

# Ileal Pouch Biopsy Triggers Investigation and Diagnosis of Systemic Mastocytosis

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## ABSTRACT

We report a unique case of systemic mastocytosis (SM) diagnosed in an ileal pouch biopsy obtained from a 44-year-old woman with ulcerative colitis. She presented with intermittent abdominal pain and watery diarrhea that did not respond to antibiotic therapy. The pouch biopsy showed expansion of the lamina propria by aggregates of CD117 and CD25-positive abnormal mast cells. A subsequent bone marrow analysis showed an increase in abnormal mast cells. Based on World Health Organization criteria, she was diagnosed with SM and responded to cromolyn sodium therapy. Systemic mastocytosis can mimic pouchitis, and thus recognition of this condition is important for appropriate clinical management.

## INTRODUCTION

Gastrointestinal (GI) involvement is being increasingly recognized in patients with systemic mastocytosis (SM) and urticarial pigmentosa. The frequency of GI symptoms in patients with SM is about 70%,<sup>1,2</sup> whereas approximately 25% of urticarial pigmentosa patients present with GI symptoms.<sup>3</sup> In a recent study, Doyle et al<sup>4</sup> reported that in 16 of 24 patients, the first diagnosis of SM was made on the basis of GI biopsy evaluation.

## CASE REPORT

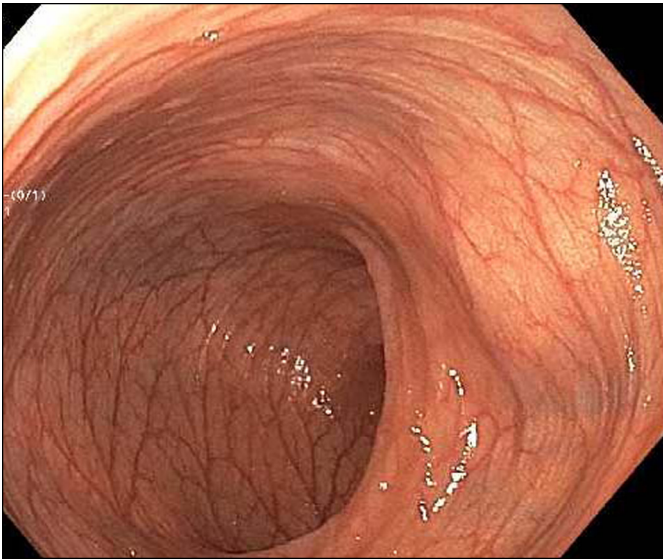
A 44-year-old woman diagnosed with ulcerative colitis (UC) in 1989 presented in March 2015 with symptoms of lower abdominal pain and watery diarrhea. She underwent total proctocolectomy for medically refractory UC in 1999, followed by an ileal-pouch anal anastomosis. She had been experiencing similar symptoms of watery diarrhea since 2007, was clinically diagnosed as pouchitis, and treated with oral antibiotics with minimal relief. Over the past few months, she developed exacerbation of symptoms, and a 10-pound weight loss. Endoscopic evaluation of the pouch revealed normal-appearing afferent limb, pouch body, and anal transitional zone (Figure 1). Biopsies obtained from the afferent limb and body of the pouch showed villous architectural distortion along with expansion of the lamina propria by lymphocytes, plasma cells, and eosinophils (Figure 2A). In addition, the biopsies also showed a subtle subepithelial collection of cells with moderately abundant pale eosinophilic cytoplasm with oval to elongated nuclei and slight indentation, fine chromatin pattern, and inconspicuous nucleoli (Figure 2). These cells were admixed with numerous eosinophils. The cellular aggregates were more prominent within the tips of the villi. In some fragments, the cells showed spindle morphology. Immunohistochemistry revealed that the cells of interest were diffusely positive for CD117 (C-KIT; Figure 2), confirming their mast cell origin. More importantly, they also showed expression of CD25 (Figure 2).

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**Figure 1.** Endoscopic view of the normal appearing pouch.

