

Endoscopic and microscopic findings of gastrointestinal tract in Henoch–Schönlein purpura

Single institute experience with review of literature

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Abstract

Asia has the highest incidence of Henoch–Schönlein purpura (HSP). Although 50% to 75% of patients with HSP manifest gastrointestinal (GI) symptoms, endoscopic, and pathologic findings of HSP have been rarely reviewed in Asia.

Patients diagnosed with HSP who had undergone endoscopic biopsy from GI tract (GIT) in Soonchunhyang University Seoul Hospital from 2000 to 2018 were evaluated and 25 cases with 44 biopsies from upper GI tract (U-GIT) or lower GI tract (L-GIT) were enrolled. Their clinical and endoscopic findings and histologic findings of endoscopic biopsy were reviewed.

Of the 25 patients, 15 were males and 10 were females. There were 6 children and 19 adults. The most common GI symptom was abdominal pain (20/25), followed by loose stool or diarrhea (9/25). Biopsied sites included 19 from U-GIT (9 stomach and 10 duodenum) and 25 from L-GIT (7 terminal ileum, 1 cecum, 4 ascending, 1 transverse, 2 descending, 7 sigmoid, and 3 rectum). Erythema/petechia was the most common endoscopic finding in U-GIT, while erosion/ulceration was the most common one in L-GIT. In U-GIT, extravasted red blood cell (RBC) (14/19) was the most common histologic finding, while leukocytoclastic vasculitis (LCV)/capillarities were identified in 7 specimens, including 5 duodenum samples. In endoscopic investigations of L-GIT, erosion/ulceration (9/14) was predominantly identified. The most common histologic finding was also extravasted RBC (22/25), while LCV/capillarities were noted in 10 specimens, including 5 specimens from terminal ileum.

The HSP commonly involves GIT. Histologic findings of our cases were not significantly different from results of previous studies in Western countries. However, endoscopic and pathologic characteristics of HSP have been rarely reviewed in Asia. Herein, we share experience of endoscopic biopsy of GIT in patients with HSP.

Abbreviations: EGD = esophagogastroduodenoscopy, EULAR = European League Against Rheumatism, GI = gastrointestinal, GIT = gastrointestinal tract, HSP = Henoch–Schönlein purpura, LCV = leukocytoclastic vasculitis, L-GIT = lower gastrointestinal tract, U-GIT = upper gastrointestinal tract.

Keywords: endoscopy, Henoch–Schönlein purpura, histology, leukocytoclastic vasculitis

1. Introduction

Henoch–Schönlein purpura (HSP) is a small-vessel vasculitis that affects both children and adults. It involves small vessels of the skin, joints, gastrointestinal tract (GIT), and kidney. Diagnosis of HSP is made when patients complain purpura or petechiae of the

skin with at least one of the following criteria: abdominal pain, histopathologically proven IgA vasculitis, arthritis or arthralgia, and renal involvement according to 2010 European League Against Rheumatism (EULAR) criteria.^[1] GI symptoms can occur in 50% to 85% of patients with HSP.^[2] Although GI symptoms include acute abdominal pain, nausea, vomiting, hematochezia or melena, and diarrhea, not every HSP patient receives endoscopic evaluation. Endoscopic evaluations are performed when patients complain severe GI symptoms or when the GI manifestations are suspicious of infectious/inflammatory etiology or when patients are suspected of HSP without skin manifestations.

Despite high incidence of HSP in Asia,^[3] the study for endoscopic and pathologic characteristics of HSP have been rarely reviewed in Asia. Therefore, we share our experience for endoscopic and its pathologic findings of GIT in patients with HSP.

2. Materials and methods

We retrieved 25 cases of HSP with 44 GIT endoscopic biopsies from archives of the Department of Pathology and Gastroenterology at Soonchunhyang University Seoul Hospital from January

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Table 1
Summarization of demographic characteristics of patients with Henoch–Schönlein purpura involving gastrointestinal tract.

