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CASE REPORT

Gastroenterology

# Protein-losing enteropathy secondary to collagenous colitis in a 2-year-old

**Hamza Hassan Khan**[1] | **David N. Lewin**[2] | **Carmine Suppa**[1]

[1]Department of Pediatrics, Division of Pediatric Gastroenterology, Shawn Jenkins Children's Hospital, Medical University of South Carolina, Charleston, South Carolina, USA

[2]Department of Pathology, Medical University of South Carolina, Charleston, South Carolina, USA

**Correspondence**

Hamza Hassan Khan, Department of Pediatrics, Division of Pediatric Gastroenterology, Shawn Jenkins Children's Hospital, Medical University of South Carolina 125 Doughty St, Suite 530, MSC 917, Charleston, SC 29425, USA.
Email: khanha@musc.edu

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## Abstract

Protein-losing enteropathy associated with collagenous colitis (CC) is a rare but described entity in the adult population. However, literature regarding this in the pediatric population is scarce. Here we describe a 2-year-old female who presented with fevers, accompanied by nonbloody, watery diarrhea, and decreased oral intake. Work-up was significant for severe hypoalbuminemia at 1.5 grams per deciliter (g/dL), pancytopenia, and elevated fecal alpha-1-antitrypsin at 1.13 milligrams per grams (mg/g). Gastrointestinal mucosal evaluation was normal endoscopically; however, histology was consistent with CC. She responded to 12-week treatment with budesonide with resolution of symptoms and laboratory values. At this point, she has not had a recurrence 1 year later.

**KEYWORDS**

diarrhea, hypoalbuminemia, pediatrics

## 1 | INTRODUCTION

Collagenous colitis (CC) is a microscopic, inflammatory mucosal disease of the colon defined by a thick layer of collagen, ≥10 mm in diameter, histologically.[1] It often results in chronic, watery diarrhea, fecal urgency, fecal incontinence, nocturnal defecation episodes, weight loss, and extraintestinal manifestations (e.g., arthralgia, arthritis, uveitis).[2] CC is well recognized in the adult population, most commonly middle-aged women, but is an uncommon entity in the pediatric population.[3] Moreover, the association of CC with protein-losing enteropathy (PLE) is rare.[4] To our knowledge, there are only two cases of CC with PLE reported in the pediatric literature.[4,5] We report a case of a 2-year-old female with 3 weeks of diarrhea who was found to have PLE secondary to CC with concomitant pancytopenia. PLE and pancytopenia resolved with successful treatment of CC.

## 2 | CASE REPORT

A 2-year-old female, previously healthy, presented with a 3-week history of four to five nonbloody, foul smelling, watery, daily bowel movements associated with intermittent fevers and decreased oral intake. She was evaluated in the Emergency Department for worsening symptoms. Her examination was significant for mild peripheral edema and tachycardia refractory to aggressive fluid resuscitation. She was admitted for rehydration and further evaluation. Her body mass index (BMI) upon admission was 15.64 kg/m$^2$ (29.59%. *Z*-score = –0.54).

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Hamza Hassan Khan and Carmine Suppa are members of NASPGHAN and are in good standing.

The patient's initial work-up was significant for severe hypoalbuminemia at 1.4 grams per deciliter (g/dL) (normal albumin range:3.5–4.5 g/dL), elevated C-reactive protein (CRP) at 3.73 milligrams per deciliter (mg/dL) (normal CRP range:0.0–0.1 mg/dL), and pancytopenia with white blood cells (WBCs) count of 2.39 Thousand per cubic millimeter (K/cumm) (normal range:5.00–11.00 K/cumm), Hemoglobin (Hb) of 10.7 g/dL (normal range:11.0–15.0 g/dL), and platelets count of 113 K/cumm (normal range:140–440 K/cumm). Infectious work-up including blood culture, respiratory viral panel, and serum parvovirus-B19 were negative. Celiac and thyroid disease screening was unremarkable. Peripheral blood smear revealed macrocytic, normochromic erythrocytes, with normal morphology, leukopenia, and mild thrombocytopenia. Due to persistent pancytopenia, bone marrow biopsy was performed, the results of which were negative for hematolymphoid neoplasm.