Based on these histologic findings, a diagnosis of involvement by SM was suggested. Further clinical work-up revealed mild dermatographism of skin, but without clear evidence of urticaria pigmentosa. Serum tryptase level was 18.6 ng/mL (reference range 1-11 ng/mL). Her peripheral blood counts were within normal limits. A bone marrow aspirate examination revealed a normocellular marrow with trilineage hematopoiesis. Immunohistochemical stains for CD117 and tryptase showed a slight increase in mast cells, distributed mostly as single cells, but without clustering or aggregate formation. The mast cells also demonstrated aberrant expression of CD25 and pSTAT5. Bone marrow analysis was negative for chromosomal abnormalities and *KIT* Asp816Val mutation. Subsequent sampling of the upper GI tract showed an abnormal mast cell population within the duodenum with an unremarkable stomach and esophageal mucosa. In accordance with the World Health Organization criteria,<sup>5</sup> the patient was diagnosed with SM. She was treated with oral cromolyn

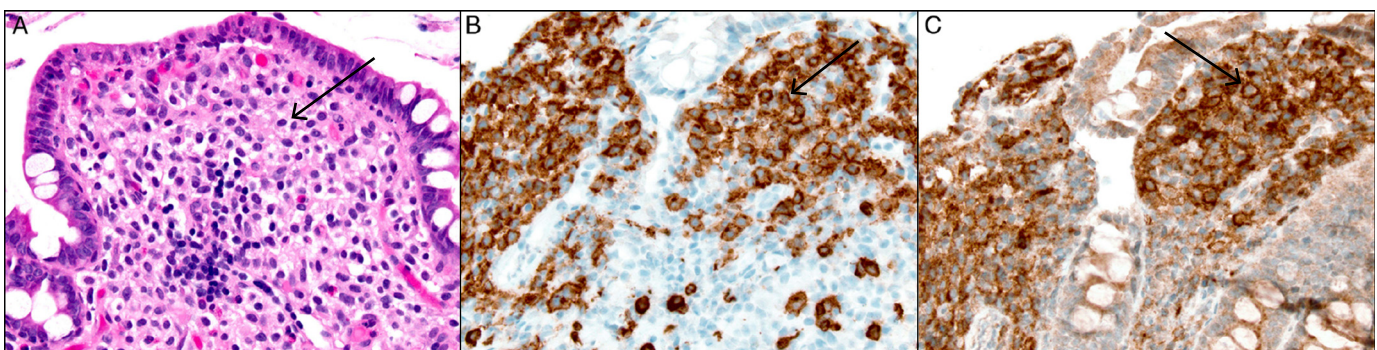
sodium (100 mg/5 mL ampule) 2 ampules, 4 times a day, and reported symptom relief within 3 weeks of therapy. She continues to be asymptomatic 10 months after her initial diagnosis.

## DISCUSSION

We present a unique case of SM diagnosed in a diagnostic pouchoscopy biopsy from a patient with long-standing UC. Lymphocytic colitis and collagenous colitis are other entities that can present with similar symptoms and have been described in the J-pouch.<sup>5</sup> However, histologically, they typically have increased intraepithelial lymphocytes with associated epithelial injury, and a thickened subepithelial collagen layer (collagenous colitis).

Considering the high frequency (up to 70%) of GI involvement in patients with SM,<sup>2</sup> mucosal biopsies can serve as an important aid in uncovering the disease. In a recent study of 24 patients with GI involvement, in two-thirds of the patients, the initial diagnosis of SM was made on the basis of endoscopic biopsy evaluation.<sup>4</sup> However, diagnosis of SM in GI biopsies can be particularly challenging since GI involvement can be patchy and subtle. In the present case, the aggregates of abnormal mast cells were present in only some of the biopsy fragments and were only identified in biopsies from the duodenum and pouch. They were best visualized by performing immunohistochemical stains (CD117).

