Henoch-Schonlein Purpura : Clinical Manifestations and Long-Term Outcomes in Thai Children

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Abstract

The clinical features of 47 children with Henoch-Schonlein purpura (HSP) are presented. The most common ages at presentation ranged from 3-5 years. Duration of data collection was 60 months. The peak incidence was from December to February. The organ involvements included skin (100%), gastrointestinal tract (74.5%), renal (46.8%) and joint (42.6%). Renal involvement was detected within the first 2 months in 16 cases (72.7%) but was delayed until 6 months after diagnosis in 6 cases. No risk factors for renal involvement could be identified. The mean duration of follow-up was 2.6 years (range 1-5 years). Six out of 16 (37.5%) patients had residual renal diseases but none were end stage. Recurrent episodes of abdominal pain and skin purpura were found in a few cases during the first year.

Overall prognosis of HSP is good and long-term morbidity is predominantly associated with renal involvement. Patients with initially normal urinalysis should have sequential urinary examination at least for 6 months.

Key word : Henoch-Schonlein Purpura, IgA Nephropathy, Nephrotic Syndrome, Proteinuria, Hypertension

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Henoch-Schonlein purpura (HSP) is the most common vasculitis disease of childhood. The incidence is 13.5-18 to 100,000 children per year[1,2]. Although multisystem involvement occurs in HSP, the long-term outcomes of patients are determined by the extent of renal involvement. Most patients have relatively mild diseases characterized by asymptomatic hematuria and resolve spontaneously. Some patients have severe renal diseases such as nephrotic syndrome. Progression to end stage renal diseases varies from 10-16 per cent[3,4]. Predictive factors of severe renal involvement in HSP are controversial and require more studies.

There is only one study on HSP in Thai children which focused on the clinical manifestations of HSP with particular emphasis on the cutaneous features but no report on long-term outcomes. This paper reports the epidemiologic data, clinical manifestations, treatment and outcomes of children with HSP at the period of 1-5 year follow-up.

PATIENTS AND METHOD

A retrospective cohort study was conducted. Children who were diagnosed with HSP from January 1995 to December 1999 were included in the study. The criteria for diagnosis of HSP were non-thrombocytopenic palpable purpura in conjunction with one or more manifestations of the following organs: gastrointestinal tract (GI), renal and joint. Demographic data such as age, sex, clinical manifestations, physical examinations, laboratory data and clinical courses of the diseases were collected. Patients who lost follow-up were called back for evaluation of symptoms, signs and urine analysis. Blood urea nitrogen and serum creatinine were evaluated in some patients if there were clinical indications.

Table 1. Age onset of Henoch-Schonlein purpura in 47 children.

Age (years)	Number	Percentage
0-2	3	6.4
3-5	21	44.7
6-8	15	31.9
9-11	3	6.4
12-14	5	10.6
Total	47	100

RESULTS

From a total of 52 patients with HSP, 47 (90.4%) medical records were available for reviewing. The ratio of male: female is 1.1:1. Their ages ranged from 1.6 to 14.7 years with the mean age of 6.3 years. The most common age group was 3-5 years

