A Rare Case of Autoimmune Enteropathy Misdiagnosed as Celiac Disease

Munraj Singh, MD, Catherine Hudson, MD, MPH
Department of Gastroenterology, Louisiana State University Health Sciences Center, New Orleans, LA

Introduction

Autoimmune enteropathy (AIE) is an increasingly rare condition characterized by immune mediated intestinal mucosal injury that manifests as intractable diarrhea. Originally thought to be a pediatric condition, increasing cases have been reported in the adult population. Further, diagnosis can be difficult and often leads to misdiagnosis and delay in treatment. Management is centered around optimizing nutritional status in addition to steroids, immunosuppression and biologic agents. Herein we present a case of a 29-year-old man with lifelong diarrhea and misdiagnosed celiac disease who presents with failure to thrive, severe vitamin deficiencies and electrolyte abnormalities, later found to have autoimmune enteropathy.

Case Presentation

A 29-year-old man with past medical history of intractable diarrhea and childhood diagnosis of celiac disease presented for weakness and electrolyte abnormalities in the setting of chronic watery diarrhea. Laboratory findings were significant for WBC 6k uL, Potassium 2.5 mmol/L, Chloride 117 mmol/L, Creatinine 2.43 mg/dL, and decreased levels of Vitamins A, B, E, Zinc. Further investigation showed negative workup for C. diff, Giardia, Cryptosporidium, and campylobacter and negative Tissue Transglutaminase IgA. Endoscopic evaluation showed atrophic duodenitis with erythema (Figure 1A,B). Histological examination of duodenal biopsies showed loss of goblet cells and Paneth cells in addition to villous blunting, intraepithelial lymphocytosis and increased apoptotic bodies consistent with autoimmune enteropathy (Figure 1C). Prolonged outpatient clinical course significant for failed steroid therapy with oral budesonide. He was then started on Infliximab but due to inconsistent adherence, patient developed undetectable levels and high antibody levels towards the biologic agent. Currently, patient is being trialed on Humira with improvement of symptoms.

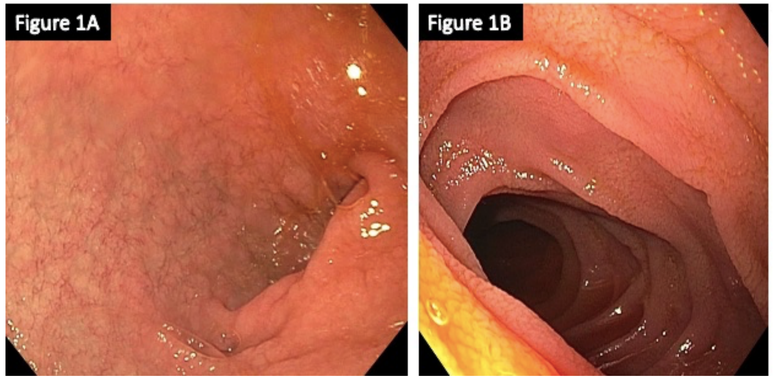
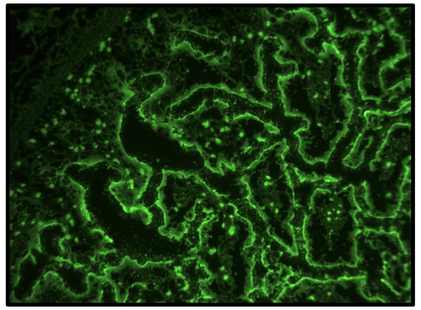
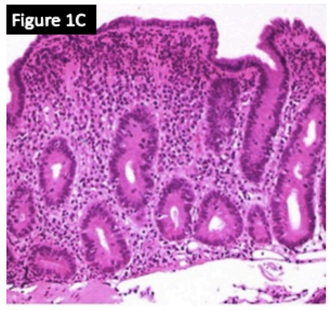


Figure 1A. Duodenal bulb inflammation. Figure 1B. Erythema of 2nd portion of duodenum. Figure 1C. High power view of duodenal biopsy shows absent villi, expansion of the lamina propria with a lymphoplasmacytic infiltrate, and absence of goblet cells. Scattered intraepithelial lymphocytes and crypt apoptotic figures can be seen.





