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Enteropathy with loss of enteroendocrine and Paneth cells in a patient with immune dysregulation: a case of adult autoimmune enteropathy

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Summary Autoimmune enteropathy (AIE) is a relatively rare condition found most frequently in children. It presents with persistent watery diarrhea and malabsorption and may require total parenteral nutrition for nutritional support. Rare cases have been reported in adults. On histology, the small intestinal villi are flattened but lack the intraepithelial lymphocytosis of celiac disease. In children and rarely in adults, some cases are linked to the IPEX syndrome (Immune dysregulation, Polyendocrinopathy, Enteropathy, X-linked inheritance). We report a 21-year-old man who presented with chronic persistent diarrhea for 4 years. The duodenal biopsies showed villous blunting, chronic inflammation, and decreased to absent goblet cells, Paneth cells, and endocrine cells by histology and electron microscopy. These changes are consistent with an AIE with involvement of non-enterocyte populations. Pathologists must be aware of the possibility of AIE in adults and consider it in the differential diagnosis of duodenitis, intraepithelial lymphocytosis, and small bowel villous flattening.

1. Introduction

In children, autoimmune enteropathy (AIE) is an uncommon condition that presents with persistent diarrhea and malabsorption accompanied by small bowel damage on histology. The terminology was first proposed by Unsworth and Walker-Smith [1], who suggested 4 criteria: presentation with diarrhea and enteropathy, no response to total parenteral nutrition (TPN) or exclusion diet, evidence of other autoimmune disease or a predisposition to this, and absence of severe immune deficiency. In a subgroup of children, the bowel changes are associated with the IPEX syndrome (Immune dysregulation, Polyendocrinopathy, Enteropathy, X-linked inheritance). Only 7 previous reports of AIE in adults have been identified [2,3], where patients

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present with villous atrophy and malapsorptive symptoms not responsive to a gluten-free diet.

We report a case of an adult male patient with chronic diarrhea requiring TPN, dysgammaglobulinemia, and autoimmune disorders with enteropathy. Marked loss of Paneth cells and endocrine cells was apparent on histology and electron microscopy.

2. Clinical history

A 21-year-old man was admitted for investigation for chronic persistent non-bloody diarrhea of 4 years' duration associated with an involuntary weight loss of more than 40 lb. His medical history included developmental delay, dysgammaglobulinemia, autoimmune hemolytic anemia, hypothyroidism, Raynaud phenomena, and exfoliative dermatitis. He had undergone upper gastrointestinal endoscopy after 1 year of symptoms and was subsequently put on a gluten-free diet after endoscopic duodenal mucosal biopsies showed mild villous atrophy and mildly increased intraepithelial lymphocytes, despite normal anti-endomysial and tissue transglutaminase results on serology. There was no response clinically or on follow-up endoscopy and histology, so the gluten-free diet was discontinued and he was then referred to St Michael's Hospital for further evaluation. On examination at admission, he appeared severely malnourished, with a hemoglobin of 108 g/L and a low total white cell count of 1.53×10^9/L (normal 4-11 $\times$ 10^9/L) and lymphocytes at 0.26×10^9/L (normal 1.0-3.2 $\times$ 10^9/L). Serum electrophoresis demonstrated abnormal immunoglobulin distribution (elevated IgG at 19.4 g/L, low to absent IgA at <0.07 g/L, and normal IgM). Anti-SSA(Ro), anti-SSB(La), anti-Smith, anti-RNP, and anti-parietal cell antibodies were all negative. Rheumatoid factor and antinuclear antibody (ANA) were initially negative. Rheumatoid factor later became positive at 37 IU/mL, and ANA was later positive in a speckled pattern with a titer of 1:160. Upper and lower gastrointestinal endoscopy demonstrated no abnormalities, but biopsies were obtained. He was then given TPN and a 2-month course of prednisone, resulting in a weight gain of 20 pounds over 4 months and diminished diarrhea.