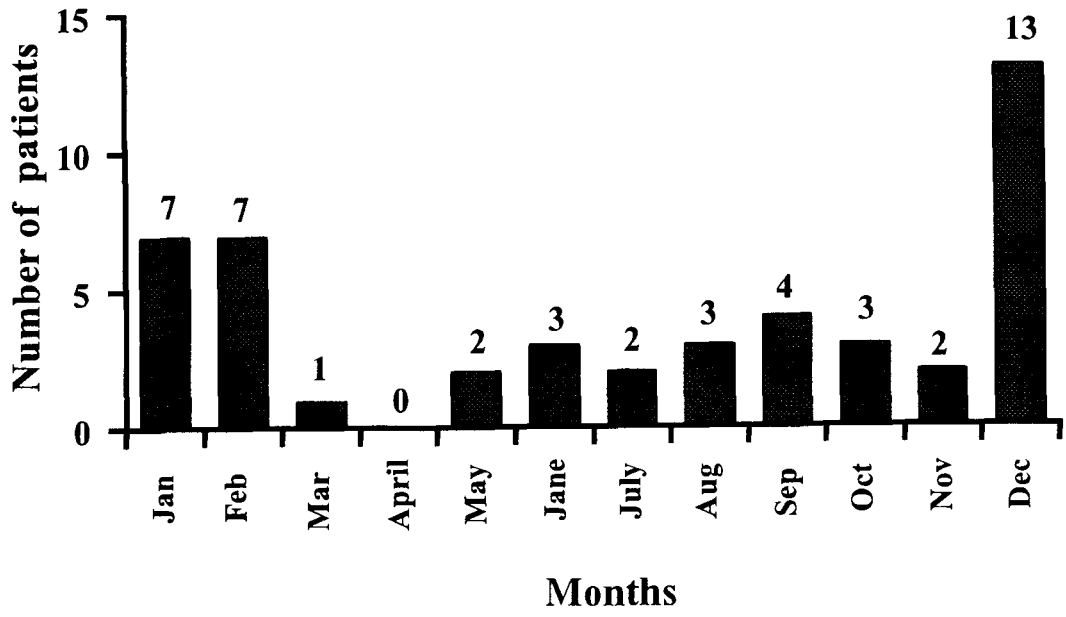

Fig. 1. Frequency of children with Henoch-Schonlein purpura by months from 1995 to 1999.

(44.6%) (Table 1). The majority of cases were diagnosed from December to February (Fig. 1). Twenty two patients (46.8%) had 2-organ involvement and 20 patients (42.6%) had 3-organ involvement. Only 5 patients (10.6%) had more than 3-organ involvement. Palpable purpura occurred in all cases. GI symptoms (74.5%) which included abdominal pain (63.8%), nausea and vomiting (42.6%) and hematochezia (23.4%), were the second most common manifestations (Table 2). Twenty two patients (46.8%) had renal involvement which included isolated hematuria (27.7%), hematuria with proteinuria (10.6%) and nephrotic syndrome with or without nephritis (8.5%). Arthralgia or arthritis occurred in 20 patients (42.6%) and involved ankle joints in 13 cases (27.7%), knee joints in 9 cases (19.1%), wrist joints in 4 cases (8.5%) and interphalangeal joints in 3 cases (6.4%).

In patients with abdominal pain, most episodes occurred 1-21 days after the appearance of skin purpura. Only 5 patients (16.7%) developed abdominal pain 3-30 days before the onset of skin purpura. Corticosteroid was given to patients with severe abdominal pain. Sixty per cent of patients with abdominal pain received corticosteroid and the mean duration of abdominal pain was 2.3 ± 1.7 weeks. Abdominal pain disappeared by 56.7 per cent, 73.3 per cent and 100 per cent within 1, 3 and 5 weeks, respectively. Recurrent abdominal pain occurred in 16.7 per cent during the first 4 months. None had recurrent abdominal pain after 1 year. The remainder did not receive corticosteroid and the mean duration of abdominal pain was 2 ± 1.7 weeks.

Skin purpura resolved by 70 per cent, 87.2 per cent and 100 per cent within 1, 3 and 5 weeks, respectively. One patient had recurrent palpable purpura without abdominal pain or arthralgia at 1 year after the onset of HSP.

Urinalysis was performed in all cases except one. Abnormal urinalysis was detected during the first 2 months of diagnosis in 16 cases (34.8%). During the first 6 months of diagnosis, 19 cases with initially normal urine findings had repeated urinalysis and abnormal findings were detected in 6 cases (31.6%). In those with late renal involvement, 2 patients had nephrotic syndrome, 1 patient had microscopic hematuria with moderate proteinuria and 3 patients had isolated microscopic hematuria.

The follow-up period ranged from 1-5 years (mean 2.7 ±1.4 years). Sixteen of 22 patients with nephritis had regular follow-up. The final outcomes were as follows: 10 patients (62.5%) had normal urinalysis and 6 (37.5%) had persistent renal diseases which were isolated hematuria in 4 cases and hematuria with moderate proteinuria in 2 cases. None had hypertension. Neither had abnormal serum creatinine nor end stage renal diseases. The other organ involvements were neither persistent nor recurrent.