Indirect Immunofluorescent Testing: Positive staining of apical and basolateral borders of enterocytes or goblet cell staining indicates the presence of anti-enterocyte and antigoblet cell antibodies

LSU Health NEW ORLEANS

Discussion

Chronic diarrhea, malabsorption and small bowel mucosal atrophy frequently represent a diagnostic dilemma. In reference to the adult population, more current diagnostic criteria were identified by Akram et al. in 2008 and include diarrhea lasting greater than 6 weeks, signs and symptoms of malabsorption, consistent small bowel histology and the exclusion of other causes of villous atrophy. In the adult population, AIE was found to have no sex predominance and an average age at diagnosis of 55.[2] Many autoimmune extra-intestinal conditions are associated with AIE and include hypothyroidism, autoimmune hepatitis, arthritis, nephrotic syndrome and rheumatoid arthritis. The pathophysiology of AIE includes a hyperactive immune state due to a defect in regulatory T-cell homeostasis.[2] Abnormal expression of self-antigens on mucosal epithelial cells activates CD4 T lymphocytes which leads to the destruction of enterocytes through cytotoxic effects and apoptosis.[7] Immunohistological studies of serum from patients affected by AIE have shown that autoantibodies can be directed against enterocytes and goblet cells. Interestingly, autoantibodies seem to play a secondary role in pathogenesis as they only appear after the onset of mucosal damage and are undetectable once treatment is initiated.[9] Therefore, the absence of anti-enterocyte and/or anti-goblet cell antibodies does not exclude the diagnosis of AIE.

While AIE can affect all parts of the GI tract, the duodenum is the most common site of GI tract involvement. Endoscopic findings include mucosal hyperemia, ulcerations and mucosal atrophy. Histopathological features include small bowel villous blunting, crypt apoptotic bodies, lymphoplasmacytic infiltration of the lamina propria, loss of goblet cells, and absence of Paneth cells. The treatment and management of AIE is challenging and aims at managing malnutrition and treating the underlying autoimmune disorder. Optimizing nutritional status is critical with effort made to maintain enteral nutrition, although many patients may eventually require parenteral nutrition. Initial recommended induction treatment is with corticosteroids such as budesonide and prednisone which has showed an 85% clinical response rate in patients with AIE. In refractory cases, immunosuppressive therapy have shown to be beneficial.
Highlighted by the case we present, AIE can go undiagnosed for years in an individual presenting with chronic diarrhea and signs of malabsorption. Establishing an early diagnosis is critical in reducing morbidity and improving long-term outcomes. Since much of what is known has been gathered from case reports or small series, more research in the underlying mechanisms and treatment of this rare disease is needed.

References

1. Ahmed Z, Imdad A, Connelly JA, Acra S. Autoimmune Enteropathy: An Updated Review with Special Focus on Stem Cell Transplant Therapy. *Dig Dis Sci.* 2019;64(3):643-654. doi:10.1007/s10620-018-5364-1
2. Akram S, Murray JA, Pardi DS, et al. Adult Autoimmune Enteropathy: Mayo Clinic Rochester Experience. *Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc.* 2007;5(11):1282-1245. doi:10.1016/j.cgh.2007.05.013
3. Unsworth DJ, Walker-Smith JA. Autoimmunity in diarrhoeal disease. *J Pediatr Gastroenterol Nutr.* 1985;4(3):375-380. doi:10.1097/00005176-198506000-00009
4. Montalto M, D'Onofrio F, Santoro L, Gallo A, Gasbarrini A, Gasbarrini G. Autoimmune enteropathy in children and adults. *Scand J Gastroenterol.* 2009;44(9):1029-1036. doi:10.1080/00365520902783691