

BACKGROUND

- Collagenous gastrointestinal (GI) disorders (CGID) include **collagenous gastritis (CG)**, **collagenous sprue or enteritis (CE)**, and **collagenous colitis (CC)**
- Symptoms include diarrhea and weight loss
- Increased reports of sprue-like enteropathy associated with angiotensin II receptor blockers (ARB), commonly Olmesartan
- Patients may develop symptoms only years after Olmesartan initiation
- Diagnosis involves exclusion of other causes of enteropathy, mainly celiac disease (CeD) and improvement in symptoms after drug cessation
- Histopathologic distinctions between causes of enteropathy are often subtle with many overlapping features

LITERATURE REVIEW

- 20 cases worldwide of collagenous changes associated with ARB use
- Anatomic involvement:**
 - Small intestine was biopsied in 100% of patients; 60% with evidence of CE
 - Gastric biopsies in 75% of patients; 33% with CG
 - Colon biopsies in 50% of patients; 40% with CC
- Diagnosis:** methods to exclude CeD were varied between use of celiac serologies (e.g., IgA tissue transglutaminase) to HLA haplotypes
- Outcomes:**
 - 65% had clinical or histologic improvement after ARB cessation
 - 15% had clinical improvement after steroid use alone
 - On average, symptoms resolved 9.3 months after ARB cessation

CASE DESCRIPTION

- 73-year-old man with GERD and HTN, on tribenzor (olmesartan-amlo地平ine-hydrochlorothiazide, 40 mg once a day) for nearly a decade, was referred to our celiac clinic for epigastric pain, diarrhea, bloating, and significant weight loss of 40 lb in nearly a year
- Absent celiac genes (HLA-DQ2-/DQ8-), normal celiac serologies** (Endomysial IgA antibody, Transglutaminase IgA, deamidated gliadin IgA and IgG antibodies), normal fecal *H. pylori* antigen
- Push enteroscopy and colonoscopy with endoscopic findings per Figure 1
- Biopsies with evidence of **collagenous gastritis** with focal intestinal metaplasia and severe oxyntic atrophy, duodenal bulb and distal duodenum with **collagenous enteritis** with severe mucosal lesions, **normal jejunum**, and right **collagenous colitis**
- Thickened subepithelial collagen with inflammatory infiltrates was noted in the antrum, duodenum, ileum, and right colon consistent with collagenous gastroenterocolitis (CGID), Figure 2
- Olmesartan was discontinued** with symptom resolution within weeks
- At his **7 week** follow up, the patient's **diarrhea and GERD have resolved**, and he endorsed a **7lb weight gain**

Figure 1. Endoscopy images with nodularity in the antrum (A), edematous duodenum with fissures and loss of folds (B), and patchy nodularity in the right colon (C). The patient had a normal appearing jejunum (D).