All cases of nephrotic syndrome were treated with corticosteroid and combination therapy was required in 2 cases. (Table 3)

The possible predictive factors for renal involvement which were age more than 7 years, GI bleeding, persistent purpura, required corticosteroid therapy for GI symptoms were analyzed. None was statistically significance.

Table 2. Clinical manifestations of Henoch-Schonlein purpura in 47 children.

	Organ involvement Percentage	Number
Skin involvement	47	100
Palpable purpura	47	100
Edema	6	12.8
GI involvement	35	74.5
Abdominal pain	30	63.8
Nausea/vomiting	20	42.6
Hematochezia	11	23.4
Renal involvement	22	46.8
Isolated hematuria	13	27.7
Hematuria with proteinuria	5	10.6
Nephrotic syndrome	4	8.5
Arthralgia or arthritis	20	42.6

Table 3. Treatment and outcome of nephrotic syndrome with or without nephritis.

Age (years)	Sex	Treatment	Duration (months)	Outcome at 1 year
4.9	F	Prednisolone	8	Isolated microscopic hematuria
8.6	M	Prednisolone	6	Microscopic hematuria with moderate proteinuria
		Cyclophosphamide	3	
5.7	F	Prednisolone	4	Microscopic hematuria with moderate proteinuria
		Cyclophosphamide	16	
		Dipyridamole	16	
13.5	F	Prednisolone	8	Isolated microscopic hematuria
		Fish oil	6	

DISCUSSION

HSP is the most common vasculitis disorder in children. The most common age group is 3-5 years. The prevalence of disease in males and females was not different in the present study. In contrast, previous studies showed that HSP are more common in males[5,6]. The majority of the presented patients were in the age group of 3-5 years and 6-8 years. This is similar to other reports both in Thailand and other countries[7,8].

The occurrence of HSP has a seasonal variation, in all previously reported series, the majority occurred in winter and spring[9]. Most patients in this study developed disease from December to February which is the lowest temperature of the year in Thailand. This suggests that HSP may be a viral-associated disease.

The most common GI manifestation is abdominal pain[7,10-12]. The serious GI complications such as intussusception, perforation and massive GI bleeding may occur[13,14]. However, there was no serious complication in the present study. Interestingly, 16.7 per cent of the presented patients developed acute abdominal pain preceding the onset of palpable purpura and the duration may last up to 30 days. Saulsbury reported that 40 per cent of patients presented with abdominal pain or joint symptoms preceding the onset of skin purpura for a period ranging from 1 day to 2 weeks[10]. Therefore, physicians should be aware of this syndrome in children who present with arthralgia and acute abdominal pain. Careful observation for palpable pupura is crucial for the diagnosis of HSP.

For the duration of abdominal pain, most of the presented patients improved in 3 weeks and the longest duration was 5 weeks. None had recurrent abdominal pain after 1 year. A previous report showed that very few patients had recurrent abdominal pain after 1 year[15]. Comparison between patients treated *versus* untreated with corticosteroid, the durations of abdominal pain were not significantly different. However, severe cases of abdominal pain were likely to receive the treatment due to the limitations of retrospective study. The benefit of corticosteroid therapy for shortening the duration of abdominal pain is conclusive. It is possible that without corticosteriod therapy the duration of abdominal pain in severe cases may be prolonged.

HSP nephritis occurred in 46.8 per cent of the patients in this study. The majority of HSP nephritis were detected by urinalysis during the first 2 months after the onset of skin purpura. However, 6 patients developed renal involvement during 2-6 months after diagnosis and 2 of them had nephrotic syndrome. The authors suggest that repeated urinalysis is required for at least 6 months even in those with normal urinalysis initially.

Most patients had only microscopic hematuria. Nephrotic syndrome was less common in the present study. Goldstein et al[16] and Scharer et al [17] reported the prevalence of nephrotic syndrome in HSP being 50 per cent and 59 per cent, respectively. These may be due to racial variability, with a high incidence in Native Americans[18].

The predictive factor for renal involvement is unknown. Previous reports showed that age onset of more than 7 years, persistent purpura and decreased of Factor XIII activity were associated with renal involvement[19]. In the present study, no predictive factor for renal involvement could be identified. One possibility is due to the small number of patients.