Stool studies were negative for infectious etiologies. Fecal pancreatic elastase was unremarkable at 286 micrograms per grams (µg/g) (normal fecal pancreatic elastase:>200 µg/g) but elevated fecal calprotectin at >3000 µg/g (normal fecal calprotectin:<50 µg/g) and elevated fecal alpha-1-antitrypsin at >1.13 milligrams per grams (mg/g) (normal fecal alpha-1-antitrypsin range:0.00–0.50 mg/g). Computed Tomography Scan (CT-Scan) of the abdomen and pelvis with contrast revealed trace bilateral pleural effusions, mild periportal edema, small volume ascites, and mild anasarca of the proximal lower limbs. No lymphatic obstruction was noted on the CT scan. Due to persistent diarrhea, esophagogastroduodenoscopy (EGD) and colonoscopy were performed which appeared grossly normal, but histology revealed chronic active gastritis (negative for Helicobacter Pylori) and collagenous colitis throughout the colon, Figure 1. She was started on budesonide 3 mg extended-release capsule opened in apple sauce or Nutella once daily in addition to a high protein and low-fat diet. She was discharged home on Day 15. She responded to 12-weeks of treatment with a decrease in the number of bowel movements, improved stool consistency, and good weight gain. After 12-weeks of treatment, she achieved normalization of laboratory values with serum albumin of 4.3 g/dL, WBCs count of 6.36 K/cumm, Hb of 12.1 g/dL, platelets of 350 K/cumm, CRP of <0.02 mg/dL, fecal alpha-1-antitrypsin level of 25 mg/dL (normal range: ≤ 54 mg/dL) and fecal calprotectin of 27.6 µg/g. At 4 months posttreatment completion follow-up, she continued to do well without any recurrence of symptoms and unremarkable follow-up blood work-up. At 1-year posttreatment, she continues to be symptom free and is growing appropriately with a body mass index (BMI) of 16.4 kilograms per meter square ($kg/m^2$) (71.66%. *Z*-score=0.57). Repeat endoscopy was not pursued given her continued growth and sustained response off therapy.

## 3 | DISCUSSION

The exact pathogenesis of CC is unknown. Common risk factors include diabetes, Celiac disease, and hypothyroidism, and common triggers include infections, drugs (e.g., nonsteroidal anti-inflammatory drugs [NSAIDs]), and environmental triggers (e.g., smoking).[2,3] In a case series published by Matta et al., patients who had upper gastrointestinal (GI) tract involvement presented with recurrent vomiting, abdominal pain, and upper GI bleeding accompanied by iron deficiency anemia while chronic diarrhea was associated with lower GI tract involvement

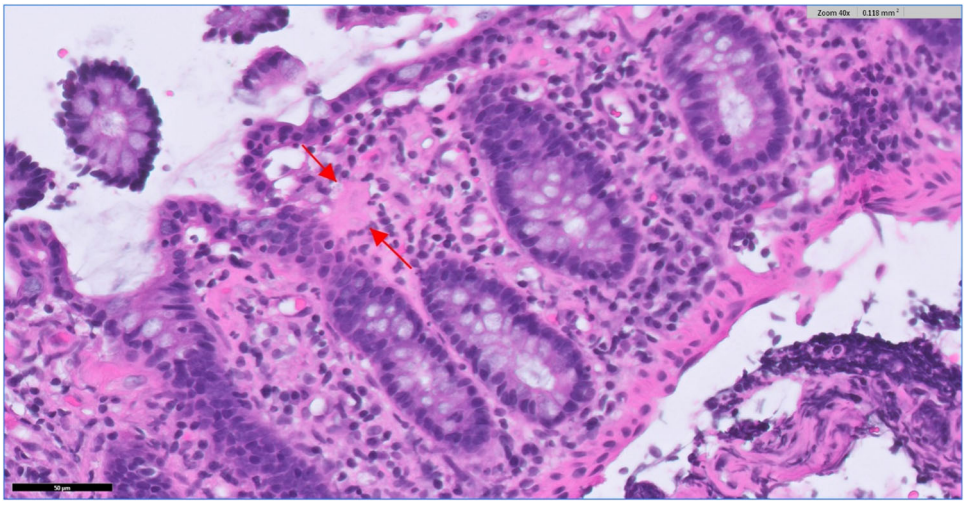

**FIGURE 1** The red arrows indicate thickened subsurface collagen deposits in the colonic mucosa. In addition, tearing or lifting of the superficial epithelium is seen (a common finding in collagenous colitis).

