

Henoch-Schönlein Purpura Presenting as Terminal Ileitis: Case Report and Review of Unusual Causes of Ileitis

Tara Sanft, MD¹
 Terrence A. Barrett, MD²
 Walter G. Barr, MD³
 Michael P. Jones, MD²

¹Department of Internal Medicine, ²Division of Gastroenterology,
³Division of Rheumatology, Feinberg School of Medicine,
 Northwestern University, Chicago, Ill.

Henoch-Schönlein purpura (HSP) is an acute vasculitic syndrome presenting with cutaneous purpura on the lower extremities and buttocks as a hallmark clinical feature.^{1,2} Arthritis and gastrointestinal and renal involvement are also frequently associated with HSP. Most often HSP occurs in children, with an annual incidence estimated at 10 per 100,000 children.^{3,4} The mean age at diagnosis is 6 years and 90% of affected individuals are less than 10 years of age. HSP is rare in adults but often more severe and more likely to manifest with renal involvement.⁵ Although gastrointestinal manifestations are common in adults, they typically occur with background systemic involvement and, as such, HSP presenting as ileitis is rarely reported in adult populations. We present such a case and discuss the relevant literature pertaining to HSP and other unusual causes of ileitis in adults.

Case Report

An otherwise healthy 21-year-old Asian American woman developed abdominal pain, nausea, vomiting, and diarrhea 2 weeks after experiencing an upper respiratory syndrome. Her only medical condition was a mild anxiety disorder, for which she took paroxetine. She was seen by two physicians within the first 4 weeks of symptom onset because of severe abdominal pain and was diagnosed with gastroenteritis and irritable bowel syndrome (IBS). Four weeks after symptom onset, she was admitted to the hospital due to persistent, severe abdominal pain. A computed tomography (CT) scan of the abdomen revealed

inflammation in the mid-ileum. A presumptive diagnosis of Crohn's disease was made. The patient was started on oral prednisone 40 mg daily and transferred to our institution for further evaluation and treatment.

On admission, the patient was experiencing moderately severe, diffuse abdominal pain. She was afebrile and her pulse and blood pressure were normal. Her abdomen was soft and nondistended and her bowel sounds were normal. There was diffuse tenderness to palpation without peritoneal findings. A violaceous, purpuric rash developed within 12 hours of admission, involving bilateral lower and upper extremities, back, and chest (Figure 1). Her white blood cell count was 18,000/ μ L and consisted of 69% neutrophils, 25% lymphocytes, 5% monocytes, and 1% eosinophils. Her hemoglobin measured 13.6 g/dL and her platelet count was 361,000/ μ L. Blood urea nitrogen and serum creatinine levels were within normal limits. Urinalysis was unremarkable. Stool studies done at the transferring facility showed no evidence for parasites, *Clostridium difficile* toxin, or enteric infection. Serologies for hepatitis B virus, hepatitis C virus, antinuclear antibody, anti-*Saccharomyces cerevisiae* antibody, perinuclear antineutrophil cytoplasmic antibody, and cytoplasmic antineutrophil cytoplasmic antibody were negative. Total complement, C3, and C4 levels were also normal. Colonoscopy revealed a grossly normal colon throughout but marked confluent ulceration of the ileum (Figure 2). Ileal biopsies showed acute inflammation with ulceration and hemorrhagic necrosis. Random biopsies from the colon were normal. A punch biopsy of a skin lesion revealed neutrophilic dermatitis with karyorrhexis.

A diagnosis of Crohn's disease with Sweet syndrome was made and the patient continued on prednisone. Her abdominal pain, diarrhea, and rash resolved, and she was discharged on the fifth day of hospitalization. Reduction

Address correspondence to:
 Michael P. Jones, MD, 251 E. Huron St., Galter Pavilion 4-104, Chicago, IL
 60611-2908; Tel: 312-926-7719; Fax: 312-926-6540; E-mail: mpjones@nmh.org.



Figure 1. Purpuric rash over the distal aspect of the lower extremities. Similar lesions were present on the upper extremities and trunk.



