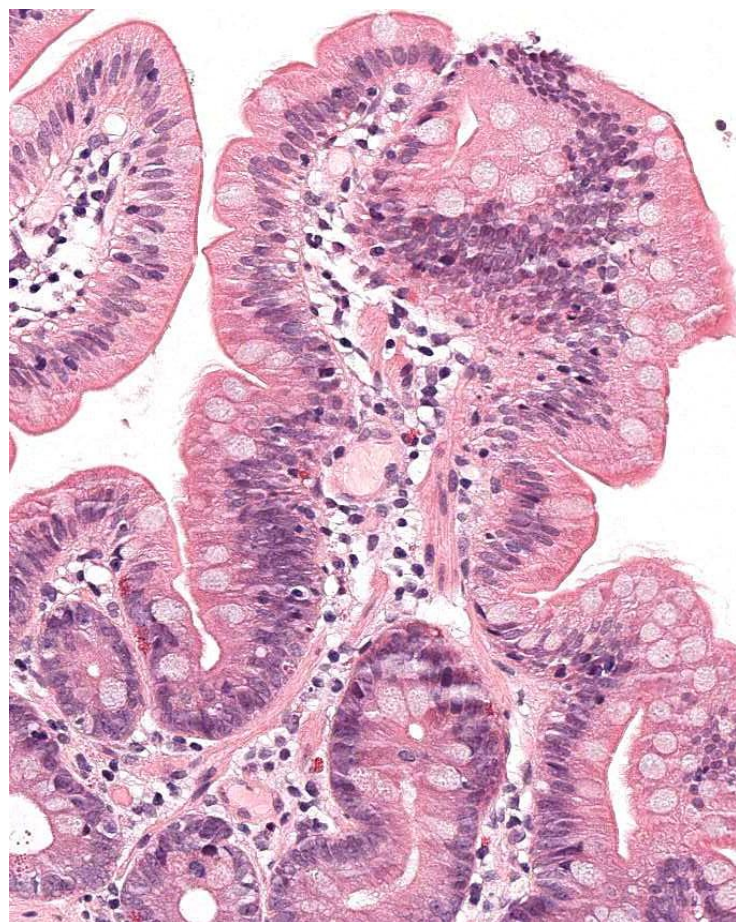


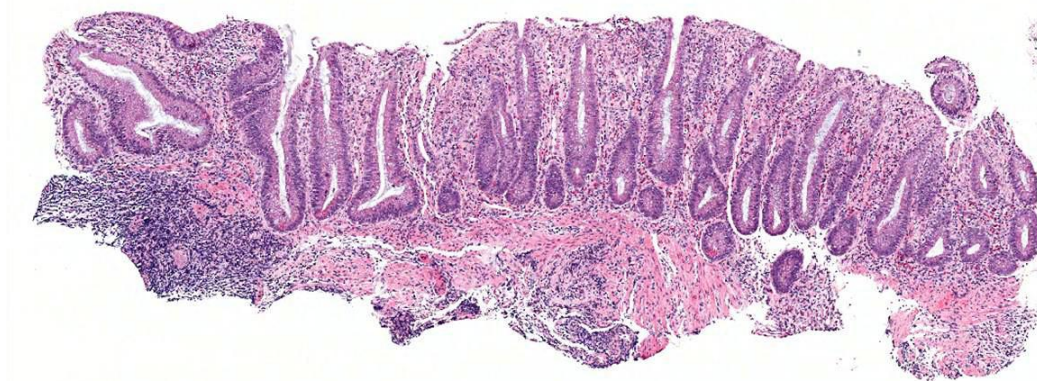
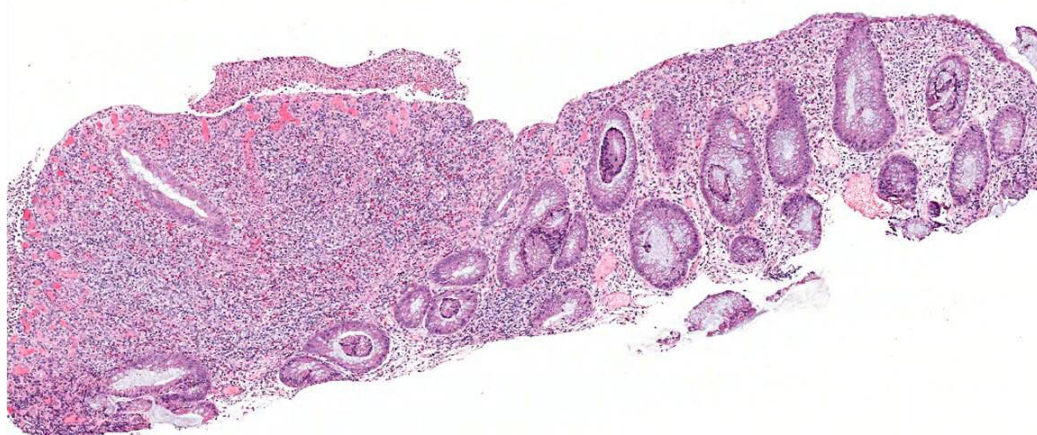
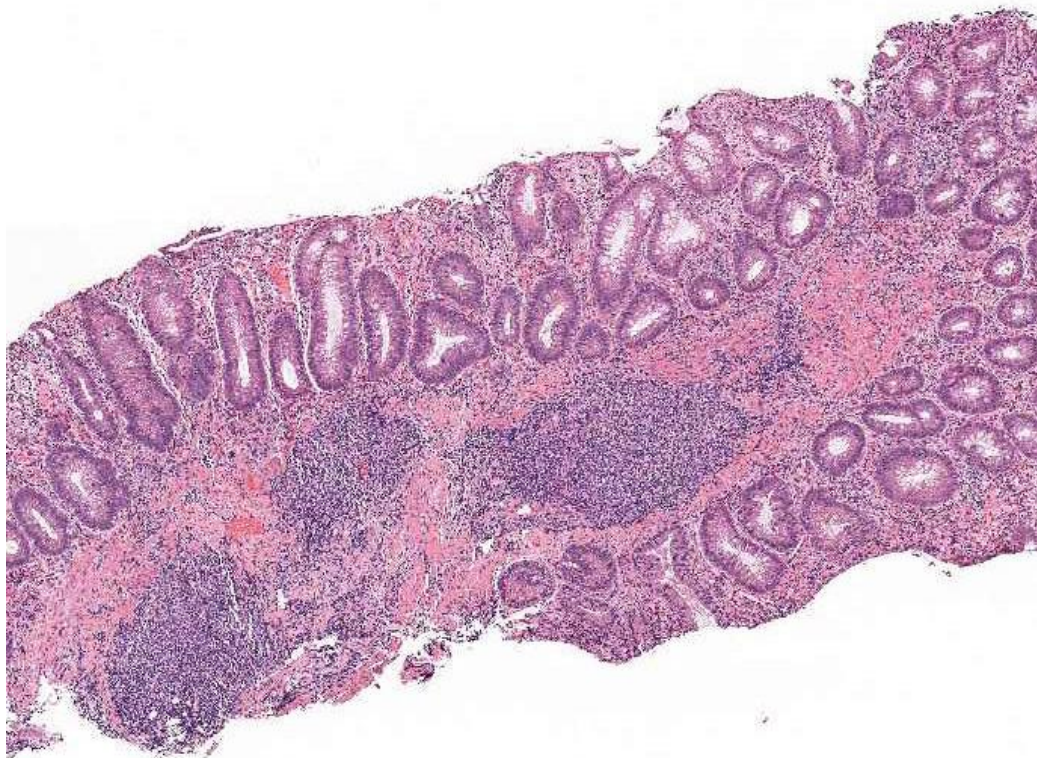
## Case History

A 24 year old male presented with fatigue, fever, watery diarrhea, and a cough with sputum production for the past three weeks. His past medical history was significant for recurrent bouts of pneumonia since childhood, frequent colds, and chronic sinusitis. After a course of antibiotics, his symptoms failed to improve and he was referred to pulmonology where they drew quantitative immunoglobulins. His IgG was 22 mg/dL (normal: 565-1765 mg/dL). IgA, IgE, and IgM were absent. He was referred to a gastroenterologist for his watery diarrhea. Colonoscopy and endoscopy demonstrated pan colitis with mucosal friability, granularity and loss of haustral folds. There was scant blood and moderate mucous throughout the colon. There was minimal erythema in the duodenum. Representative histologic sections of biopsies from the duodenum and descending colon are shown below.

