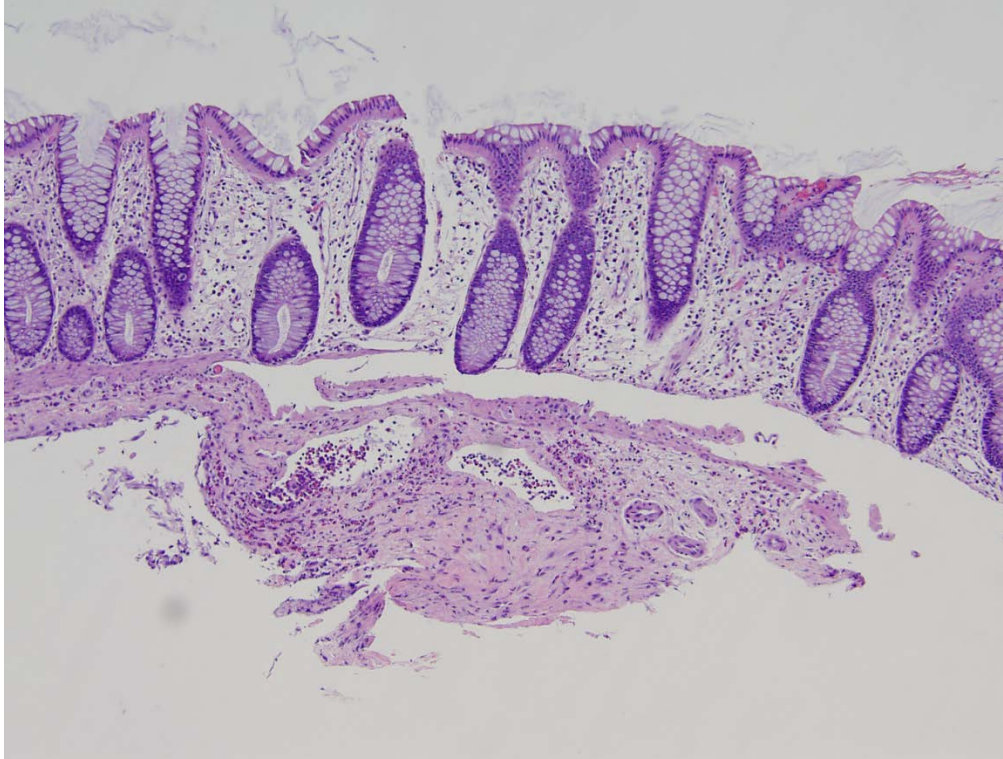
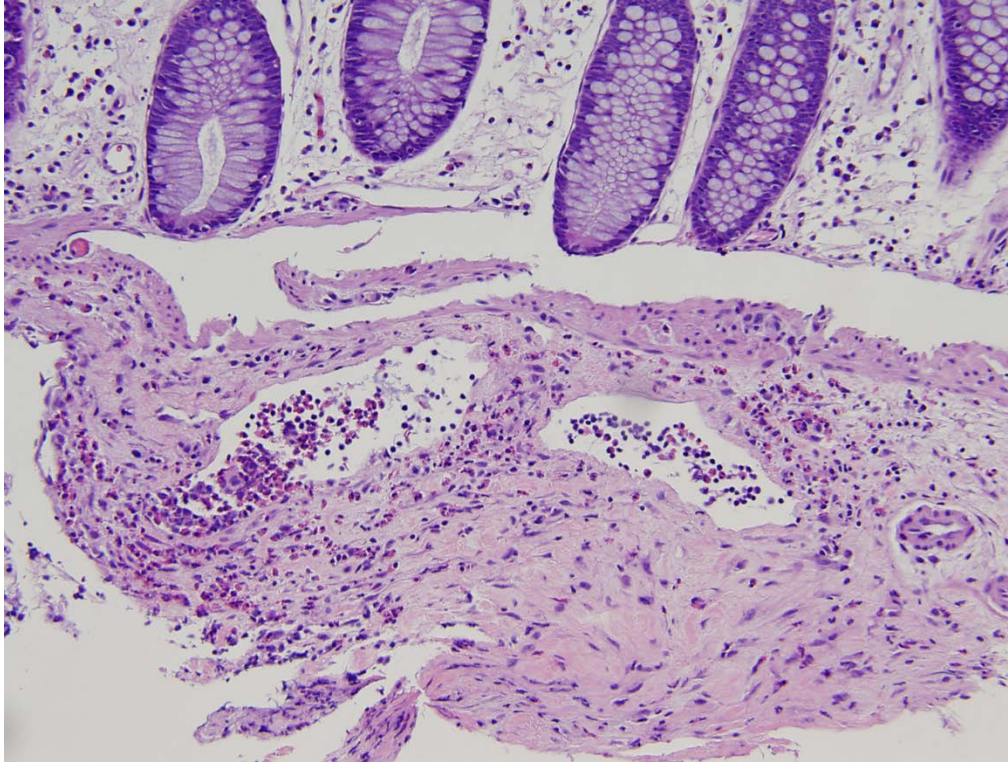