Figure 2. Endoscopic appearance of the cecum (left) and terminal ileum (right). The cecum is grossly normal although the ileocecal valve is patulous and erosions can be seen at the orifice. The terminal ileum is diffusely ulcerated. Biopsies of ileal mucosa revealed only ischemic necrosis.

of the prednisone dosage as an outpatient led to recurrent abdominal pain and reemergence of the violaceous purpuric rash. She was readmitted, at which time urinalysis revealed greater than 4 grams protein and red blood cell casts. Because of concerns for vasculitis and glomerulonephritis, a renal biopsy was performed. The biopsy demonstrated active nephritis with immunoglobulin A deposition in the mesangium. A (IgA) diagnosis of HSP was made based on renal biopsy findings along with the purpuric rash and ileitis. Intravenous steroids were administered followed by oral prednisone with resolution of symptoms over the next several days. She was discharged on prednisone 40 mg daily. Over the following several weeks, prednisone was gradually tapered without recurrence of symptoms. After 6 months, the patient remains asymptomatic with no evidence of either ileitis or nephritis.

Discussion

This case demonstrates two important clinical points. First, although Crohn's disease remains the leading cause of ileitis in young adults, evaluation of alternate causes is warranted when associated with extraintestinal symptoms (eg, rash) or when response to therapy is atypical. Further, although HSP most often presents with arthralgias, rash, colicky abdominal pain, and renal involvement in children, it may rarely present as isolated ileitis in young adults.

Vasculitis represents just one of the many uncommon causes of ileitis that are summarized in Table 1.⁶ *Yersinia enterocolitica* is the most common bacterial infection causing ileitis.^{7,8} Less commonly reported infections include cytomegalovirus, salmonella, shigella, *Entamoeba histolytica*, actinomycosis, and *Mycobacterium tuberculosis*.⁹⁻¹⁵ The latter two entities are capable of causing intestinal fistulization and mimicking Crohn's disease.^{16,17} Malignant involvement of the terminal ileum may mimic ileitis. Lymphomas and carcinomas are the most common tumors in this location, with lymphomas often presenting in patients with longstanding IBS.¹⁸ Adenocarcinoma arising from the ileocecal valve can also give this appearance.^{19,20} Medications that cause ileal inflammation include nonsteroidal anti-inflammatory drugs (NSAIDs), oral contraceptives, ergot derivatives, and digoxin.⁶ NSAIDs can also cause thin fibrotic strictures that are easily distinguished from the thick inflammatory strictures of Crohn's disease.²¹ Ileal involvement is common in patients with spondyloarthropathies but typically goes undetected unless diagnostic colonoscopy is warranted.⁶ Ulcerative ileojejunitis is a rare but potentially severe illness that may occur in association with celiac sprue.²² Eosinophilic gastroenteritis may present with ileal

involvement, abdominal pain, and diarrhea associated with full-thickness eosinophilic infiltrates of the bowel.²³

Ischemia of the terminal ileum also causes ileitis, usually with cecal involvement.^{24,25} The most common causes of ischemic ileitis are atherosclerotic vascular disease and “low-flow” states resulting in nonocclusive mesenteric ischemia. Because the ileocolic branches are the longest branches of the superior mesenteric artery, the ileocecal region is most susceptible to ischemia from poor perfusion. Ischemic ileitis has also been reported as a complication of sickle cell disease.²⁶

Vasculitis involving the mesenteric circulation can also result in ischemia. Mesenteric vasculitis is most commonly associated with HSP, polyarteritis nodosa, and systemic lupus erythematosus.²⁷ In general, visceral vasculitis presents with abdominal pain, nausea, vomiting, diarrhea, and gastrointestinal bleeding. Small-vessel or leukocytoclastic vasculitis is characterized by mucosal ischemia whereas vasculitis involving medium-size or larger vessels may more likely result in transmural involvement, leading to peritoneal findings or frank perforation of the digestive tract.

In general, isolated intestinal involvement is unusual in vasculitis as these are systemic conditions typically manifesting signs and symptoms in multiple organ systems. In particular, HSP presenting as ileitis is uncommon and a review of the English-language literature uncovered only eight case reports, including this one.²⁸⁻³³ In only three of these eight cases did ileitis initially present without associated rash, arthralgias, or renal involvement. Our patient was similar in that she presented with abdominal pain and did not develop rash and nephritis until 1 month later. It is interesting that the syndrome is dominated by involvement of IgA deposits in cutaneous and renal tissue. IgA is predominantly induced in mucosal lymphoid structures (eg, Peyer patches) where it is essential in defending against enteric microbes.³⁴ As Peyer patches abound in the distal ileum, it is possible that induction of IgA at these sites may be involved in the pathogenesis of ileal inflammation in HSP with subsequent spread to other involved tissue (kidney and skin) due to antigen mimicry.