	No. of patients (%)
Age, yr	
Children (≤ 18)	6 (24%)
Adults (> 18)	19 (76%)
Sex	
Male	15 (60%)
Female	10 (40%)
Endoscopy	
Upper gastrointestinal tract	17 (68%)
Lower gastrointestinal tract	14 (56%)
Kidney biopsy	6 (24%)
Leukocytoclastic vasculitis or Proliferative glomerulonephritis with IgA deposit	6
Skin biopsy	13 (52%)
Leukocytoclastic vasculitis	12
Others	1
Total	25 (100%)

1, 2000 to May 5, 2018. Search terms of “HSP,” “IgA vasculitis,” “esophagogastroduodenoscopy (EGD),” “colonoscopy,” and “biopsy” were used. A total of 44 biopsied specimens from these 25 patients with HSP were collected. Their clinical data such as age, sex, symptoms, and endoscopic findings were obtained from electronic medical records. Microscopic findings of biopsied slides were also reviewed. The Research Ethics Committee at the Soonchunhyang University Seoul Hospital approved the study (IRB No: 2018-08-009-001).

3. Results

We identified 25 patients who fulfilled the EULAR criteria of HSP and underwent GI endoscopic investigations (Table 1). These patients include 15 males and 10 females. There were 6 children and 19 adults.

The most common GI symptom was abdominal pain (20/25), followed by loose stool/diarrhea (9/25), nausea/vomiting (7/25), hemochezia (3/25), and melena (3/25). Seventeen patients underwent U-GIT investigations with EGD. Fourteen patients underwent L-GIT investigations with colonoscopy. Six patients were received both evaluations. Of the total of 44 biopsied specimens, 19 were from U-GIT and 25 were from L-GIT (Table 2). Of the 19 biopsied specimens from U-GIT, 9 were

Table 2
Composition of biopsy sites.

	No. of biopsied specimens
Upper gastrointestinal tract (n=19)	
Stomach	9
Duodenum	10
Lower gastrointestinal tract (n=25)	
Terminal ileum	7
Cecum	1
Ascending colon	4
Transverse colon	1
Descending colon	2
Sigmoid colon	7
Rectum	3
Total	44

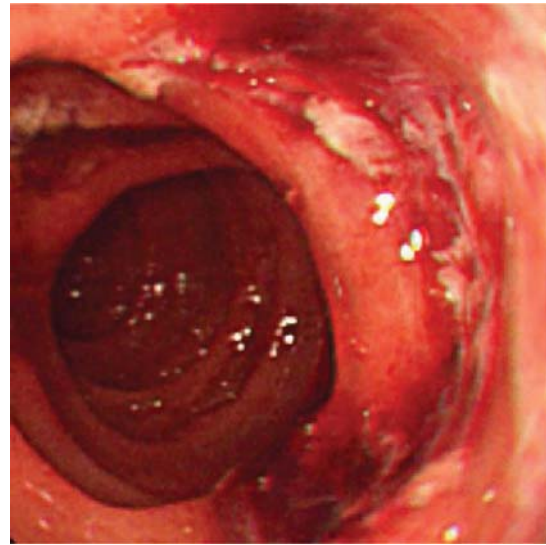


Figure 1. Esophagogastroduodenoscopy shows erosive lesion with erythematous change covered with inflammatory exudates in the duodenum.

stomach specimens and 10 were duodenum specimens. Specimens from L-GIT (n=25) included 7 terminal ileum, 1 cecum, 4 ascending colon, 1 transverse colon, 2 descending colon, 7 sigmoid colon, and 3 rectum specimens. Nine patients showed involvement of multiple GIT sites and 6 of them had both U-GIT and L-GIT specimens. The most commonly biopsied site was the duodenum (10/25) in U-GIT and sigmoid colon (7/25) in L-GIT.

The EGD findings of U-GIT included erythema/petechiae (11/17) (Fig. 1), erosion/ulceration (10/17), edema (2/17), atrophy (1/17), and hemorrhage (1/17). Early gastric cancer was incidentally found in 1 patient (Table 3). Colonoscopic findings included erosion/ulceration (9/14) (Fig. 2), erythema/petechiae (7/14), edema (2/14), vascular ectasia (2/14), vascular eruption (1/14), hemorrhage (1/14), and unremarkable endoscopic finding (1/14) (Table 4).

