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Case Report

Adult Autoimmune Enteropathy: A Case Report

Rongcai Wu [1], Xiaohui Jiang [2], Xinxiang Huang [3], Jin Chen [1*]

[1]Department of Medical Laboratory, The People' s Hospital of Guangxi Zhuang Autonomous Region (Guangxi Academy of Medical Sciences), China

[2]Department of Gastroenterology, The People' s Hospital of Guangxi Zhuang Autonomous Region (Guangxi Academy of Medical Sciences), China

[3]Department of Rheumatology and Immunology, The People' s Hospital of Guangxi Zhuang Autonomous Region (Guangxi Academy of Medical Sciences), China

***Corresponding Author:** Jin Chen, Department of Medical Laboratory, The People' s Hospital of Guangxi Zhuang Autonomous Region (Guangxi Academy of Medical Sciences), China

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Abstract

Adult autoimmune enteropathy (AIE) is a rare and challenging condition primarily characterized by severe, refractory diarrhea, malabsorption, and immune-mediated gastrointestinal injury. Diagnosing AIE requires the consideration of specific diagnostic criteria, including chronic diarrhea, malabsorption syndrome, small intestinal pathological findings such as villus atrophy, crypt inflammation, and elevated intraepithelial lymphocytes, and the exclusion of other causes such as celiac disease and intestinal lymphoma. This case report describes a 32-year-old male who presented with intractable diarrhea, which persisted despite multiple treatments. Following a comprehensive diagnostic workup, including autoantibody testing and gastrointestinal endoscopy, AIE was highly suspected and later confirmed through pathological examination. The patient's condition was differentiated from other causes of villus atrophy, including chronic infectious diseases, inflammatory bowel disease, and small intestinal neoplasia. Treatment with immunosuppressive therapy, including glucocorticoids and antiviral agents, along with supportive care, resulted in clinical stability. This case highlights the complexity of diagnosing AIE and the importance of a multidisciplinary approach in identifying rare causes of chronic diarrhea. AIE remains a diagnostic challenge, requiring careful consideration of clinical, pathological, and serological findings.

Keywords: adult autoimmune enteropathy; refractory diarrhea; malabsorption syndrome; autoantibodies; gastrointestinal pathology; immunosuppressive therapy

Introduction

Autoimmune Enteropathy (AIE) is an extremely rare autoimmune disease with unclear etiology, which usually occurs in infants and young children, especially in children aged 1 to 3 years [1]. AIE patients are presents with prolonged unhealed and severe diarrhea, malabsorption syndrome and failure to respond to any dietary restriction [2]. In adults AIE is much rarer, and the global incidence rate is about 1/100,000 [3]. As of March 2009, a total of 27 cases of adults with AIE were reported worldwide [4]. Because most of the related literatures are single case reports without epidemiological data, the treatment is also based on empirical treatment.

The clinical symptoms of AIE are similar to those of other small intestinal malabsorption diseases, such as gluten-induced enteropathy, and the diagnosis is quite difficult [5]. Currently, the understanding of AIE is still under research , resulting in a high rate of misdiagnosis. In addition, untimely treatment will lead to significant nutritional disorders and serious harm. Therefore, in view of the rarity and high clinical complexity of AIE in adults, this study aims to further explore the clinical characteristics, diagnostic process and treatment strategy of adult AIE through the detailed analysis of an adult AIE case, and to provide experience reference for the diagnosis and treatment of adult AIE in the future. At the same time, this study will help deepen the understanding of this rare disease, promote the early diagnosis and treatment standardization of this disease in clinical practice, fill the research gap in the field of adult AIE, and provide support for further clinical research and multi-center data collection.

Presentation

A 32-year-old male patient presented with a 3-month history of diarrhea, characterized by loose stools occurring approximately five times a day, predominantly after meals. He also reported occasional dull periumbilical pain and discomfort, but denied any presence of bloody stools, black stools,

or mucopurulent stool. Additionally, he did not experience other symptoms such as chills, fever, chest tightness, or shortness of breath. The patient had sought medical care at another hospital over five months ago, where routine stool examination revealed the presence of white blood cells and pus cells, and enteroscopy indicated proctitis and hemorrhoids. Despite treatment with acid suppression, gastric protection, and antidiarrheal medications, his symptoms showed minimal improvement. The patient then visited a higher-level hospital for further evaluation. Enteroscopy revealed internal hemorrhoids with multiple superficial ulcers, external hemorrhoids, and no significant abnormalities in the colorectal mucosa. Small bowel CT enterography (CTE) showed thickening of the rectal mucosa, suggesting inflammatory changes, increased gallbladder density, suspected cholestasis, and an accessory spleen. Despite treatment involving antidiarrheal medications, intestinal flora regulation, gastric protection, antispasmodic therapy, and promotion of gastric motility, the patient continued to experience persistent diarrhea and discomfort. Thus the patient was referred to our hospital （The people's hospital of Guangxi Zhuang Autonomous Region） for further diagnosis and treatment.

