

# Chasing the Common Variable Immunodeficiency Zebra – Endoscopic/histopathologic Findings and Treatment

Daniela Fluxa, MD; Maryam AlAhmad, MBBS; Lauren Loeb, MD; Jaqueline Squire, MD; Christina Ha, MD; FACG; Darrell S. Pardi, MD; Yan Bi, MD; Jami R. Kinnucan, MD, FACG; Michael F Picco, MD, PhD, FACG; Jonathan Leighton, MD, FACG; Francis A. Farraye, MD, MSc, MACG; Jana G. Hashash, MD, MSc, FACG

## INTRODUCTION

- Common variable immunodeficiency (CVID) is a rare disease.
- Few studies have described endoscopic (endo) and histopathological (histo) findings or outlined effective treatment strategies.

## AIM

- Characterize CVID presenting gastrointestinal (GI) symptoms.
- Describe endoscopic and histological findings.
- Describe real-world experience with treatment of patients with CVID with GI involvement.

## METHODS

- Retrospective review of patients ≥16 years of age with diagnosis of CVID who underwent endoscopic evaluation for GI symptoms at a major three site academic medical center.
- Patients with secondary CVID were excluded.
- Patients were identified by searching our institution's database using CVID, upper endoscopy and/or colonoscopy as key words.
- Procedures with indication of screening/surveillance were excluded.
- Demographics, clinical symptoms, endoscopic and histological findings, and treatments were abstracted.
- Descriptive statistics were used to analyze the results.

## RESULTS

- 38 patients were included; 47% female, median age at CVID diagnosis was 31 years (range 4-66).
- 100 procedures were included (Table 1)
- The most common GI symptoms leading to endoscopic evaluation were
  - Diarrhea (45%)
  - Abdominal pain (20%)
  - Nausea (17%) and Vomiting (10%)
  - Weight loss (14%)
  - Hematochezia/rectal bleeding, bloating, heartburn, dysphagia, anorexia/early satiety, iron and vitamin B12 deficiency (<10% each).
- Endoscopic and histological findings are described in Table 1 and 2, respectively.
- Patients were diagnosed with:
  - CVID enteropathy (CVIDe) (7)
  - Microscopic colitis (6)
  - Autoimmune enteropathy (1)
  - CMV colitis (1)
  - Lichen planus
  - Lymphocytic gastritis (2)
- Patients diagnosed with CVIDe were treated with intravenous or subcutaneous immunoglobulin in addition to:
  - Steroids: Budesonide (5) or Prednisone (1)
  - Mesalamine (1)
  - Sirolimus (1)
  - Biologic therapy: Vedolizumab (2), Infliximab (2), Ustekinumab (1)
  - One patient underwent bone marrow transplant for medically refractory disease

## TABLE 1. ENDOSCOPIC FINDINGS

Type of procedure	Number of procedures n = 100 (%)
- EGD	48 (48)
- Colonoscopy	44 (44)
- Flexible sigmoidoscopy	7 (7)
- Lower DBE	1 (1)
<b>EGD endoscopic findings (n=48)</b>	
- Normal	22 (46)
- Esophagitis	2 (4)
- Gastric erythema and/or erosions	19 (40)
- Gastric atrophy	1 (2)
- Duodenal erythema	2 (4)
- Villous blunting	4 (8)
- Scalloping duodenum	4 (8)
- Nodular mucosa duodenum	1 (2)
- Ulcer duodenum	1 (2)
<b>Colonoscopy/Flexible sigmoidoscopy/Lower DBE endoscopic findings (n=52)</b>	
- Normal	29 (56)
- Nodular mucosa terminal ileum	1 (2)
- Atrophic mucosa terminal ileum	1 (2)
- Aphtha/erosion/ulcer terminal ileum	1 (2)
- Granularity terminal ileum	1 (2)
- Inflammatory changes in 1 or more colonic segments	11 (21)
- Pseudopolyps	1 (2)

EGD = upper endoscopy, DBE = double balloon enteroscopy, CMV = Cytomegalovirus  
\*Same patient was found to have CMV on biopsies twice

## TABLE 2. HISTOPATHOLOGICAL FINDINGS

EGD histopathology findings (n=48)	Number of procedures n = 100 (%)
- Normal	8 (17)
- Apoptosis	1 (2)
- Decreased/absent plasma cells	10 (21)
- Villous blunting	9 (19)
- Crypt distortion	2 (4)
- Lymphoid aggregates	1 (2)
- Prominent lymphoid follicle	1 (2)
- Increased intraepithelial lymphocytes (duodenum)	7 (13)
- Active duodenal inflammation	3 (6)
- Chronic duodenal inflammation (peptic and non-peptic)	7 (15)
- Increased eosinophils	5 (10)
- Reactive gastropathy	4 (8)
- Chronic gastritis	10 (21)
- Lymphocytic gastritis	2 (4)
- Multinucleated giant cells	1 (2)
- Increased epithelial lymphocytes esophagus	2 (4)
<b>Colonoscopy/Flexible sigmoidoscopy/Lower DBE histopathological findings (n=52)</b>	
- Normal	18 (35)
- Apoptosis	4 (8)
- Decreased/absent plasma cells	7 (13)
- Villous blunting terminal ileum	2 (4)
- Lymphoid aggregates	6 (12)
- Prominent lymphoid follicle	1 (2)
- Active ileitis	5 (10)
- Active colitis	5 (10)
- Active on chronic colitis	2 (4)
- Chronic colitis/crypt distortion	3 (6)
- Increased subepithelial collagenous band	4 (8)
- Increased intraepithelial lymphocytosis	5 (10)
- Pseudopolyp	1 (2)
- CMV	2 (4)*

## DISCUSSION

- **Patients with CVID often experience GI manifestations, with CVIDe occurring in up to 15-20% of patients in the literature and 18% in our series.**
- **While endoscopic and histological findings may be normal, biopsies are important as a range of histological findings can be found and this may impact treatment decisions.**
- **Although specific treatment guidelines are lacking, CVID patients with GI manifestations may require treatment with immunomodulators/biologics to improve morbidity and mortality.**