Most patients had good long-term outcome. Sixteen of 22 (72.7%) cases with nephritis were followed-up. Urinalysis returned to normal in 10 cases, but remained abnormal in 6 cases, of which 4 had isolated microscopic hematuria and 2 had persistent hematuria with moderate proteinuria. Interestingly, Goldstein et al studied the long-term outcome (mean 23.4 years) and found that although all patients had normal kidney function at 1 year, 44 per cent of the patients with nephrotic syndrome developed renal insufficiency later[16]. Due to a shorter follow-up period in the present study, renal impairment was not found. Hence, long-term sequential evaluations are required for early detection and intervention.

To date, standard treatment for HSP nephritis has not been established. However, therapy with corticosteroid and other immunosuppressive drugs may improve renal pathology[20-23]. Treatment and outcome of 4 patients with nephritic syndrome are summarized in Table 3. All of them had an improvement in renal manifestation. Further study is required for the evaluation of the outcome of these treatment regimens.

SUMMARY

HSP is a common disease in young children. In Thailand, the peak incidence occurs from December to February and multisystem involvements are common. Corticosteroid therapy may be required in some cases with severe abdominal pain and nephrotic syndrome. Renal involvement is not uncommon. Most cases presented in the first 2 months, but the presentation may be delayed until 6 months after the onset of skin purpura. Urinalysis in HSP patients should be intermittently repeated at least for 6 months. Isolated hematuria is the most common presentation in HSP nephritis. After 1-5 years follow-up, persistent renal diseases can be found in one-third of patients with HSP nephritis.

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REFERENCES

1. Stewart M, Savage Jm, Bell B, McCord B. Long-term renal prognosis of Henoch-Schonlein purpura in an unselected childhood population. Eur J Pediatr 1988; 147: 113-5.
2. Nielsen HE. Epidemiology of Schonlein-Henoch purpura. Acta Paediatr Scand 1988; 77: 125-31.
3. Yoshikawa N, Ito H, Yoshiya K, et al. Henoch-Schonlein nephritis and IgA nephropathy in children: A comparison of clinical course. Clin Nephrol 1987; 27: 233-7.
4. Coppo R, Mazzucco G, Cagnoli L, Lupo A, Schena FP. Long-term prognosis of Henoch-Schonlein nephritis in adults and children. Nephrol Dial Transplant 1997;12: 2277-83.
5. Robson WL, Leung AK. Henoch-Schonlein purpura. Adv Pediatr 1994; 41: 163-94.
6. Meadow SR, Glasgow EF, White RH, Moncrieff MW, Cameron JS, Ogg CS. Schonlein-Henoch nephritis. Q J Med 1972; 41: 241-58.
7. Wananukul S, Watana D, Pongprasit P. Henoch-Schonlein purpura in Thailand: Review of 41 children. J Med Assoc Thai 1997; 80: 686-92.
8. Wedgwood RJP, Klaus MH. Anaphylactoid purpura (Schonlein-Henoch Syndrome): A long-term follow-up study with special reference to renal involvement. Pediatric 1955; 16: 196-206.
9. Farley TA, Gillespie S, Rasoulpour M, Tolentino N, Hadler JL, Hurwitz E. Epidemiology of a cluster of Henoch-Schonlein purpura. Am J Dis Child 1989; 143: 798-803.
10. Saulsbury FT. Henoch-Schonlein purpura. Pediatr Dermatol 1984; 1: 195-201.
11. Nussinovitch M, Prais D, Finkelstein Y, Varsano I. Cutaneous manifestations of Henoch-Schonlein purpura in young children. Pediatr Dermatol 1998; 15: 426-8.
12. Kumar L, Singh S, Goraya JS, et al. Henoch-Schonlein purpura : The Chandigarh experience. Indian Pediatr 1998; 35: 19-25.
13. Martinez-Frontanilla LA, Haase GM, Ernster JA, Bailey WC. Surgical complications in Henoch-Schonlein purpura. J Pediatr Surg 1984; 19: 434-6.
14. Choong CK, Beasley SW. Intra-abdominal manifestations of Henoch-Schonlein purpura. J Paediatr Child Health 1998; 34: 405-9.
15. Nathan K, Gunasekaran TS, Berman JH. Recurrent gastrointestinal Henoch-Schonlein purpura. J Clin Gastroenterol 1999; 29: 86-9.
16. Goldstein AR, White RH, Akuse R, Chantler C. Long-term follow-up of childhood Henoch-Schon-