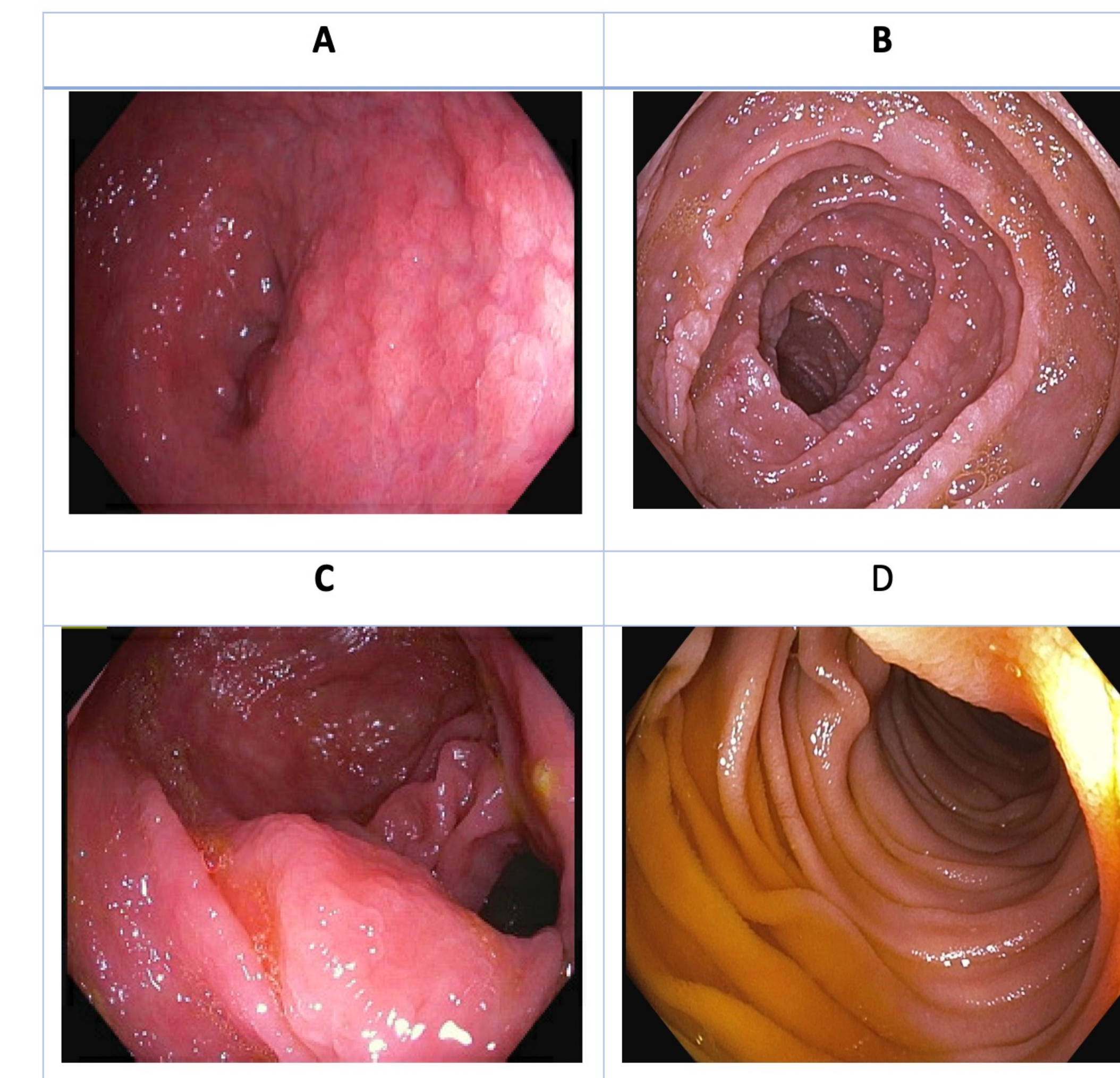
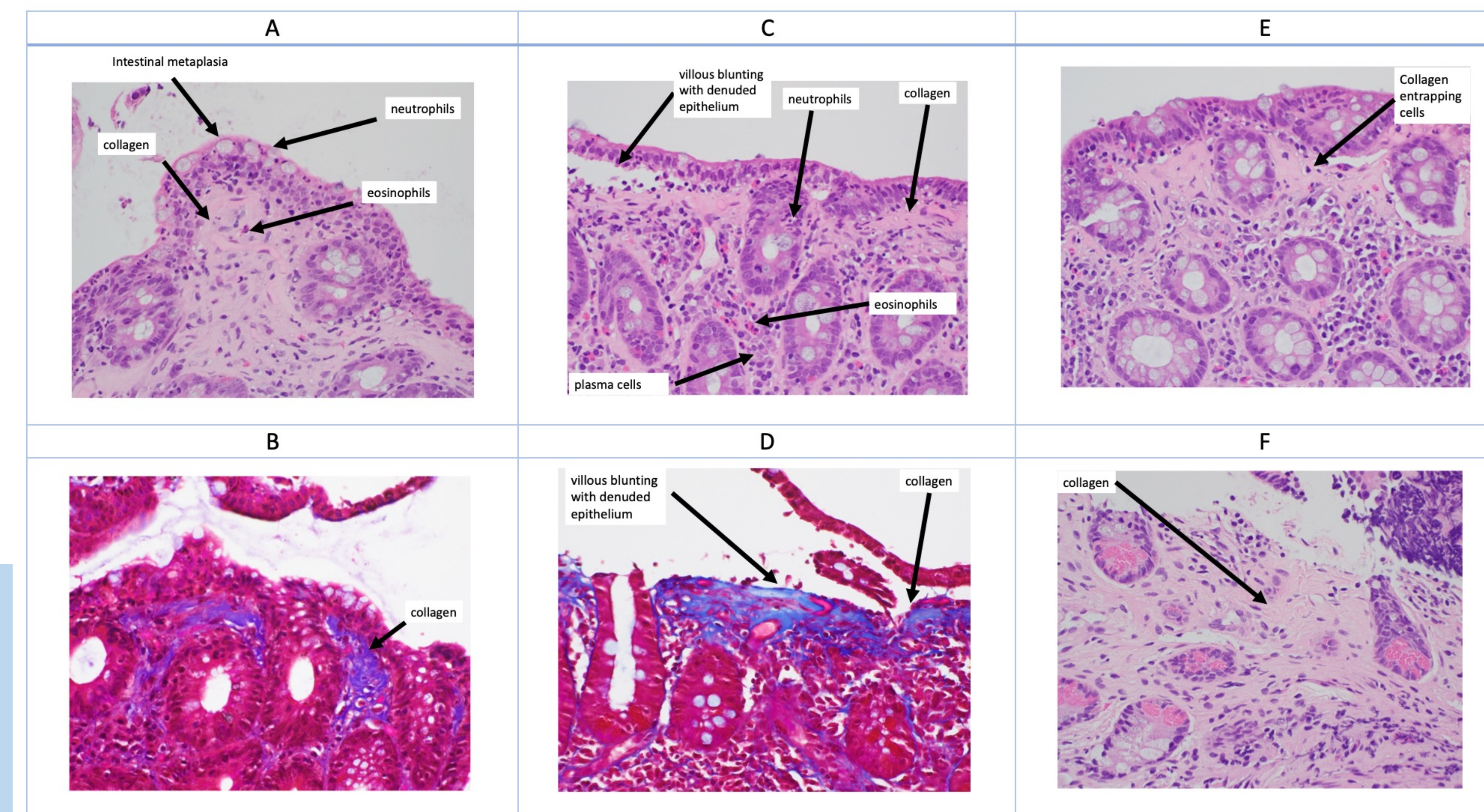


