

Case Report

Henoch-Schönlein without Purpura: A Case Report and Review Literature

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Henoch-Schönlein purpura (HSP) is a multi-organ vasculitis involving skin, joints, gastrointestinal tract, and kidneys. The present study reported a 5-year-old boy presenting with intense abdominal pain, bloody diarrhea, and protein-losing enteropathy. Investigations for infectious enteritis were negative. Esophagogastroduodenoscopy showed swelling and erythematous mucosa with hemorrhagic spots at duodenal bulb to the third part of duodenum. Histopathology of endoscopic biopsies revealed non-specific duodenitis. HSP was suspected, based on duodenitis and the presence of inflammatory markers without identifiable causes. Corticosteroid was started resulting in marked improvement of his clinical symptoms. Two weeks later, he developed nephrotic-range proteinuria, thus kidney biopsy was performed. Renal histology was consistent with IgA nephropathy, supporting the diagnosis of HSP. This report emphasizes that patients with HSP may not always show visible purpura, and the diagnosis requires a high index of suspicion. GI endoscopy and renal biopsy may be helpful for the diagnosis in selected patients presenting with atypical presentations.

Keywords: Abdominal pain, Gastrointestinal hemorrhage, Henoch-Schönlein purpura, IgA nephropathy, Vasculitis

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Henoch-Schönlein purpura (HSP) is the most common immune complex-mediated vasculitis in childhood that results in multi-organ involvement. The European League against Rheumatism and Pediatric Rheumatology European Society (EULAR/PReS) defined the diagnostic criteria composed of skin purpura and one of the following: diffuse abdominal pain, any biopsy showing predominant IgA deposition, arthritis or arthralgia, and renal involvement⁽¹⁾. Thus, the presence of palpable purpura or petechiae is mandatory for the diagnosis of HSP. However, there have been some reports of the patients presented with gastrointestinal (GI) involvement without purpura^(2,3). This could be an atypical form of HSP. The present study report a young child presented with GI and renal involvement of HSP without purpura.

Case Report

A previously healthy 5-year-old boy presented with colicky abdominal pain, vomiting, and watery diarrhea for 8 days. He was admitted to the hospital,

and antibiotics were given intravenously for suspected infective colitis. Seven days after admission, he developed bloody diarrhea and was referred to our hospital. He had no history of drug use or significant underlying disease. Physical examination revealed normal body weight (17.2 kg, 25th percentile) and height (115 cm, 90th percentile). Vital signs showed body temperature 37.8°C, pulse rate 130/minute, and blood pressure 118/82 mmHg. There were puffy eyelids without pallor. Abdominal examination revealed mild tenderness at left para-umbilical area, without abdominal distention or hepatosplenomegaly. No skin rash or purpura was observed.

Laboratory investigations showed hemoglobin 13.4 g/dL, hematocrit 40%, white blood cells (WBC) 43,000/mm³ (87% neutrophil), and platelets 632,000/mm³. Serum urea nitrogen, creatinine, and liver profiles were normal except albumin of 14.7 g/L (normal 35-45 g/L). Other blood tests showed C-reactive protein (CRP) of 45.9 mg/L (normal <5 mg/L), complement C3 level of 518 µg/mL (normal 900-1,800 µg/mL) and C4 of 83.1 µg/mL (normal 100-400 µg/mL). Antistreptolysin-O titer, antinuclear antibodies, and anti-double-stranded DNA were negative. Urinalysis showed WBC 3-5/HPF, red blood cells (RBC) 5 to 10/HPF, and proteinuria 3+. A 24-hour urine protein was 35 mg/m²/hour. Stool examination showed numerous RBC with moderate

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WBC but no parasite or ova was found. Stool culture was negative for enteric pathogens. Protein losing enteropathy was demonstrated by fecal alpha-1 antitrypsin of 36.3 mg/dL (normal 0.25-5.3 mg/dL). A computed tomography scan of the whole abdomen showed dilated entire colon without evidence of bowel wall thickening or gut obstruction.

An esophagogastroduodenoscopy showed generalized swelling, erythematous mucosa, and hemorrhagic spots at the duodenal bulb to the third part of duodenum. Macroscopic and microscopic examinations of the colonoscopy were unremarkable. Histopathology showed mild active duodenitis without vasculitis and was otherwise unremarkable. The immunohistochemistry revealed no IgA deposit in the capillary wall.