In fact, it was only after the renal biopsy in this case disclosed mesangial immunoglobulin A deposits that the diagnosis of HSP was made. The painful, purpuric rash had raised the possibility of leukocytoclastic vasculitis but the biopsy was nondiagnostic. In fact, the biopsy had actually suggested the possibility of Sweet syndrome. Sweet syndrome is a neutrophilic dermatosis that can occur as an isolated finding or may accompany a variety of conditions, chiefly inflammatory bowel disease, rheumatoid arthritis, and lymphoproliferative disorders.³⁵ Whereas neutrophilic dermatosis is histologically characterized by a dense neutrophilic infiltrate without evidence of vascu-

Table 1. Conditions Associated with Ileitis

Infectious	
<ul style="list-style-type: none"> • <i>Yersinia enterocolitica</i> • <i>Yersinia pseudotuberculosis</i> • <i>Mycobacterium tuberculosis</i> • <i>Mycobacterium avium-intracellulare complex</i> 	<ul style="list-style-type: none"> • <i>Histoplasma capsulatum</i> • <i>Salmonella</i> • Cryptococcosis • <i>Anisakiasis</i> • <i>Actinomycosis israelii</i> • <i>Entamoeba histolytica</i> • Typhlitis
Inflammatory	
<ul style="list-style-type: none"> • Appendicitis • Appendiceal abscess 	<ul style="list-style-type: none"> • Torsion of the appendiceal epiploica • Cecal diverticulitis
Gynecologic	
<ul style="list-style-type: none"> • Pelvic inflammatory disease • Tubo-ovarian abscess • Ovarian cyst or tumor 	<ul style="list-style-type: none"> • Ovarian torsion • Ectopic pregnancy • Endometriosis
Neoplastic	
<ul style="list-style-type: none"> • Cecal or small bowel (ileal) adenocarcinoma • Lymphoma 	<ul style="list-style-type: none"> • Lymphosarcoma • Carcinoid tumor • Metastatic cancer
Drug-related	
<ul style="list-style-type: none"> • Nonsteroidal anti-inflammatory drug-related ulcer or stricture 	<ul style="list-style-type: none"> • Ischemic <ul style="list-style-type: none"> - Oral contraceptives - ergotamine - Digoxin - Diuretics - Antihypertensives
Vascular	
<ul style="list-style-type: none"> • Vasculitides <ul style="list-style-type: none"> - Polyarteritis nodosa - Churg-Strauss syndrome - Takayasu arteritis - Wegener granulomatosis - Lymphomatoid granulomatosis - Giant-cell arteritis - Rheumatoid arthritis vasculitis - Thromboangiitis obliterans 	<ul style="list-style-type: none"> • Henoch-Schönlein purpura • Systemic lupus erythematosus • Behçet syndrome • Ischemia
Infiltrative and Other	
<ul style="list-style-type: none"> • Eosinophilic gastroenteritis • Amyloidosis • Lymphoid nodular hyperplasia (normal or suggestive of immunoglobulin G deficiency) 	<ul style="list-style-type: none"> • Ileitis associated with spondyloarthropathy • Backwash ileitis arising in ulcerative colitis • Radiation enteritis • Ulcerative ileojejunitis (celiac sprue)

litis, Sweet syndrome has been described in association with vasculitis.^{36,37} Additionally, biopsies of advanced lesions in leukocytoclastic vasculitis may demonstrate a predominant neutrophilic infiltrate without prominent vasculitic features. Finally, Crohn's disease is associated with both vasculitis and thromboembolic events.^{6,38}

In summary, HSP, a disease chiefly affecting children, can occasionally affect adults. The diagnosis can be delayed, particularly when it presents without the classic triad of purpura, colicky abdominal pain, and arthritis. Gastrointestinal involvement in HSP is common, but reports in the literature describing isolated involvement of the terminal ileum are rare. This case highlights both the broad differential diagnosis of ileitis and the importance of this uncommon presentation of HSP as isolated ileitis in an adult.