Figure 2. Histology findings showed thickened subepithelial collagen and mixed inflammatory infiltrates of the gastric antrum with collagen wrapping around cells and vessels (A, trichrome B). Evidence of thickened subepithelial collagen with villous blunting and denuded epithelium was present in the duodenum (C, trichrome D). Thickened subepithelial collagen wrapping around cells was also present in the right colon (E) and ileum (F).



DISCUSSION

- Previous studies have focused on collagenous enteritis, with few reports including biopsies from the stomach or colon
 - Unknown if prior cases had more widespread involvement of the GI tract
- Methods to exclude celiac disease are inconsistent in the literature (celiac serologies vs. genotyping)
 - Of the cases that included haplotypes, 64% were positive for either HLA DQ2 or HLA DQ8
 - Celiac haplotypes may predispose an individual to developing CGID in addition to celiac disease
 - Prior cases of CGID in HLA DQ2+/-8 patients may have misdiagnosed seronegative CeD (<5% of celiacs)
- We present a case of confirmed collagenous gastroenterocolitis with sparing of the jejunum and left colon in a patient with GERD and weight loss
- Our patient was seronegative with absent HLA-DQ2 and HLA-DQ8, making the diagnosis of celiac disease highly unlikely
- Symptoms resolved upon discontinuation of Olmesartan
- Effects of ARBs on the GI tract may be more diffuse than previously reported & Olmesartan associated gastritis should be considered when evaluating patients for ARB related collagenous enterocolitis
- We coin the term **Collagenous Gastrointestinal Disorders (CGID)** to include collagenous disorders of the stomach, and/or small bowel, and/or colon, and in this case **ARB-associated CGID**

CONCLUSION

While Olmesartan has been implicated in sprue-like enteropathy, our case highlights the effects of Olmesartan on the entire GI tract and is the first time patchy collagenous pan-gastroenterocolitis, or collagenous GI disorders (CGID), as we prefer to term it, have been associated with angiotensin II receptor blockers

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