Extravasated red blood cells (RBCs) (14/19) were the most common histologic findings of U-GIT. Leukocytoclastic vasculitis (LCV)/capillarities were observed in 7 specimens (Fig. 3, Table 5). Other findings were edema (10/19), erosion/ulceration (8/19), fibrin exudates in lamina propria (4/19), and lymphangiectasia or dilated lymphatics (4/19). These 19 specimens were classified into 3 groups according to the severity of inflammation: 6 mild, 6 moderate, and 7 severe inflammation. Histologic findings of L-GIT included extravasated RBCs (22/25), edema (14/25), erosion/ulceration (10/25), LCV/capillarities (10/25) (Fig. 4), and fibrin deposition (6/25) (Table 6). Two specimens from the terminal ileum and ascending colon revealed lymphangiectasia or dilated lymphatics. Like U-GIT specimens, 25 L-GIT specimens were also evaluated according to the severity of inflammation. Results showed 12 cases, 9 cases, and 4 cases with mild, moderate, and severe inflammation, respectively.

Additionally, of the 25 patients, 6 patients also underwent kidney biopsies and 13 patients underwent skin biopsies (Table 1). All the kidney specimens showed LCV or proliferative glomerulonephritis with IgA deposit, which are consistent with HSP. Twelve skin specimens (12/13) disclosed LCV and the remaining 1 specimen showed histologic findings for nonspecific inflammation.

Table 3
Summarization of endoscopic and histologic characteristics of upper gastrointestinal tract.

Age/sex	Symptoms at presentation	Endoscopic findings	Biopsy site	Severity of inflammation	Histologic findings				
					Leukocytoclastic vasculitis (capillarities)	Extravasated RBC	Erosion/ulceration	Edema	Fibrin exudates
1 33/F	Abdominal pain, loose stool	Erosion	Stomach	Mild	-	+	+	-	-
2 54/M	Diarrhea, melena	Ulceration	Duodenum	Moderate	-	+	+	+	-
3 26/F	Nausea/vomiting, abdominal pain, melena	Edema, erosion multiple ulcer, petechiae	Stomach	Severe	+	-	+	-	-
4 11/F	Nausea/vomiting, abdominal pain, melena	Erythema	Duodenum	Severe	+	+	+	+	+
			Duodenum	Mild	+	-	-	-	+
5 57/M	Abdominal pain	Erythema, atrophy	Stomach	Severe	+	+	-	-	-
6 56/M	Abdominal pain, loose stool	Early gastric cancer	Stomach	Mild	+	-	-	-	-
7 14/M	Abdominal pain, petechia	Ulceration, erythema	Duodenum	Mild	+	-	-	-	+
8 44/M	Abdominal pain, petechiae	Petechiae	Stomach	Severe	+	+	-	-	-
9 14/M	Petechiae	Ulceration	Duodenum	Severe	-	+	+	+	+
10 15/M	Abdominal pain, petechiae	Erythema, ulceration	Duodenum	Moderate	-	+	-	-	-
11 64/M	Abdominal pain	Multifocal hemorrhage	Stomach	Severe	+	+	+	+	-
12* 24/M	Abdominal pain, loose stool, petechiae	Erythema, erosion	Stomach	Severe	-	+	+	+	-
13* 32/F	Abdominal pain	Erythema	Stomach	Moderate	-	+	+	-	-
14* 41/F	Abdominal pain, petechiae	Erosion	Duodenum	Moderate	+	-	+	+	-
15* 39/M	Nausea/vomiting, abdominal pain, diarrhea	Erythema, ulceration	Stomach	Mild	-	-	+	+	-
			Duodenum	Moderate	+	-	-	-	-
16* 26/F	Abdominal pain, arthralgia	Erosion, erythema	Duodenum	Mild	-	-	+	+	-
17* 66/M	Hematochezia, petechiae, arthralgia	Erosion, edema	Duodenum	Moderate	-	-	-	+	+

* Patients who underwent both upper and lower gastrointestinal tract investigations.
 RBC = red blood cell.

Table 4
Summary of endoscopic and histologic characteristics of lower gastrointestinal tract.