References

- Saulsbury FT. Henoch-Schonlein purpura. *Curr Opin Rheumatol*. 2001;13:35-40.
- Jennette JC, Falk RJ. Small-vessel vasculitis. *N Engl J Med*. 1997;337:1512-1523.
- Nielsen HE. Epidemiology of Schonlein-Henoch purpura. *Acta Paediatr Scand*. 1988;77:125-131.
- Farley TA, Gillespie S, Rasoulpour M et al. Epidemiology of a cluster of Henoch-Schonlein purpura. *Am J Dis Child*. 1989;143:798-803.
- Tancrede-Bohin E, Ochonisky S, Vignon-Pennamen MD, et al. Schonlein-Henoch purpura in adult patients. Predictive factors for IgA glomerulonephritis in a retrospective study of 57 cases. *Arch Dermatol*. 1997;133:438-442.
- Sands BE. From symptom to diagnosis: clinical distinctions among various forms of intestinal inflammation. *Gastroenterology*. 2004;126:1518-1532.
- Vantrappen G, Geboes K, Ponette E. Yersinia enterocolitidis. *Med Clin North Am*. 1982;66:639-653.
- Stolk-Engelaar VM, Hoogkamp-Korstanje JA. Clinical presentation and diagnosis of gastrointestinal infections by Yersinia enterocolitica in 261 Dutch patients. *Scand J Infect Dis*. 1996;28:571-575.
- Vilaichone RK, Mahachai V, Eiam-Ong S, et al. Necrotizing ileitis caused by cytomegalovirus in patient with systemic lupus erythematosus: case report. *J Med Assoc Thai*. 2001;84(suppl 1):S469-S473.
- Sebastian JJ, Uribarrena R. Cytomegalovirus ileocolitis: different manifestations of the same illness in the terminal ileum and colon. *Endoscopy*. 1996;28:729.
- Balthazar EJ, Charles HW, Megibow AJ. Salmonella- and Shigella-induced ileitis: CT findings in four patients. *J Comput Assist Tomogr*. 1996;20:375-378.
- Meza AD, Bin-Sagheer S, Zuckerman MJ, et al. Ileal perforation due to cytomegalovirus infection. *J Natl Med Assoc*. 1994;86:145-8.
- Schneebaum CW, Novick DM, Chabon AB, et al. Terminal ileitis associated with Mycobacterium avium-intracellulare infection in a homosexual man with acquired immune deficiency syndrome. *Gastroenterology*. 1987;92(5 pt 1):1127-1132.
- Perkins DJ, Newstead GL. Campylobacter jejuni enterocolitis causing peritonitis, ileitis and intestinal obstruction. *Aust N Z J Surg*. 1994;64:55-58.
- Lambert M, Marion E, Coche E, Burtzler JR. Campylobacter enteritis and erythema nodosum. *Lancet*. 1982;1:1409.
- Nair A, Patel R, Monypenny JJ. Tuberculous peritonitis presenting as coloenteric fistula. *Br J Clin Pract*. 1993;47:214-215.
- Klaaborg KE, Kronborg O, Olsen H. Enterocutaneous fistulization due to Actinomyces odontolyticus. Report of a case. *Dis Colon Rectum*. 1985;28:526-527.
- Vanbockrijck M, Cabooter M, Casselman J, et al. Primary Hodgkin disease of the ileum complicating Crohn disease. *Cancer*. 1993;72:1784-1789.
- Petroski D. Carcinoma in Crohn's ileitis. *Gastroenterology*. 1982;83:1160-1161.
- Traube J, Simpson S, Riddell RH, et al. Crohn's disease and adenocarcinoma of the bowel. *Dig Dis Sci*. 1980;25:939-944.
- Levi S, de Lacey G, Price AB, et al. "Diaphragm-like" strictures of the small bowel in patients treated with non-steroidal anti-inflammatory drugs. *Br J Radiol*. 1990;63:186-189.
- Coupe MO, Barnard ML, Stamp G, Hodgson HJ. Ulcerative ileojejunitis associated with pulmonary fibrosis and polymyositis. *Hepatogastroenterology*. 1988;35:144-146.
- Talley NJ, Shorter RG, Phillips SF, Zinsmeister AR. Eosinophilic gastroenteritis: a clinicopathological study of patients with disease of the mucosa, muscle layer, and subserosal tissues. *Gut*. 1990;31:54-58.
- Marshak RH, Lindner AE, Maklansky D. Ischemia of the small intestine. *Am J Gastroenterol*. 1976;66:390-400.
- Sarda AK, Mathur M, Kapur M. Non-occlusive ischaemic enteritis. *Ann R Coll Surg Engl*. 1990;72:18-21.
- Engelhardt T, Pulitzer DR, Etheredge EE. Ischemic intestinal necrosis as a cause of atypical abdominal pain in a sickle cell patient. *J Natl Med Assoc*. 1989;81:1077, 1080-1084, 1087-1088.
- Passam FH, Diamantis ID, Perisinaki G, et al. Intestinal ischemia as the first manifestation of vasculitis. *Semin Arthritis Rheum*. 2004;34:431-441.
- Kawasaki M, Hizawa K, Aoyagi K, et al. Ileitis caused by Henoch-Schonlein purpura. An endoscopic view of the terminal ileum. *J Clin Gastroenterol*. 1997;25:396-398.
- Machet L, Vaillant L, Machet MC, et al. Schonlein-Henoch purpura associated with gastric Helicobacter pylori infection. *Dermatology*. 1997;194:86.
- Scherbaum WA, Kaufmann R, Vogel U, Adler G. Henoch-Schonlein purpura with ileitis terminalis. *Clin Invest*. 1993;71:564-567.
- Das CH, Raju MP. Acute regional ileitis with concomitant pulmonary tuberculosis. *Int Surg*. 1982;67:377-379.
- Ortego-Centeno N, Callejas-Rubio JL, Lopez-Manas JG, et al. Ileitis terminalis in a patient with Henoch-Schonlein purpura. *Dig Dis Sci*. 1999;44:1590-1593.
- Karagozian R, Turbide C, Szilagyi A. Henoch-Schonlein purpura presenting with ileal involvement in an adult. *Dig Dis Sci*. 2004;49:1722-1726.
- Fagarasan S, Honjo T. Regulation of IgA synthesis at mucosal surfaces. *Curr Opin Immunol*. 2004;16:277-283.
- Lear JT, Atherton MT, Byrne JP. Neutrophilic dermatoses: pyoderma gangrenosum and Sweet's syndrome. *Postgrad Med J*. 1997;73:65-68.
- Gouliaris A, Papadakis P, Kranias D, et al. Sweet's syndrome with arthritis and vasculitis. *Clin Rheumatol*. 2003;22:244-247.
- Malone JC, Slone SP, Wills-Frank LA, et al. Vascular inflammation (vasculitis) in sweet syndrome: a clinicopathologic study of 28 biopsy specimens from 21 patients. *Arch Dermatol*. 2002;138:345-349.
- Mader R, Segol O, Adawi M, et al. Arthritis or vasculitis as presenting symptoms of Crohn's disease. *Rheumatol Int*. 2004.