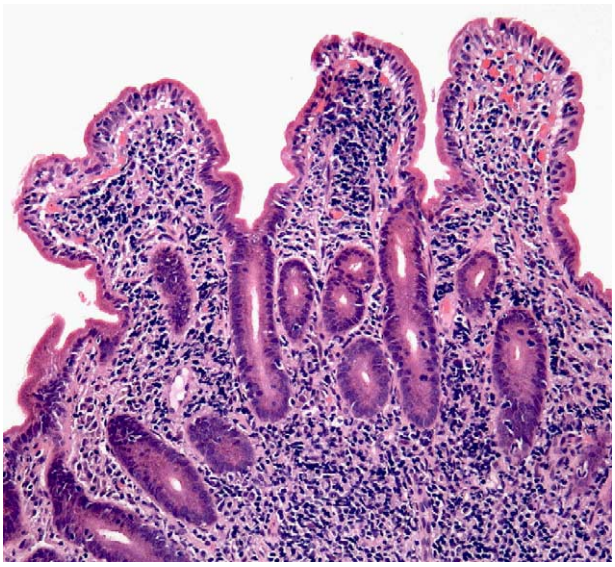

Fig. 1 Duodenal mucosa demonstrating mild villous atrophy and crypt hyperplasia. Intraepithelial lymphocytes are increased. Note the loss of goblet cells and Paneth cells (H&E, ×100).

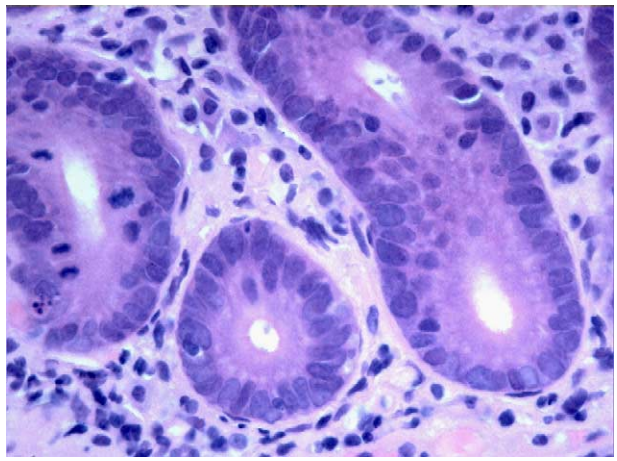

Fig. 2 High-power view of crypt bases in the duodenal mucosa; Paneth cells, endocrine cells, and goblet cells are not evident (H&E, ×400).

3. Pathological findings

Small bowel biopsies done at the time of his first two endoscopies had similar features of mild villous atrophy with associated crypt hyperplasia and mildly increased intraepithelial lymphocytes. Occasional neutrophils were present within the lamina propria. Goblet cells were evident but Paneth cells and endocrine cells were not identified on

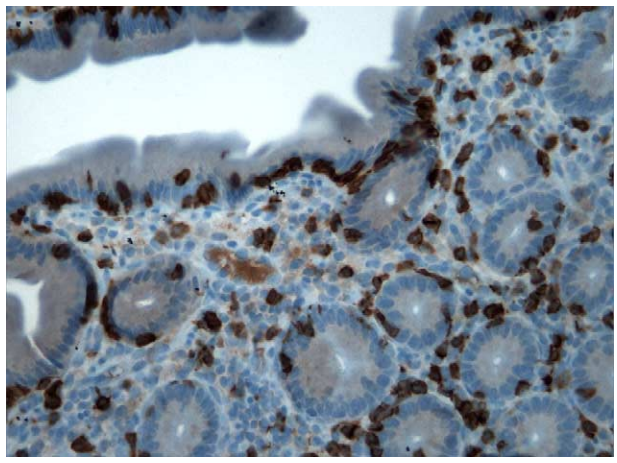

Fig. 3 Immunohistochemistry for CD8 demonstrates scattered CD8-positive T cells within the lamina propria, with a marked preponderance in the intraepithelial compartment.