Age/sex	Symptoms at presentation	Endoscopic findings	Biopsy site	Severity of inflammation	Leukocytoclastic vasculitis (capillarities)	Histologic findings				
						Extravasated RBC	Erosion/ulceration	Edema	Fibrin exudates	Lymphangiectasia/dilated lymphatics
1	29/F Nausea/vomiting, abdominal pain, loose stool	Erythema, vascular ectasia	Sigmoid colon	Mild	-	-	-	-	-	-
2	42/M Nausea/vomiting, hematochezia, petechiae, arthralgia	Erythema, erosion	Sigmoid colon	Mild	-	+	+	+	+	-
3	18/F Nausea/vomiting, abdominal pain	Unremarkable	Sigmoid colon	Moderate	+	-	+	+	-	-
4	39/F Abdominal pain, diarrhea, hematuria	Edema, erythema, ulceration	Terminal ileum	Moderate	+	-	-	+	-	-
5	33/M Abdominal pain, petechiae	Erythema, ulceration	Sigmoid colon	Severe	-	+	+	+	-	-
			Terminal ileum	Mild	+	+	-	-	+	-
			Cecum	Mild	-	+	+	+	-	-
			Ascending colon	Mild	-	+	+	+	-	-
			Ascending colon	Mild	-	+	-	-	-	-
			Sigmoid colon	Mild	-	+	-	-	-	-
			Rectum	Mild	-	+	-	-	-	-
			Descending colon	Moderate	-	+	+	+	-	-
			Sigmoid colon	Mild	-	+	-	-	-	-
8	14/F Abdominal pain, loose stool	Ulceration, hemorrhage	Sigmoid colon	Severe	-	+	+	-	-	-
9	24/M Abdominal pain, loose stool, petechiae	Ulceration	Transverse colon	Moderate	+	+	+	-	+	-
10	32/F Abdominal pain	Ulceration	Terminal ileum	Moderate	+	+	+	+	+	-
			Ascending colon	Moderate	+	+	-	-	-	-
			Descending colon	Moderate	+	+	-	-	-	-
			Rectum	Moderate	+	+	-	-	-	-
11	41/F Abdominal pain, petechiae	Ulceration	Terminal ileum	Severe	+	+	+	+	+	+
12	39/M Nausea/vomiting, abdominal pain, diarrhea	Erythema, ulceration	Ascending colon	Moderate	-	-	-	+	+	-
13	26/F Abdominal pain, arthralgia	Vascular eruption	Terminal ileum	Mild	-	-	-	-	-	-
14	66/M Hematochezia, petechiae, arthralgia	Edema, vascular ectasia	Terminal ileum	Severe	+	+	+	+	+	+

* Patients who underwent both upper and lower gastrointestinal tract investigations.
RBC = red blood cell.

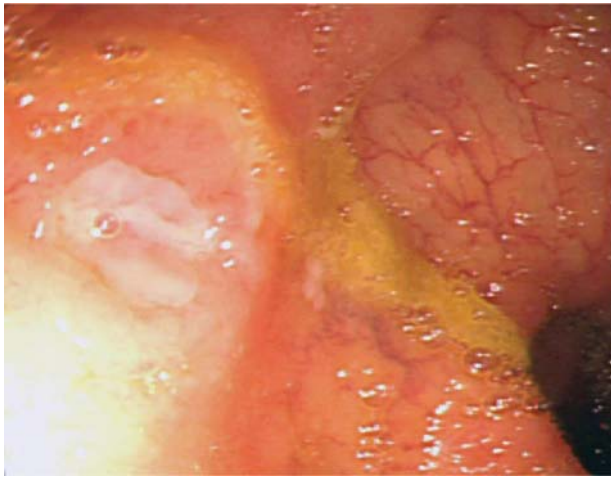


Figure 2. Colonoscopy shows shallow ulcerative lesion in the terminal ileum.