He continued to have intense abdominal pain, bloody diarrhea, and anemia requiring blood transfusion despite intravenous antibiotic therapy. Duodenitis in combination with inflammatory markers including high CRP, leukocytosis, and thrombocytosis without identifiable causes, suggested a diagnosis of HSP. Intravenous methylprednisolone (2 mg/kg/day) was started on the third day of admission. Abdominal pain and bloody diarrhea improved significantly following three days of methylprednisolone, and CRP decreased to 9 mg/L. Then, treatment was continued with oral prednisolone. He stayed in the hospital for 13 days.

Two weeks later at the outpatient follow-up visit, his urinalysis showed proteinuria 3+ with WBC >20/HPF and numerous dysmorphic RBC. A 24-hour urine protein was 79 mg/m²/hour, which was in the nephrotic range. A kidney biopsy showed focal endocapillary proliferation with moderate mesangial hypertrophy. The immunofluorescence stain revealed IgA and fibrinogen deposition in the mesangium, which were compatible with IgA nephropathy (Fig. 1). Electron dense deposits were identified in the mesangium on the electron microscopy. According to the renal histology and GI involvement, the diagnosis of HSP was made. His renal disease resolved following 5 months of oral prednisolone therapy. Skin rash had never been observed during 12-month follow-up.

Discussion

HSP or IgA vasculitis is characterized by IgA1-dominant immune deposition in the small vessels and often involves the skin, joints, GI tract, and kidneys⁽⁴⁾. Our previous study in 47 children with HSP showed that 83% presented with abdominal pain occurred following purpura with an interval of one to

21 days and 17% had abdominal pain before purpura with an interval of three to 30 days⁽⁵⁾. According to the EULAR/PRES criteria 2006, the presence of skin purpura or petechiae is mandatory for diagnosis of HSP⁽¹⁾. Our patient had two main clinical features, GI and renal involvement, which are compatible with HSP. Differential diagnoses include other systemic vasculitis and severe gastrointestinal infection. Based on the finding of mesangial IgA deposition on renal histology, while excluding enteric pathogens, the most likely diagnosis in this patient was HSP; although there was no rash during his clinical course.

HSP without purpura or HSP variant has been described. Gunasekaran et al reported three children presented with acute colicky abdominal pain and endoscopic findings of duodenojejunitis predominantly at the descending duodenum with additional laboratory results supporting HSP diagnosis⁽³⁾. The authors proposed that duodenojejunitis could be the primary manifestation of HSP, even in the absence of the characteristic purpura. Another study from Japan reported nine children with gastroduodenitis with clinical characteristics and endoscopic findings mimicking HSP without skin rash⁽²⁾. The authors reported that characteristic IgA deposition, particularly IgA1, in the capillaries in lamina propria was found in six patients, which was similar to another report⁽⁶⁾. They also demonstrated the proportion of IgA deposition was higher in patients who had HSP without rash as compare to the control group who had various gastrointestinal disorders (64% vs. 9%)⁽⁶⁾.

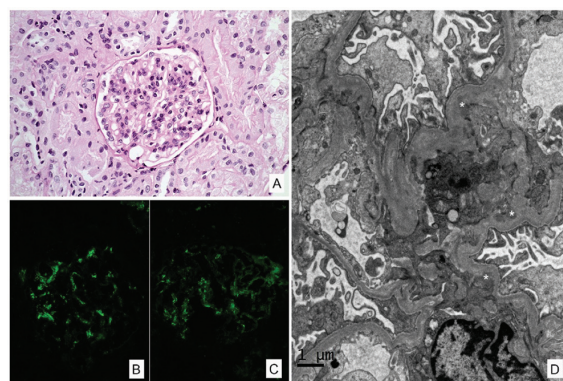


Fig. 1 Histopathology of kidney biopsy. (A) The glomerulus showed mesangial hyperplasia with occasional leukocytes (PAS x400). Fluorescent microscopy demonstrated IgA (B) and fibrinogen (C) staining in the mesangium. (FITC x400). (D) Dense deposits (*) were identified in the mesangium (TEM x8,000).

