

Dysphagia as a Presentation of Celiac Disease

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ABSTRACT

Dysphagia is an uncommon symptom for celiac disease (CD). Typically, patients with CD present with abdominal pain, diarrhea, steatorrhea, weight loss, growth failure, anemia, or fatigue. We report a case of dysphagia in a pediatric patient with negative celiac serologies and positive histologic findings suspicious for CD. Our patient's dysphagia resolved after being placed on a gluten-free diet. Repeat interval endoscopy on a gluten-free diet to assess for resolution of histological changes confirmed the diagnosis of CD. In patients with dysphagia, CD should be considered in the differential diagnosis despite negative celiac serologies.

INTRODUCTION

A variety of diseases present with dysphagia: neuromuscular disorders, achalasia, systemic scleroderma, motility disorders, eosinophilic esophagitis (EoE), anatomical abnormalities such as esophageal web/rings, or obstructive lesions. Dysphagia is a known but an uncommon symptom of celiac disease (CD). We present a pediatric case who presented with dysphagia with negative celiac serologies, subsequently diagnosed with CD.

CASE REPORT

An 18-year-old woman presented 2 years ago with 1 month of dysphagia. Solid food was getting stuck in her throat. She denied abdominal pain, diarrhea, vomiting, fevers, unintentional weight loss, rashes, or joint pains. With clinical suspicion of EoE, she was started on a proton-pump inhibitor (PPI). Complete blood count, comprehensive metabolic panel, erythrocyte sedimentation rate, celiac serology, thyroid panel, and stool for *Helicobacter pylori* were all normal except for an elevated C-reactive protein (CRP) of 7.0 mg/L. Her esophagogastroduodenoscopy on PPI therapy was visually and histologically normal with esophageal, gastric, and duodenal biopsies. With continued dysphagia, her PPI was increased to twice daily for 1 month with no improvement. Esophageal manometry showed a normal lower esophageal sphincter pressure (LES), but on 9 of 10 swallows, she had an incomplete clearance of her fluid bolus. A 24-hour impedance probe was recommended but she refused. Her dysphagia continued to worsen with complaints of large "bubbles" in her chest and abdomen. She trialed IBgard (IM HealthScience, Boca Raton, FL), a peppermint-oil-based medication used to relax the smooth muscle of her gastrointestinal tract.

Lost to follow up for 1 year, she returned with dysphagia with soft foods and prolonged gurgling in her chest. Given her abnormal esophageal motility a year ago, there were concerns for achalasia, scleroderma, chronic reflux, and EoE. Further workup included a normal upper gastrointestinal series and laboratory test results remarkable for elevated CRP 8.7 mg/L, positive antinuclear antibody (ANA), and an elevated anticentromere antibody 3.3 AI. Repeat esophageal manometry showed ineffective motility. Of 10 swallows, 8 of them were not followed by peristalsis. She was referred to rheumatology for her laboratory test results. She lacked definitive clinical findings to suggest localized or diffuse cutaneous systemic scleroderma. Bethanechol was started to increase smooth muscle tone and promote esophageal motility.

Two months later, her symptoms improved but were still present. Repeat esophagogastroduodenoscopy was performed, which showed villous blunting and focally increased intraepithelial lymphocytes in the duodenum, concerning for CD (Figure 1). Gastric and esophageal biopsies were normal. Serologies remained negative (serum IgA 142, tissue transglutaminase IgA < 2, tissue transglutaminase IgG < 2, deamidated gliadin IgA 4, deamidated gliadin IgG 5, endomysial IgA negative), and celiac genetics showed DQ2

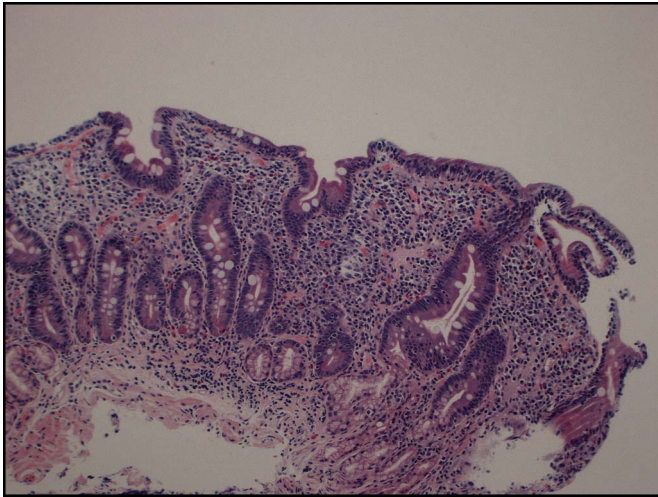


Figure 1. Esophagogastroduodenoscopy of the duodenal mucosa taken in July 2017 with almost completely blunted villi marked an increased number of intraepithelial lymphocytes, hyperplastic crypts, and expanded lamina propria by chronic inflammation (hematoxylin and eosin stain, 40× magnification).

positive/DQ8 negative. CD was considered. Immunodeficiencies were not considered with normal immunoglobulins in an otherwise healthy patient. As a therapeutic trial, the patient was started on a strict gluten-free diet (GFD).