Another challenge in diagnosing SM in the GI tract is that the abnormal infiltrate is often admixed with numerous eosinophils, which can obscure the mast cell population. Biopsies from the pouch often show a variable increase in the number of intramucosal eosinophils.<sup>6</sup> Prominent eosinophils were observed in 44% of the involved biopsies.<sup>4</sup> Thus, a low threshold for utilizing CD117 stain to confirm the presence of subtle mast cell aggregates can be very helpful. Expression of CD25, a low-affinity receptor for interleukin-2, is a reliable diagnostic tool for distinguishing neoplastic mast cells from reactive proliferations,<sup>7</sup> and has been included as a minor



**Figure 2.** Pouch biopsy shows expansion of flattened villous tip with spindled appearing mast cells admixed with eosinophils (A, arrows). Immunohistochemistry shows that the mast cells are diffusely positive for CD117 (B, arrows) and CD 25 (C, arrows).

criterion for the diagnosis of SM.<sup>1</sup> All cases of SM showed coexpression of CD25 within the abnormal mast cell population, whereas none of the patients with urticarial pigmentosa or other inflammatory conditions showed CD25 expression.<sup>8</sup>

Increased intramucosal mast cells have been described in the setting of inflammatory bowel disease. However, they are usually scattered as single cells and do not show aggregate formation.<sup>9,10</sup> A case of SM was reported in a 47-year-old man that mimicked Crohn's disease.<sup>11</sup> Four years later, biopsies from the duodenum and colon revealed an abnormal mast cell infiltrate with aberrant CD25 expression. Biopsies from her cutaneous lesions as well as a bone marrow biopsy subsequently confirmed the diagnosis of SM. The symptoms of SM may mimic those of pouchitis, and thus, awareness of uncommon conditions affecting the pouch and GI tract is important to facilitate proper clinical management.

## DISCLOSURES

Author contributions: A.A.S.R. Mannan wrote and revised the manuscript. B. Shen and F. Hsieh edited the manuscript. D.T. Patil edited the manuscript and is the author guarantor.

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## REFERENCES

1. Horny HP, Metcalfe DD, Bennett JM, Bain BJ. Mastocytosis. In: Swerdlow SH, Campo E, Harris NL, et al. eds. *WHO Classification of Tumors of Hematopoietic and Lymphoid Tissues*. 4th ed. Lyon, France: IARC; 2008:54-63.
2. Jensen RT. Gastrointestinal abnormalities and involvement in systemic mastocytosis. *Hematol Oncol Clin North Am*. 2000;14(3):579-623.
3. Topar G, Staudacher C, Geusen F, et al. Urticaria pigmentosa: A clinical, hematologic, and serologic study of 30 adults. *Am J Clin Pathol*. 1998; 109(3):279-85.
4. Doyle LA, Sepehr GJ, Hamilton MJ, et al. A clinicopathologic study of 24 cases of systemic mastocytosis involving gastrointestinal tract and assessment of mucosal mast cell density in irritable bowel syndrome and asymptomatic patients. *Am J Surg Pathol*. 2014;38(6):832-43.
5. Shen B, Bennett AE, Fazio VW, et al. Collagenous pouchitis. *Dig Liver Dis*. 2006;38(9):704-9.
6. Shen B, Plesec T, Remzi FH, et al. Evaluation of tissue eosinophilia in the pouch and afferent limb in patients with restorative proctocolectomy. *Inflamm Bowel Dis*. 2008;14(6):744-9.
7. Sotlar K, Horny HP, Simonitsch I, et al. CD 25 indicates the neoplastic phenotype of mast cells. *Am J Surg Pathol*. 2004;28(10):1319-25.
8. Hahn HP, Hornick JL. Immunoreactivity for CD 25 in gastrointestinal mucosal mast cells is specific for systemic mastocytosis. *Am J Surg Pathol*. 2007;31(11):1669-76.
9. He SH. Key role of mast cells and their major secretory products in inflammatory bowel disease. *World J Gastroenterol*. 2004;10(3):309-18.
10. King T, Biddle W, Bhatia P, et al. Colonic mucosal mast cell distribution at line of demarcation of active ulcerative colitis. *Dig Dis Sci*. 1992; 37(4):490-5.
11. Bedeir A, Jukic DM, Wang L, et al. Systemic mastocytosis mimicking inflammatory bowel disease: A case report and discussion of gastrointestinal pathology in systemic mastocytosis. *Am J Surg Pathol*. 2006; 30(11):1478-82.