4. Discussion

The HSP shows a small-vessel vasculitis and its involvement of GIT is noted in about 2/3 patients. There have been a few studies for the endoscopic and microscopic findings of HSP patients in western countries. However, similar studies about GI findings in patients with HSP have been rarely studied in Asia in despite of its high incidence of HSP.^[3,4]

Although peak incidence of HSP is 4 to 7 years old, GI involvement rate of HSP is higher in adults.^[5] In our study, there were 24% of childhood cases and 76% of adult cases. As involvement of GIT in HSP is higher in adult group and endoscopic investigations are readily accessible diagnostic tools in Korea, more adult cases are included in this study. We thought that there could be selection bias for the following causes. First, in Korea, it is easy to access endoscopic evaluation because of low medical cost by national health insurance. Nevertheless, a large number of patients receive only supportive treatment without endoscopic examination and biopsy. Another cause is that endoscopic examination might be limited in pediatric patients for

Table 5

Summarization of endoscopic, histologic characteristics in Henoch–Schönlein purpura involving upper gastrointestinal tract.

Endoscopic findings	No. of patients (%)
Edema	2 (12%)
Erythema/petechiae	11 (65%)
Erosion/ulceration	10 (58%)
Etc.	3 (18%)
Total	17 (100%)

Histologic findings	No. of biopsied specimens (%)
Severity of inflammation	
Mild	6 (32%)
Moderate	6 (32%)
Severe	7 (37%)
Leukocytoclastic vasculitis/capillarities	7 (37%)
Extravasated RBCs	14 (74%)
Erosion/ulceration	8 (42%)
Edema	10 (53%)
Fibrin exudates	4 (21%)
Lymphangiectasia/dilated lymphatics	4 (21%)
Etc.	1 (5%)
Total	19 (100%)

RBC = red blood cell.

various reasons. Although HSP is well known as childhood disease, our study includes only 24% of pediatric cases. Additionally, there is no well-established guideline for the endoscopic approach of patients with HSP with GI symptoms. Additional studies should be needed, considering different approaches in adult and pediatric patients.

The most commonly presented symptom was abdominal pain followed by loose stool/diarrhea. As adult group showed higher frequency of diarrhea,^[5] many cases underwent L-GIT investigations. In other studies, the duodenum was found to be the predominantly involved site.^[4,6] Ten cases involved duodenum, which occupied the largest proportion of U-GIT biopsy in the present study. Erythema/petechiae was identified as the most common endoscopic finding in U-GIT followed by erosion/ulceration. In L-GIT, erosion/ulceration was the predominant

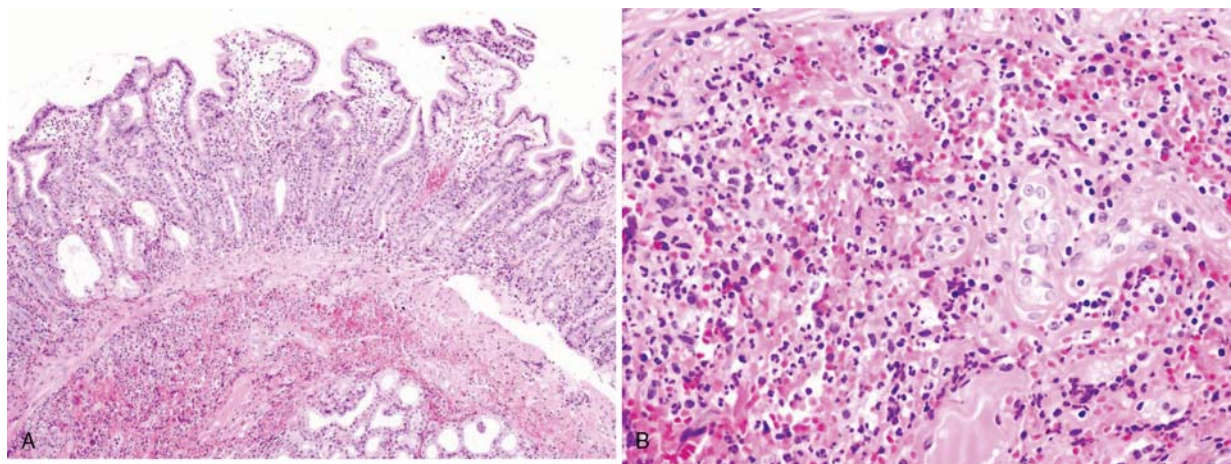


Figure 3. (A) Duodenal biopsy exhibits infiltration of inflammatory cells in mucosa and acute inflammation with hemorrhage in submucosa (hematoxylin and eosin [H&E], ×100). (B) On detailed view of (A), submucosa shows neutrophilic infiltration around vessels and nuclear debris with swelling of endothelial cells and surrounding fresh hemorrhage is also seen, suggesting leukocytoclastic vasculitis (H&E, ×400).