Three months after this intervention, she had complete resolution of her esophageal dysmotility and “gurbling.” She remained hesitant to wean bethanechol therapy because she was finally asymptomatic. Currently, she reports arthralgias, and her CRP remains elevated at 9.7 mg/L with persistent significantly high ANA titers and anticentromere antibody. After 8 months of a GFD and bethanechol, dysphagia has resolved and she rarely complains of “gurples.” Her repeat endoscopy revealed normalization of her duodenum on histopathology (Figure 2).

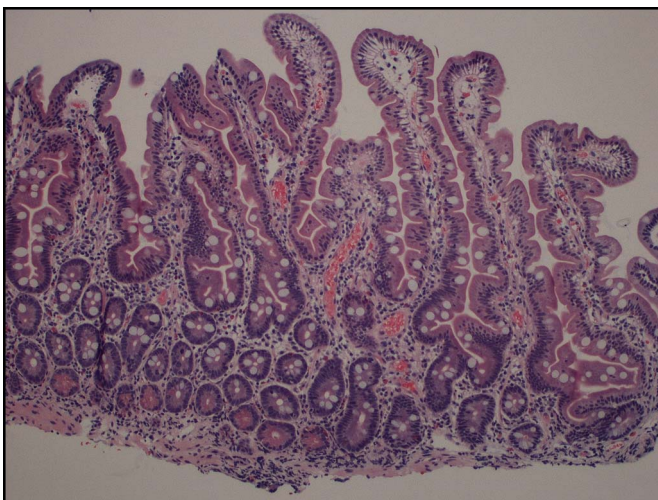


Figure 2. Esophagogastroduodenoscopy of the duodenal mucosa taken in July 2018 after a gluten-free diet with intact slender villi and scattered intraepithelial lymphocytes (hematoxylin and eosin stain, 40× magnification).

DISCUSSION

Patients with CD commonly present with abdominal pain, diarrhea, steatorrhea, weight loss, growth failure, anemia, fatigue, bone disease, abnormal liver function test, or be asymptomatic.^{1,2} Dysphagia is a known but an uncommon symptom of CD.^{3,4} Association of esophageal dysmotility has been reported in adult celiac patients. One study analyzed motility disorders in adult celiac patients using esophageal manometry and found nutcracker esophagus and low LES associated with simultaneous and frequently repetitive contractions.³ Patients with untreated CD may have reflux symptoms, and there is an association with EoE. Hypothetical physiopathological interactions between CD and gastroesophageal reflux disease include reduced nutrient absorption leading to delayed gastric emptying, increased plasma levels of endogenous glucagon, and neurotensin, which can decrease LES pressure and increase levels of somatostatin or plasma peptide YY that can reduce gastric emptying, secretions, and LES pressure.³

Initial testing for CD includes serological testing for endomysial, tissue transglutaminase, and deamidated gliadin antibodies. These testing were negative in our patients; 5% to 10% of patients with CD can have negative celiac serologies.^{5,6} Small intestinal biopsy remains the gold standard in diagnosing CD. Histological changes of the small intestinal mucosa include lymphocytic infiltration in the epithelium, increased density and depth of crypts, and flattening of the villi. Villous atrophy can be seen in other disease processes such as autoimmune enteropathy, food allergies, Crohn’s disease, and infections.^{2,7} These were ruled out based on the absence of diarrhea, lack of blood in the stool, and negative histology for eosinophils. Thus, the clinical history, celiac serologies, histological findings, and histological response to a strict GFD are all important components to confirm the diagnosis of CD. In these patients, if HLA-DQ2 or DQ8 is negative, then it is highly unlikely for the patient to have CD.^{1,8} Our patient was DQ2 positive. Histological response to GFD strongly supports the diagnosis of CD. Seronegative CD is speculated to be due to a lack of passage of autoantibodies produced in the intestine into the circulation or immaturity of the immune system.⁹ Our patient was diagnosed with seronegative CD after confirmation with complete resolution of our patient’s symptoms and normalization of her histologic findings on a GFD.

This patient has no clinical signs for scleroderma currently. An association of scleroderma and CD has been reported in the adult literature.^{10,11} Studies have shown patients with undifferentiated connective tissue disease with systemic scleroderma-like symptoms have an increased prevalence of CD.¹² The patient continues to have elevated CRP, persistent positive ANA and anticentromere antibody while on a GFD with complete resolution of her gastrointestinal symptoms. Other autoimmune diseases remain a consideration in patients with CD. She continues to have ongoing monitoring by rheumatology.

In conclusion, in a patient with dysphagia and esophageal dysmotility, CD should be in the differential diagnosis even in

the setting of negative celiac serology. Our patient's dysphagia resolved after being on a GFD and has been diagnosed with seronegative CD. In subjects with esophageal symptoms and histological changes suspicious for CD, a trial of GFD is recommended. In serology-negative patients, repeat interval endoscopy on a GFD should be performed to assess for a histologic resolution to confirm the diagnosis of CD.

DISCLOSURES

Author contributions: A. Lee wrote the manuscript and is the article guarantor. M. Tobin and A. Chawla reviewed the literature and revised the manuscript for intellectual content. J. Cherian revised the manuscript for intellectual content.

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Informed consent was obtained for this case report.

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