

## CLINICAL VIGNETTE

# A Rare Cause of Diarrhea in the Elderly

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### Case

A 73-year-old female presented to the Emergency Department (ED) with acute onset of nausea, vomiting, and approximately ten episodes of watery diarrhea in one day. She had recently finished a ten-day course of clindamycin for a tooth extraction.

The patient also has known chronic obstructive pulmonary disease, obstructive sleep apnea, deep venous thrombosis, hypertension, hyperlipidemia, insulin-dependent diabetes mellitus type 2, heart failure with preserved ejection fraction, granuloma annulare, depression, osteoarthritis, overactive bladder, restless leg syndrome, and gastroesophageal reflux disease. She reports taking bupropion, citalopram, fenofibrate, furosemide, gabapentin, insulin, lisinopril, metformin, metoprolol, mometasone nasal spray, nystatin cream, oxybutynin, oxycodone-acetaminophen, rivaroxaban, ropinirole, inhalers, and vitamin D.

The patient's vitals on admission to the ED were temperature of 36.9 degrees Celsius, heart rate of 124 beats per minute, blood pressure of 72/52 mmHg, and pulse oxygenation at 93% on room air. Laboratory test results were significant for leukocytosis of  $10.84 \times 10^3/\mu\text{L}$  (reference 4.16-9.95  $\times 10^3/\mu\text{L}$ ) with absolute neutrophil count 8.48  $\times 10^3/\mu\text{L}$  (reference 1.80-6.90  $\times 10^3/\mu\text{L}$ ) and absolute eosinophil count 1.13  $\times 10^3/\mu\text{L}$  (reference 0.00-0.10  $\times 10^3/\mu\text{L}$ ), blood lactate 36 mg/dL (reference 5-25 mg/dL), and creatinine 1.9 mg/dL (reference 0.6-1.3 mg/dL). Her chest x-ray did not show any acute disease; her abdominal x-ray was unremarkable, free of dilated bowel loops or bowel thickening.

The ED attending physician treated her for sepsis and started intravenously vancomycin, ceftriaxone, and normal saline 500cc bolus. Upon admission to the hospital and review of patient's history, the admitting resident physician continued her on intravenous (IV) fluids and changed her antibiotics to oral vancomycin for presumed *Clostridium difficile* stool infection. Stool was collected and sent for *C. difficile* polymerase chain reaction (PCR), bacterial pathogen PCR, and giardia/cryptosporidium.

The patient's *C. difficile* stool test returned negative on hospital day one. She continued to have approximately twelve episodes of diarrhea daily. She was started on loperamide twice a day on hospital day two, which was titrated up to four times a day and reduced her stool frequency to five to seven bowel movements daily. In addition to the ongoing diarrhea, she continued to have persistent leukocytosis with eosinophilia. Gastroenterology was consulted when the stool culture tests returned negative for ova and parasite, giardia-cryptosporidium

antigen, enterovirus PCR, viral stool culture, bacteria enteric pathogen panel PCR, and rotavirus antigen.

Gastroenterology recommended additional tests including stool for helminths given persistent eosinophilia. Noninfectious inflammatory etiologies, such as inflammatory bowel disease, were thought to be less likely as the patient did not have any bright red blood per rectum or abdominal pain. Osmotic diarrhea causes were also thought to be less likely as the diarrhea was not associated with certain foods and was relatively acute in nature. Malabsorptive diarrhea was considered less likely given the acute presentation; lack of greasy, foul smelling stools; and presence of a normal albumin level. Finally, secretory causes of diarrhea were considered as the patient reported flushing during bowel movements and had ongoing large amounts of watery, voluminous stool. Vasoactive intestinal peptide and 24-hour urine 5-hydroxyindoleacetic acid (5-HIAA) were ordered.

A colonoscopy was done on hospital day nine, which showed colon polyps and an ascending colon lipoma. That day her white blood cell count was  $17.5 \times 10^3/\mu\text{L}$  with an absolute eosinophil count of  $6.64 \times 10^3/\mu\text{L}$ . On hospital day ten, a pathology report indicated eosinophils in the colonic mucosa and terminal ileum and tubular adenoma.

The patient was diagnosed with eosinophilic colitis, without a definitive etiology, and was started on budesonide 9mg orally daily. Three days later, her stool frequency improved to two stools daily, and her white blood cell count was within normal limits, although she still had eosinophilia. On further medication reconciliation, the patient reported taking an increased amount of NSAIDs in the days leading up to presentation due to pain from her tooth extraction. She was discharged to a skilled nursing facility for reconditioning. Seven days after discharge from the hospital, she was titrated off loperamide and urine 5-HIAA, VIP, and helminthic stool tests returned negative.

### Discussion

Eosinophilic colitis (EC) is one of the primary eosinophilic gastrointestinal disorders (EGIDs) in which eosinophils infiltrate the gut in the absence of a known cause for the tissue eosinophilia.<sup>1-2</sup> It is exceptionally rare, and its etiology is unknown. It usually has a bimodal distribution in infants and young adults. The only characteristic feature is an intense eosinophilic infiltration in the colon that can be segmental or diffuse. Symptoms vary depending on the colonic segment and

layer of mucosa involved. EC frequently occurs independently of blood eosinophilia, which can make it even more challenging to diagnose. Up to 23% of patients with primary EGID have no peripheral eosinophilia.<sup>3</sup>

The differential diagnosis for eosinophilic colitis includes parasitic colitis, eosinophilic gastroenteritis, hypereosinophilic syndrome, inflammatory bowel disease, drug-induced colitis, allogeneic bone marrow transplant, vasculitis, and acute radiation colitis.

It is presumed that the patient in this clinical vignette had non-steroidal anti-inflammatory drug (NSAID)-induced eosinophilia and colitis. Drug-induced eosinophilia from NSAIDs has been reported to induce respiratory disease associated with eosinophilia and is often underreported.<sup>4-6</sup> Other reported cases of NSAID-induced eosinophilic disease include a case of eosinophilic meningitis associated with ibuprofen therapy<sup>7</sup> and a case of indomethacin-induced acute renal failure with eosinophilia.<sup>8</sup> The literature is sparse on cases regarding NSAID-induced eosinophilia causing colitis. However, NSAIDs have been known to affect the large bowel and are associated with diarrhea in addition to colonic bleeding, iron deficiency anemia, strictures, ulcerations, and perforations. The pathogenesis is likely multifactorial and thought to be related to inhibition of prostaglandin synthesis.<sup>9</sup>

In an elderly patient with persistent eosinophilia and diarrhea, consider the less likely etiologies of diarrhea and review medications in detail.

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