Review

Gurinder Luthra, DO

Assistant Professor

The University of Texas Medical Branch

Joseph Sellin, MD

Professor of Medicine

Director, C² Create

The University of Texas Medical Branch

Crohn's disease diagnosis can prove elusive and may also be subject to overdiagnosis, especially when considering the relatively inaccessible small intestine. An increasingly sophisticated armamentarium of imaging modalities (eg, capsule endoscopy) and laboratory tests (eg, inflammatory bowel disease serologies) may lure clinicians into a diagnosis of Crohn's disease that is unwarranted. The report by Sanft and associates is such an example.

HSP is an IgA-mediated, small-vessel vasculitis that often presents with purpuric rash, abdominal pain, kidney involvement, and arthritis. Common gastrointestinal (GI) symptoms are colicky abdominal pain, nausea, vomiting, hematemesis, hematochezia, and diarrhea. Intestinal perforation, intussusception, ischemia, and necrosis are

rare complications of HSP. HSP-associated vasculitis can affect any part of the gastrointestinal tract.

It is true that gastrointestinal symptoms generally occur with associated systemic involvement of the skin, joints, or kidney. There have been several reports in which gastrointestinal symptoms preceded other systemic symptoms. Involvement of the terminal ileum has led to the diagnosis of Crohn's disease in these cases.

These patients typically present with gastrointestinal symptoms at least 4 weeks before the purpuric rash. In the absence of any other systemic symptoms, midileal inflammation as detected by CT scan suggests the diagnosis of Crohn's disease. At this point, treatment with steroids for this presumptive diagnosis seems appropriate. Subsequent development of purpuric rash, when viewed through the diagnostic prism of Crohn's disease, appears to be an associated complication, Sweet syndrome. Again, with the diagnosis of Crohn's disease assumed well-established, the endoscopic and histologic changes in the terminal ileum are made to fit, even though the presence of hemorrhagic necrosis on histology is not a common finding of Crohn's disease. However, given this presentation, and improvement of symptoms with prednisone, it is easy to conclude that the patient has Crohn's disease.

These inconsistencies are easily detected after the correct diagnosis of HSP is confirmed by renal biopsy. Indeed this case, as Sanft and associates report, "highlights both the broad differential diagnosis of ileitis and the importance of this uncommon presentation of HSP." However, atypical presentations can be misleading and in some cases only manifestations brought on by the passage of time can lead to the right diagnosis.

Address correspondence to:

Joseph Sellin, MD, Division of Gastroenterology, University of Texas Medical Branch, Galveston, TX 77555-0764.