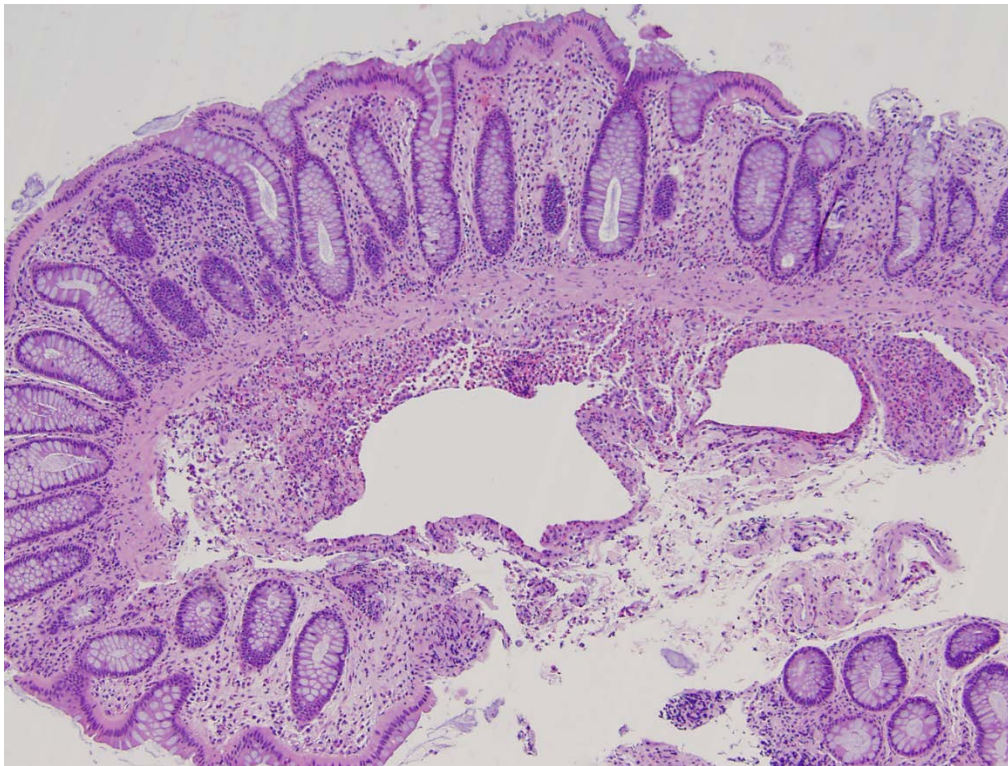
A 43-year-old female with a history of squamous cell carcinoma, status post hemi-glossectomy and multiple complications resulting in PEG-tube dependence, presented with chronic diarrhea. On endoscopic exam, she was found to have congested, inflamed, and erythematous mucosa in the transverse, descending, sigmoid colon and proximal rectum. Biopsies were obtained and histologic sections are featured below.