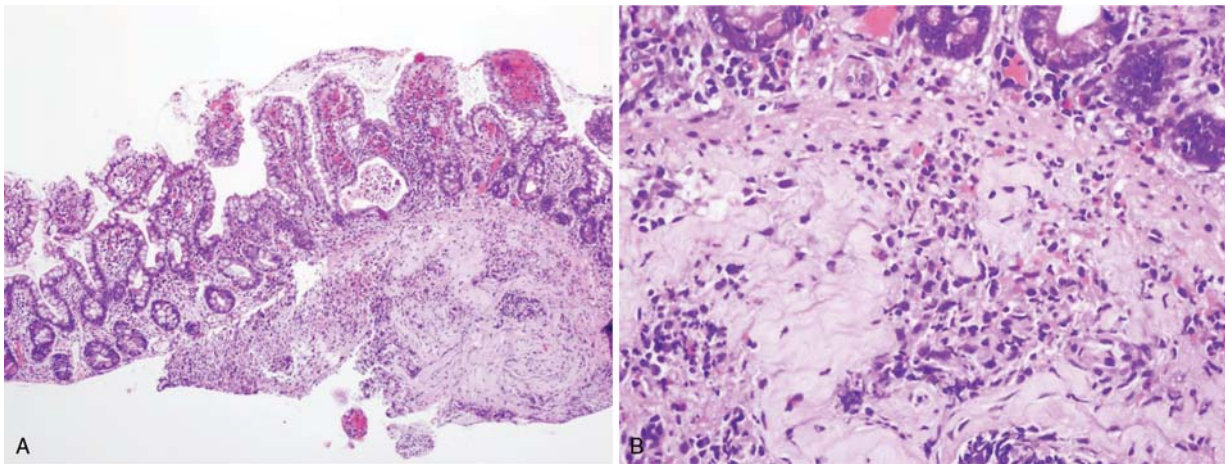


Figure 4. (A) Terminal ileum biopsy exhibits acute cryptitis and neutrophilic infiltration in submucosal layer (hematoxylin and eosin [H&E], $\times 100$). (B) On detailed view of (A) reveals vasculitis with infiltration of neutrophils around vessels and nuclear debris in submucosa (H&E, $\times 400$).

finding and erythema/petechiae was the 2nd most common finding. These findings were fairly correlated with results of previous studies.^[2,7–9]

The LCV is recognized as the characteristic histologic finding of HSP. Antigen antibody (mostly composed of IgA) complexes are formed by multiple etiologies. These complex will deposit in walls of small vessels and activate alternate complement pathway, resulting in neutrophilic accumulation.^[3] This inflammation of vessel will cause RBC extravasation and fibrin deposition in interstitial tissues, leading to edema. In our slide reviews, vasculitis was identified in 7 (37%) specimens (5 duodenum and 2 stomach) in U-GIT and 10 (40%) specimens (5 terminal ileum, 1 ascending colon, 1 transverse colon, 1 descending colon, 1 sigmoid colon, and 1 rectum) in L-GIT. These rates were similar to results of previous studies.^[4,10]

Our microscopic findings were similar to those of other studies. One case of L-GIT was unremarkable at colonoscopic investigation. However, the biopsy specimen showed capillarities. Akkari et al have reported IgA deposition despite the absence of lesion at endoscopy previously.^[11] One patient who visited hospital for abdominal pain and loose stool underwent EGD and early gastric cancer was incidentally found and histologically confirmed as well-differentiated adenocarcinoma.

While patients with HSP generally have favorable prognosis, some might have poor prognosis due to renal sequelae. There might be connections between intestinal IgA vasculitis and IgA nephropathy.^[12] Therefore, it is important to start appropriate treatment when there are GI manifestations. Proper treatment should be based on proper diagnosis after recognizing histologic findings of HSP in GIT.