Table 1. Summarized features of reported cases of Henoch-Schönlein purpura without rash

Author, year	n	Age (year)	GI manifestations	Other systemic symptoms	GI lesions and evidences supporting diagnosis	Response to glucocorticoid
Gunasekatan et al. ⁽³⁾ , 2000	3	7-9	Acute colicky abdominal pain, vomiting, diarrhea	Not mentioned	Duodenojejunitis predominantly descending part of duodenum Absent serum F XIII activity and high serum IgA level	Prompt recovery within 48 hours
Kato et al. ⁽²⁾ , 2004	9	3-12	Abdominal pain, hematemesis, hematochezia	Joint pain (2), renal disease (2) (hematuria, NS)	Duodenitis, predominantly distal part of duodenum IgA deposition in duodenal biopsy	3 patients who received glucocorticoid responded well
Nakamura et al. ⁽⁷⁾ , 2010	1	61	Intermittent abdominal pain, bloody diarrhea	NS with subsequent acute renal failure	Ulcers at terminal ileum with active bleeding IgA deposition in surgically resected ileum and kidney biopsy	Effective
The present study	1	5	Colicky abdominal pain, bloody diarrhea, protein losing enteropathy	Nephrotic range proteinuria	Duodenitis IgA deposition in kidney biopsy	Prompt recovery within 72 hours

F = factor; GI = gastrointestinal; IgA = immunoglobulin A; NS = nephrotic syndrome

Nakamura et al reported a 61-year-old Japanese patient with massive intestinal bleeding and acute renal failure. Further investigations demonstrated ulcers at the terminal ileum with active bleeding requiring surgical resection⁽⁷⁾. Histological examination revealed IgA and C3 in the small vessels of intestine and renal mesangium. Although skin rash was absent, the authors stated that IgA-related enteropathy could be a subclass of HSP. To our knowledge, only few cases of HSP without purpura were reported in English literature and were summarized in Table 1.

GI involvement is common in children with HSP (51-74%)⁽⁸⁾. The symptoms include nausea, vomiting, abdominal pain, and hemorrhage. GI hemorrhage was reported in 8 to 18% of patients with massive hemorrhage in 2%^(9,10). Hypoalbuminemia without evidence of significant renal loss is caused by intestinal protein loss due to mucosal injury, even without abdominal symptoms⁽¹⁰⁾. Protein losing enteropathy occurs in 3% of patients in a large pediatric report from Finland⁽¹⁰⁾. The reported endoscopic findings of HSP vary from erythema, edema, erosion, and ulcers to submucosal hematoma^(2,3,11). Lesions are commonly found at small intestine (91%), particularly descending duodenum (64%). Other sites include stomach (70%), terminal ileum (50%), and colon (60%)⁽¹¹⁾. Most histologic studies showed nonspecific inflammation^(8,11). Evidence of vasculitis in the intestinal mucosa is likely to be found in those who have multiple ulcers and hematoma-like protrusions⁽⁸⁾. Immunohistochemistry may be helpful in distinguishing HSP from other causes of GI inflammation. Our patient

presented with abdominal pain, bloody diarrhea, and protein losing enteropathy. Endoscopic findings of duodenitis with hemorrhagic spots, and histology of nonspecific inflammation not compatible with other causes, made HSP more likely. Vasculitis and IgA deposition in the duodenal biopsy could not be demonstrated in our patient, the findings were consistent with previous report that the positivity of IgA deposition is low in the duodenal endoscopic biopsies, even with macroscopic abnormality⁽⁶⁾.

Nephritis occurs in 30 to 50% of HSP patients^(12,13). The severity of HSP nephritis (HSPN) range from isolated hematuria and/or proteinuria to acute nephritis and/or nephrotic syndrome⁽¹⁴⁾. Interval urinalysis is recommended for six months after the disease onset⁽¹⁴⁾. Severe abdominal pain, older age at onset, persistent purpura, and recurrence of disease are risk factors described in previous reports^(13,15). Demonstration of IgA deposition in the renal mesangium is the hallmark of HSPN as well as IgA nephropathy (IgAN). The two diseases are believed to share same pathogenic mechanism⁽¹⁶⁾. However, they have different clinical presentations and outcomes. HSPN presents at a younger age with more extra-renal manifestations but has favorable renal outcome compare to IgAN^(16,17). Moreover, severe GI symptoms such as bloody diarrhea and protein losing enteropathy, like in our patient, are unlikely in IgAN⁽¹⁷⁾. Secondary forms of IgAN, such as Crohn's disease, celiac disease, lymphoproliferative disorders, and drug-induced, have been described but they rarely reported to cause urinary or renal function abnormalities⁽¹⁶⁾.