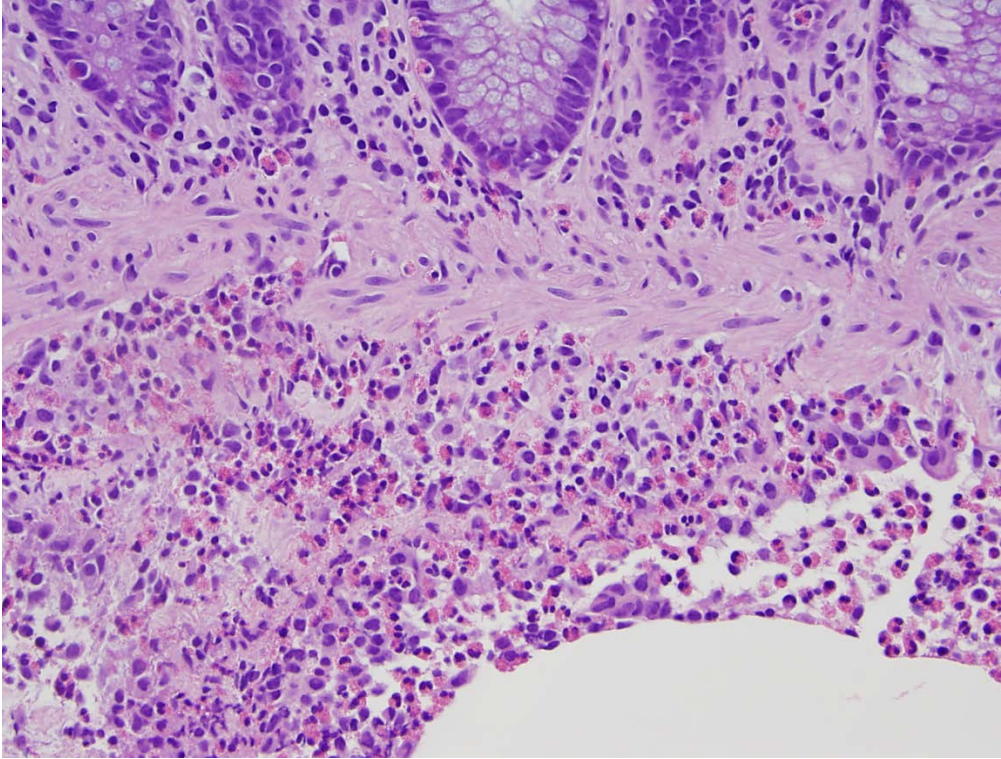
**Figure 1.** Transverse colon, H&E (10x magnification)



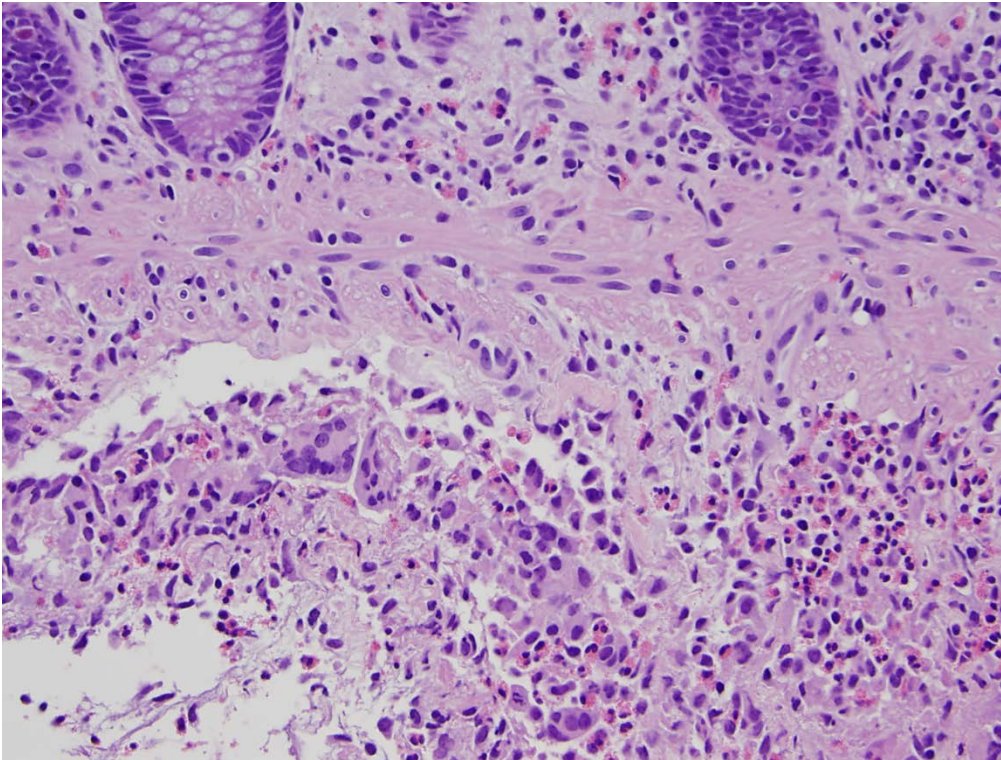
**Figure 2.** Transverse colon, H&E (20x magnification)