lein purpura nephritis. Lancet 1992; 339: 280-2.
17. Scharer K, Krmar R, Querfeld U, Ruder H, Waldherr R, Schaefer F. Clinical outcome of Schonlein-Henoch purpura nephritis in children. Pediatr Nephrol 1999; 13: 816-23.
18. Smith SM, Tung KS. Incidence of IgA-related nephritides in American Indians in New Mexico. Hum Pathol 1985; 16: 181-4.
19. Kaku Y, Nohara K, Honda S. Renal involvement in Henoch-Schonlein purpura: A multivariate analysis of prognostic factors. Kidney Int 1998; 53: 1755-9.
20. Bergstein J, Leiser J, Andreoli SP. Response of crescentic Henoch-Schonlein purpura nephritis to corticosteroid and azathioprine therapy. Clin Nephrol 1998: 49: 9-14.
21. Oner A, Tinaztepe K, Erdogan O. The effect of triple therapy on rapidly progressive type of Henoch-Schonlein nephritis. Pediatr Nephrol 1995; 9: 6-10.
22. Niaudet P and Habib R. Methylprednisolone pulse therapy in the treatment of severe forms of Henoch-Schonlein purpura nephritis. Pediatr Nephrol 1998; 12: 238-43.
23. Iijima K, Ito-Kariya S, Nakamura H, Yoshikawa N. Multiple combined therapy for severe Henoch-Schonlein nephritis in children. Pediatr Nephrol 1998; 12: 244-8.

Henoch–Schonlein Purpura : อาการแสดงและการติดตามผลระยะยาวในผู้ป่วยเด็กไทย

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การศึกษานี้ได้รวบรวมข้อมูล ผู้ป่วยอายุน้อยกว่า 15 ปี ที่ได้รับวินิจฉัยว่าเป็นโรค Henoch–Schonlein purpura (HSP) ที่คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี ตั้งแต่เดือนมกราคม 2538 ถึงเดือนธันวาคม 2542 โดยเก็บข้อมูลในคนไข้ 47 คน พบว่า ช่วงอายุที่เป็นมากที่สุดคือ 3–5 ปี และเป็นช่วงเดือนธันวาคม ถึงเดือนกุมภาพันธ์ มากที่สุด อาการและอาการแสดงที่พบได้แก่ อาการทางผิวหนังร้อยละ 100 อาการทางระบบทางเดินอาหารร้อยละ 74.5 อาการทางไตร้อยละ 46.8 และอาการทางข้อร้อยละ 42.6 ความผิดปกติทางไตส่วนใหญ่ 16 ราย (ร้อยละ 72.7) ตรวจพบตั้งแต่ 2 เดือนแรก แต่ในผู้ป่วย 6 ราย ความผิดปกติทางไตสามารถตรวจพบได้หลังจากวินิจฉัยโรค HSP นาน 2–6 เดือน เมื่อติดตามผู้ป่วยเป็นเวลานานเฉลี่ย 2.6 ปีจำนวน 16 ราย พบว่ายังตรวจพบความผิดปกติทางไต 6 ราย คิดเป็นร้อยละ 37.5 โดยไม่มีผู้ใดเป็นโรคไตระยะสุดท้าย

กล่าวโดยสรุป การพยากรณ์โรค HSP ขึ้นกับอาการและความผิดปกติทางไตเป็นหลัก ผู้ป่วยที่มีความผิดปกติทางไตควรได้รับการติดตามระยะยาวและผู้ป่วยที่ผลการตรวจปัสสาวะปกติในระยะแรกก็ควรได้รับการติดตามตรวจปัสสาวะต่อเนื่องอย่างน้อย 6 เดือน

คำสำคัญ : Henoch–Schonlein purpura, ไตอักเสบชนิด Ig A, โรคไตเนโฟรติก, โปรตีนในปัสสาวะ, แรงดันโลหิตสูง

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