Hypocomplementemia has been reported in 6 to 15%⁽¹⁸⁾. This phenomenon is transient and not relate to disease severity. The patient's complement level return to normal within four weeks, similar to previous studies. There was no evidence of other emerging autoimmune diseases during 12-month follow-up.

In conclusion, the present report emphasizes that patients with HSP may not always show visible purpura and the diagnosis requires high index of suspicion. GI endoscopy and renal biopsy may be helpful for the diagnosis in patients presenting with atypical presentations.

What is already known on this topic?

1. HSP is the most common immune complex-mediated vasculitis in childhood. It involves multi-organ system including skin, joints, GI tract, and kidney.

2. The diagnosis of HSP generally requires the presence of purpura.

3. HSP patients can present with GI involvement before the presence of purpura.

What this study adds?

1. Patients with HSP may not always show purpura.

2. HSP should be considered in patients who present with unexplained gastrointestinal symptoms despite of absence of purpura.

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Potential conflicts of interest

None.

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โรค *Henoch-Schönlein* ที่ไม่แสดงอาการผื่น: รายงานผู้ป่วยและทบทวนวรรณกรรม

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Henoch-Schönlein purpura (HSP) เป็นโรคที่มีอาการแสดงหลายระบบ ได้แก่ ผิวน้ำขุ่น ข้อ ทางเดินอาหาร และไต รายงานผู้ป่วยนี้ รายงานผู้ป่วยเด็ก อายุ 5 ปี ที่มีอาการปวดท้องรุนแรง ท้องร่วง ถ่ายอุจจาระเป็นเลือดร่วมกับมีโปรตีนรั่วทางอุจจาระ การตรวจทางห้องปฏิบัติการอื่น ๆ ไม่พบหลักฐานการติดเชื้อที่ล่าช้า การส่องกล้องตรวจทางเดินอาหารส่วนบนและล่างพบลำไส้เล็กส่วนต้นบวมแดง และมีจุดเลือดออก ผลตรวจจุลพยาธิวิทยาพบการอักเสบของคูโอดินัมแบบไม่จำเพาะ การวินิจฉัยเบื้องต้น คือ *HSP* เนื่องจากมีอาการทางเดินอาหารและคูโอดินัมอักเสบ ร่วมกับหลักฐานของการอักเสบในร่างกาย ได้แก่ ค่า *C-reactive protein* ในเลือดสูง ภาวะเม็ดเลือดขาวและเกล็ดเลือดสูง โดยตรวจไม่พบสาเหตุอื่น ผู้ป่วยจึงได้รับการรักษาด้วยยาคอร์ติโคสเตียรอยด์ ทำให้อาการปวดท้องดีขึ้นมาก และอาการถ่ายอุจจาระเป็นเลือดหายไป ในเวลาต่อมาตรวจพบว่า ผู้ป่วยมีโปรตีนไข่ขาวรั่วในปัสสาวะร่วมด้วย จึงได้รับการตัดชิ้นเนื้อไตเพื่อหาสาเหตุ และผลจุลพยาธิวิทยาของไตเข้าได้กับ *IgA nephropathy* จึงเป็นการสนับสนุนการวินิจฉัยโรค *HSP* รายงานผู้ป่วยนี้แสดงให้เห็นว่า ผู้ป่วย *HSP* อาจไม่แสดงอาการผื่น นอกจากนี้ การส่องกล้องทางเดินอาหาร และการตรวจชิ้นเนื้อไตอาจมีประโยชน์ช่วยยืนยันการวินิจฉัยในผู้ป่วยที่มีอาการสงสัยโรคนี้ แต่อาการทางคลินิกยังไม่ครบตามเกณฑ์การวินิจฉัย