**Figure 3.** Rectosigmoid colon, H&E (10x magnification)



**Figure 4.** Rectosigmoid colon, H&E (40x magnification)



**Figure 5.** Rectosigmoid colon, H&E (40x magnification)

**Question:** What is the likely diagnosis?

- A) Acute infectious colitis
- B) Pneumatosis coli
- C) Mucosal pseudolipomatosis
- D) Eosinophilic/allergic colitis, intramural variant

**Answer: B)**

**Discussion:**

B) Pneumatosis coli may be idiopathic, or associated with intestinal obstruction and certain chronic diseases.<sup>1</sup> There have been four proposed mechanisms for the pathophysiology of pneumatosis coli.<sup>2</sup> The mechanical theory states that gas dissects into the bowel wall at the site of prior mucosal injury, due to increased intraluminal pressure,<sup>2</sup> which may develop secondary to obstruction, repeated vomiting, or blunt trauma.<sup>3</sup> The pulmonary theory states that barotrauma causes alveolar rupture, allowing air to dissect through the mediastinum, mesentery, and subserosal bowel wall.<sup>2</sup> The bacterial theory proposes that invasive bacteria produce gas that dissects through the bowel wall.<sup>2</sup> Infectious agents include *Clostridium difficile*, *Clostridium perfringens*, and *Clostridium septicum*.<sup>3</sup> The fourth theory proposes that increased mucosal permeability allows for intraluminal gas to dissect between the bowel wall layers. The causative agents in the fourth theory include bowel ischemia, cytotoxic drugs, and immunodeficiency.<sup>2</sup>

Clinically, patients may be asymptomatic or show a wide range of presentations including constipation, diarrhea, abdominal pain and distention, and weight loss.<sup>3</sup> Pneumatosis coli is seen in all age groups, but is most common in the 5<sup>th</sup>-8<sup>th</sup> decades.<sup>3</sup> Computed tomography is the most sensitive radiologic diagnostic approach, which can demonstrate air within the colonic wall.<sup>3</sup> Clinical risk factors include chronic parenteral tube feedings, immunosuppressive therapy, and surgery.<sup>3</sup>

Microscopically, cyst-like spaces are present within the submucosa or subserosa.<sup>3</sup> These spaces are lined by multi-nucleated giant cells, a key diagnostic feature. Eosinophils may be prominent around cystic spaces and can be easily misdiagnosed as eosinophilic/allergic colitis. The overlying mucosa may show cryptitis, crypt abscesses, chronic inflammation, or granulomas, which may mimic inflammatory bowel disease.<sup>1</sup> The pericyclic stroma stains positive for podoplanin, suggesting a possible lymphatic origin of the cysts.<sup>1,4</sup>

The patient in this case had multiple risk factors for pneumatosis coli, such as a recent *C. difficile* infection, oral chemotherapy, and chronic parenteral tube feedings. The colonic biopsies showed prominent tissue eosinophilia surrounding cystic spaces lined with occasional giant cells (Figures 4 & 5). The overlying mucosa did not show epithelial damage.

A) Acute infectious colitis presents with acute diarrhea and abdominal pain.<sup>3</sup> Endoscopically, mucosal friability, erosions, and bleeding may be present. Histologically, the hallmark feature is neutrophilic cryptitis with preserved crypt architecture.<sup>3</sup> In this case, eosinophilic infiltrate is present mainly in the submucosa. However, the use of immunosuppressors puts acute infectious colitis on the differential diagnosis.

C) Mucosal pseudolipomatosis consists of small gas-filled cysts limited to the lamina propria. Pseudolipomatosis mimics pneumatosis endoscopically, and is thought to occur due to air insufflation at the time of endoscopy.<sup>1</sup> Differentiation of pseudolipomatosis from pneumatosis coli is based on location of the the gas-filled cysts. Giant cells are also not a feature of pseudolipomatosis.

D) Eosinophilic/ allergic colitis is most common in neonates and young adults. Histologically, numerous eosinophils are present in the epithelium, lamina propria and submucosa. Eosinophilic degranulation is common.<sup>3</sup> Cystic spaces and giant cells are not part of eosinophilic/allergic colitis.

**Key Points:**

- The pathogenesis of pneumatosis coli is multifactorial.
- Clinical presentations of pneumatosis coli vary significantly.
- Risk factors include chronic parenteral feedings, immunosuppression, and surgery.
- Pathologic features of pneumatosis coli consists of submucosal cyst-like spaces with surrounding foreign body-type reaction and giant cells.
- Tissue eosinophilia is often a prominent component of the local inflammatory reaction.

**References:**

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