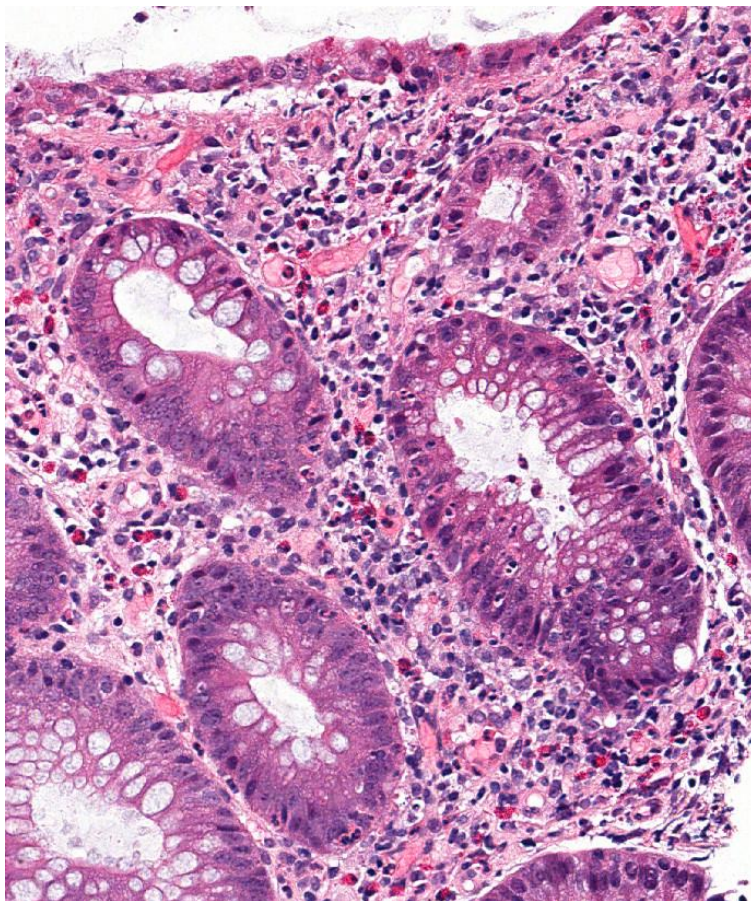
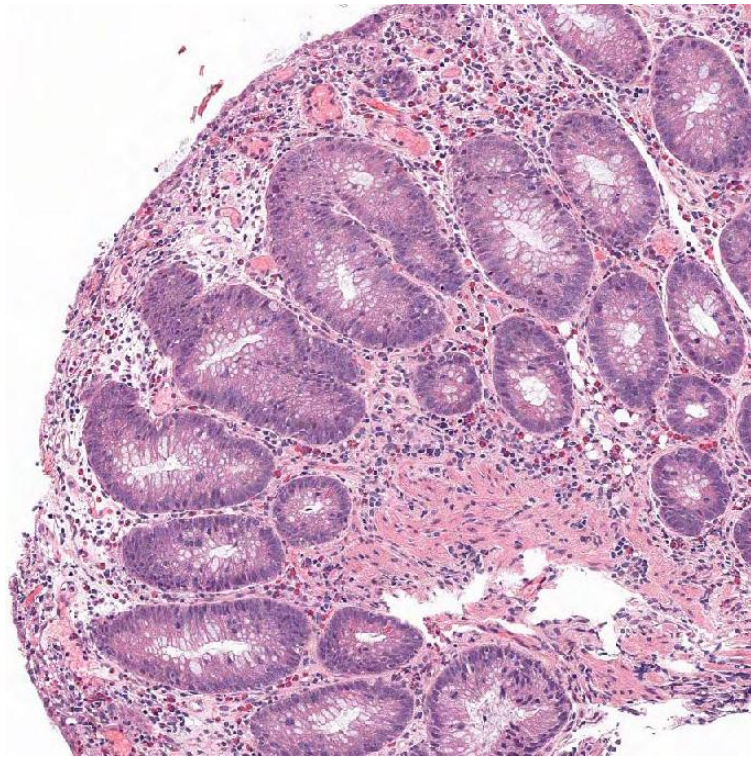