5. Conclusion

Although this study contains several limitations, there has been extremely rare data for endoscopic and histopathologic findings of GIT in HSP. Therefore, an accumulation of endoscopic and pathologic findings of HSP presented in this study will be basic data of HSP-related researches and will help to develop endoscopic guidelines for patients with HSP with GI symptoms. The results of this study are very similar to some previous Western studies, and we think that these findings provide a basis for generalization in other peoples. Herein, we share our 18 years of experience in single institute for endoscopic and histologic findings of GIT in patients with HSP.

Author contributions

Conceptualization: Yeeun Han, In Ho Choi.

Data curation: Yeeun Han.

Methodology: Yeeun Han, In Ho Choi.

Supervision: In Ho Choi.

Visualization: Yeeun Han.

Writing – original draft: Yeeun Han.

Writing – review & editing: So-Young Jin, Dong Won Kim, Yoon Mi Jeon, Yon Hee Kim, In Ho Choi.

Table 6	
Summarization of endoscopic, histologic characteristics in Henoch–Schönlein purpura involving lower gastrointestinal tract.	
Endoscopic findings	No. of patients (%)
Edema	2 (14%)
Erythema/petechiae	7 (50%)
Erosion/ulceration	9 (60%)
Etc.	5 (36%)
Total	14 (100%)
Histologic findings	No. of biopsied specimens (%)
Severity of inflammation	
Mild	12 (48%)
Moderate	9 (36%)
Severe	4 (16%)
Leukocytoclastic vasculitis/capillarities	10 (40%)
Extravasated RBCs	22 (88%)
Erosion/ulceration	10 (40%)
Edema	14 (56%)
Fibrin exudates	6 (24%)
Lymphangiectasia/dilated lymphatics	2 (8%)
Total	25 (100%)

RBC = red blood cell.

References

- [1] Ozen S, Pistorio A, Iusan SM, et al. EULAR/PRINTO/PRES criteria for Henoch-Schonlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part II: Final classification criteria. *Ann Rheum Dis* 2010;69:798–806.
- [2] Chen MJ, Wang TE, Chang WH, et al. Endoscopic findings in a patient with Henoch-Schonlein purpura. *World J Gastroenterol* 2005;11:2354–6.
- [3] Sohagia AB, Gunturu SG, Tong TR, et al. Henoch-Schonlein purpura - a case report and review of the literature. *Gastroenterol Res Pract* 2010;2010:597648.
- [4] Louie CY, Gomez AJ, Sibley RK, et al. Histologic features of gastrointestinal tract biopsies in IgA vasculitis (Henoch-Schonlein purpura). *Am J Surg Pathol* 2018;42:529–33.
- [5] Kang Y, Park JS, Ha YJ, et al. Differences in clinical manifestations and outcomes between adult and child patients with Henoch-Schonlein purpura. *J Korean Med Sci* 2014;29:198–203.
- [6] Kato S, Shibuya H, Naganuma H, et al. Gastrointestinal endoscopy in Henoch-Schonlein purpura. *Eur J Pediatr* 1992;151:482–4.
- [7] Tomomasa T, Hsu JY, Itoh K, et al. Endoscopic findings in pediatric patients with Henoch-Schonlein purpura and gastrointestinal symptoms. *J Pediatr Gastroenterol Nutr* 1987;6:725–9.
- [8] Goldman LP, Lindenberg RL. Henoch-Schoenlein purpura. Gastrointestinal manifestations with endoscopic correlation. *Am J Gastroenterol* 1981;75:357–60.
- [9] Banerjee B, Rashid S, Singh E, et al. Endoscopic findings in Henoch-Schonlein purpura. *Gastrointest Endosc* 1991;37:569–71.
- [10] Esaki M, Matsumoto T, Nakamura S, et al. GI involvement in Henoch-Schonlein purpura. *Gastrointest Endosc* 2002;56:920–3.
- [11] Akkari I, Mrabet S, Jazia EB. Gastrointestinal biopsy in Henoch-Schonlein purpura: a great diagnostic contribution. *Eur J Case Rep Intern Med* 2017;4:000662.
- [12] Coppo R. The intestine-renal connection in IgA nephropathy. *Nephrol Dial Transplant* 2015;30:360–6.