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**TABLE 1** Published reports of collagenous colitis associated with protein-losing enteropathy in pediatric population.

| Reference | Age | Gender | Presenting symptoms | Significant laboratory work-up | Diagnosis | Treatment |
|---|---|---|---|---|---|---|
| Almadhoun et al.[4] | 15 months | Male | Diarrhea, vomiting, and peripheral edema | WBCs: 14.5/mm$^3$,<br>Plasma albumin: 2.4 mg/dL,<br>Fecal alpha-1 antitrypsin: >1.33 mg/g | Collagenous colitis with protein-losing enteropathy | Budesonide 3 mg for 5 days<br>Symptoms continued<br>Budesonide 3 mg + Intravenous Methylprednisolone 2 mg/kg for 1 week<br>Symptoms improved<br>Prednisolone 1 mg/kg/dose + Budesonide 3 mg for 2 months<br>Symptoms resolved<br>Budesonide 3 mg continued<br>Continued Symptomatic remission + Persistent histological remission at 5 months<br>Budesonide 3 mg continued<br>Continued Symptomatic remission + achieved histological remission at 12 months |
| Remien et al.[5] | 3 years | Female | Diarrhea, decreased oral intake, decreased urination, and peripheral edema | Plasma albumin: 2.0 g/dL,<br>Triglyceride: 834 mg/dL,<br>Fecal alpha-1 antitrypsin: 64 mg/dL,<br>Fecal Calprotectin: 329 µg/g | Collagenous gastroenteritis and colitis with protein-losing enteropathy | Budesonide 1 week |

Abbreviation: WBC, white blood cell.

(e.g., CC).[6] CC is a histological diagnosis with subepithelial collagenous thickening accompanied by increased inflammation of lamina propria with increased lymphocytes, plasma cells, and possibly eosinophils.[5] The exact pathogenesis of PLE is unknown, however, it is hypothesized that it may be related to abnormalities in the superficial capillaries, peri-cryptal fibroblast, and surface epithelium.[4]

The association of CC with PLE is rare. To our knowledge, there are only two cases reported in the pediatric literature, Table 1. Almadhoun et al. reported the first case in a 15-month-old male who presented with diarrhea, vomiting, and peripheral edema.[4] Remien et al. recently reported another case of a 3-year-old female who presented with diarrhea, decreased oral intake, and peripheral edema. Our case also highlights the presence and resolution of pancytopenia. Although no source of infection was identified in our case, it is theorized that our patient's disease was triggered by an infectious agent that contributed to pancytopenia.

There are no guidelines regarding standard treatment strategies, duration of treatment, or follow-up for mucosal evaluation for CC.[1] Some patients respond to symptomatic treatment while others require immunosuppressive therapy including steroids, aminosalicylates, or tumor necrosis factor inhibitors, and so on.[1] Matta et al. reported clinical, endoscopic, and histologic improvement in only one of their three patients with collagenous gastritis accompanied by CC who were treated with corticosteroids and azathioprine.[6] Interestingly, Windon et al. reported partial symptoms relief in one of their CC patients with dietary modification and discontinuation of prior NSAIDs use.[7]

In contrast, our patient responded to 12 weeks of budesonide. Remien et al. describe treatment with 8 weeks of budesonide; however, their patient only took 1 week of budesonide with symptom improvement.[5] The patient from the Alhadhoun et al. case did not respond to enteral steroids initially, requiring the addition of parental steroids to reach symptomatic remission. He successfully weaned off prednisolone in 2 months, however, weaning budesonide led to recurrence of symptoms.[4]

In conclusion, microscopic colitis, such as CC, should be considered in patients with refractory diarrhea. This entity can be accompanied by PLE in those with hypoalbuminemia.

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## CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

## ETHICS STATEMENT

Informed patient consent was obtained from the parents of the child for publication of the case report.

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