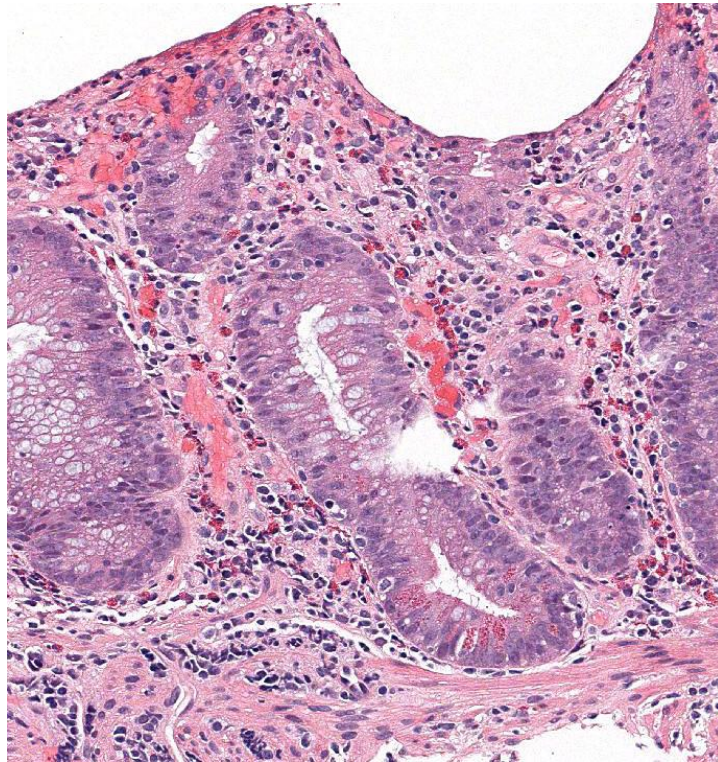












What is your diagnosis?

- a. Lymphocytic colitis
- b. Collagenous colitis
- c. Common variable immunodeficiency (CVID) associated colitis
- d. Inflammatory bowel disease/ulcerative colitis
- e. Graft versus host disease

## Answer and Discussion:

### C. Common variable immunodeficiency associated colitis

Common variable immunodeficiency (CVID) is a rare disorder with patients presenting at any age, however it most commonly presents in the 2<sup>nd</sup> and 3<sup>rd</sup> decades. Common symptomatic manifestations include recurrent bacterial infections of the upper and lower respiratory tract, diarrhea, weight loss and autoimmune dysfunction. Chronic diarrhea due to *Giardia* infection is a common complication. CVID is characterized by a failure of B-cell differentiation/maturation, resulting in hypogammaglobulinemia involving multiple classes. T-cell abnormalities may also be present.

Chronic gastrointestinal disorders occur in about 20% of patients with CVID and may result in malabsorption, diarrhea and weight loss. The small bowel findings are variable with celiac like manifestations (i.e. villous blunting and increased intraepithelial lymphocytes) in some patients and retained villous architecture in others. Lymphoid hyperplasia or epithelial cell apoptosis within the crypts may be present. There is usually a paucity or absence of plasma cells within the lamina propria. However, this feature is only present in approximately two-thirds of patients.

In some patients, the inflammatory process is limited to the colon. CVID-associated colitis is quite variable in morphology. Histologic features in the colon may include features of chronic mucosal injury characterized by architectural distortion with crypt branching, crypt destruction, and Paneth cell metaplasia. Neutrophilic inflammation is often present in the lamina propria and within crypt epithelium causing cryptitis. These chronic and active changes may mimic inflammatory bowel disease (IBD), however the crypt distortion is usually less pronounced in CVID than in IBD and there is a paucity of plasma cells within the lamina propria. Milder cases of colitis in CVID may present with increased intraepithelial lymphocytes resembling a lymphocytic colitis. In some cases, increased crypt epithelial cell apoptosis is seen accompanying crypt destruction, which may resemble graft versus host disease. Due to the variable histologic patterns, patients with CVID have been mistakenly characterized as celiac sprue, lymphocytic colitis or inflammatory bowel disease.

The pathogenesis of CVID associated colitis is unknown for the most part. In some patients, the development of GI inflammatory disorders is thought to be either a response to acute and chronic infections for which these patients are at risk for or the manifestation of an autoimmune response. Patients with CVID are also at risk for GI malignancies and other chronic inflammatory disorders.



#### References:

- 1) Cunningham-Rundles C, Bodian C. Common variable immunodeficiency: clinical and immunological features of 248 patients. *Clin Immuno*. 92(1):34-48, 1999.
- 2) Daniels JA, Lederman HM, Maitra A, Montgomery EA. Gastrointestinal tract pathology in patients with common variable immunodeficiency (CVID): a clinicopathologic study and review. *Am J Surg Pathol*. 31(12):1800-12, 2007.
- 3) Harris E and Washington K. Manifestations of Immunodeficiency in the GI Tract. In: Surgical Pathology of the GI Tract, Liver, Biliary Tract and Pancreas. 2009. 2<sup>nd</sup> ed. Eds. Odze R and Goldblum J. Saunders Elsevier, pp. 283-286.
- 4) Washington K, Stenzel TT, Buckley RH, Gottfried MR. Gastrointestinal pathology in patients with common variable immunodeficiency and X-linked agammaglobulinemia. *Am J Surg Pathol*. 20(10):1240-52, 1996.

#### Case contributed by:

Michael Lee, M.D. (GI/Liver Pathology Fellow, UCLA Medical Center)

Bitu V. Naini, M.D.