายโรคไตชนิดรุนแรงในเด็กที่เป็น Henoch-Schoenlein purpura (HSP)*

วัสดุและวิธีการ*: เก็บรวบรวมข้อมูลอาการทางคลินิกและผลการตรวจทางห้องปฏิบัติการในเด็กที่ได้รับการวินิจฉัยเป็นโรค HSP ที่มารับการตรวจรักษาที่สถาบันสุขภาพเด็กแห่งชาติมหาราชินี ในช่วงระหว่างเดือนมกราคม พ.ศ. 2546 ถึง เดือนธันวาคม พ.ศ. 2550 นำมาวิเคราะห์ทางสถิติ*

ผลการศึกษา*: ในช่วงเวลาที่ทำการศึกษามีผู้ป่วยที่ได้รับการวินิจฉัยเป็น HSP จำนวน 168 ราย เป็นเด็กชาย 86 คน เด็กหญิง 82 คน (อัตราส่วน ชาย: หญิง = 1.05: 1.0) อายุระหว่าง 2-15 ปี (เฉลี่ย 6.9 ปี ค่าเบี่ยงเบนมาตรฐาน 2.6 ฐานนิยม 6.8 ปี) หลังการติดตามพบเด็กเป็นโรคไตชนิดรุนแรง 11 ราย (ร้อยละ 6.6) ผลการตรวจปัสสาวะที่ผิดปกติ (มีไข่ขาวหรือเม็ดเลือดแดง) ในวันที่วินิจฉัยโรคเป็นปัจจัยที่มีความสำคัญทางสถิติในการทำนายการที่จะเกิดโรคไตชนิดรุนแรง ($p < 0.001$) นอกจากนี้ยังพบว่าการให้สเตียรอยด์ตั้งแต่แรกในรายที่มีอาการปวดท้องไม่มีความแตกต่างกันทางสถิติในผู้ป่วยที่ไม่เกิดหรือเกิดโรคไตชนิดรุนแรง*

สรุป*: ผลการตรวจปัสสาวะที่ผิดปกติในวันที่วินิจฉัยโรคเป็นปัจจัยที่มีความสำคัญทางสถิติในการทำนายการที่จะเกิดโรคไตชนิดรุนแรงในเด็กที่เป็น Henoch-Schoenlein purpura การให้สเตียรอยด์ตั้งแต่แรกในรายที่มีอาการปวดท้องไม่สามารถป้องกันการเกิดโรคไตชนิดรุนแรงได้*