Since the onset of the disease, the spirit and appetite of the patient have been poor, the sleep is fair, the urination is low, the stool is as mentioned above, and the body weight has decreased by 35 kg in the past three months.The patient has a history of "small three positive" but has not taken antiviral drugs, and the specific condition remains unclear. He denies having hypertension, diabetes mellitus, coronary heart disease, hepatitis, tuberculosis, bacillary dysentery, typhoid fever, or any other infectious diseases. Five years ago, he underwent minimally invasive surgery for varicocele and denies any other surgeries, blood transfusions, or trauma. There is no known history of drug or food allergies, and his vaccination history is unknown. A review of systems revealed no significant abnormalities. The patient was born locally and has no history of long-term residence outside the area or exposure to epidemics, chemicals, or radiation. He denies tobacco and alcohol use, as well as any history of sexually transmitted diseases, though he has a history of consuming fish. He is married, in an age-appropriate marriage, and both his children and spouse are healthy. There is no family history of infections, hereditary diseases, or similar medical conditions. On physical examination, his vital signs were: temperature 36.2 ℃, pulse rate 93 beats/min, respiratory rate 19 breaths/min, and blood pressure 86/64 mmHg. His body height is 178 cm and weight 59 kg. He appeared normally developed with moderate nutrition, was active, with clear consciousness, coordinated movements, and fluent speech, demonstrating a healthy orthotonic body type.

Examination after admission

Laboratory examination: Elevated high-sensitivity C-reactive protein of 1.78mg/L, elevated white blood cell count of 11.22*10^9/L, reduced hemoglobin of 126g/L, reduced hematocrit of 37.8%, platelet count of 247*10^9/L, elevated granulocyte ratio of 86.9%. Reduced potassium of 2.44 mmol/L, reduced phosphorus of 0.67 mmol/L, reduced magnesium of 0.64 mmol/L, elevated creatine kinase isoenzyme of 57U/L, elevated hepatitis B e antibody of 1.04PEIU/ml, elevated hepatitis B surface antigen> 250.00IU/mL, elevated hepatitis B core antibody>45.00PEIU/ml.

Autoantibody test: increased antinuclear antibody nuclear dot type 1:320, increased antinuclear antibody proliferative nuclear antigen type 1:320.

Food intolerance: corn of 268.55 U/ml; mushroom of 65.29 U/ml; milk of 113.82 U/ml; rice of 102.39 U/ml; tomato of 140.41 U/ml; wheat of 314.21 U/ml.

Electrocardiogram: early ventricular repolarization of sinus rhythm reverse clock transposition.

Painless enteroscopy: colonoscope into the terminal ileum: entering the terminal ileum about 10cm, did not continue to enter due to much residual stool, with short flat mucosal villi and no erosion and ulcer. Scattered patchy mucosal edema, fuzzy vascular texture and soft biopsy were visible in descending colon, sigmoid colon and rectum. (Figure 1)

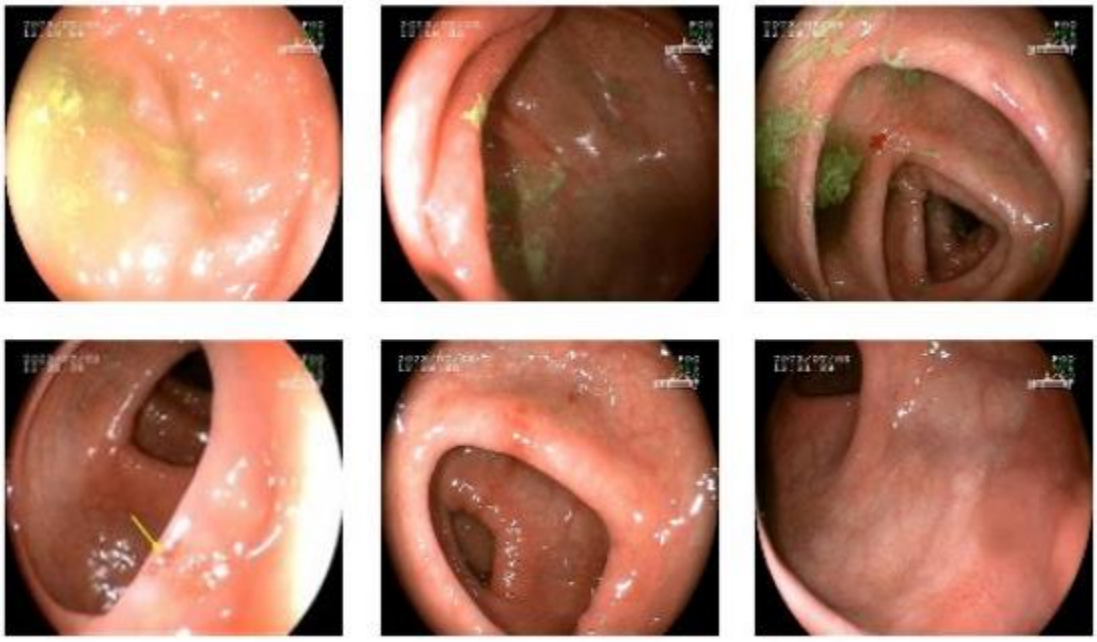

Figure 1: Painless enteroscopy

Painless gastroscopy: revealed chronic atrophic gastritis (C2) and suspected duodenitis. (Figure 2)

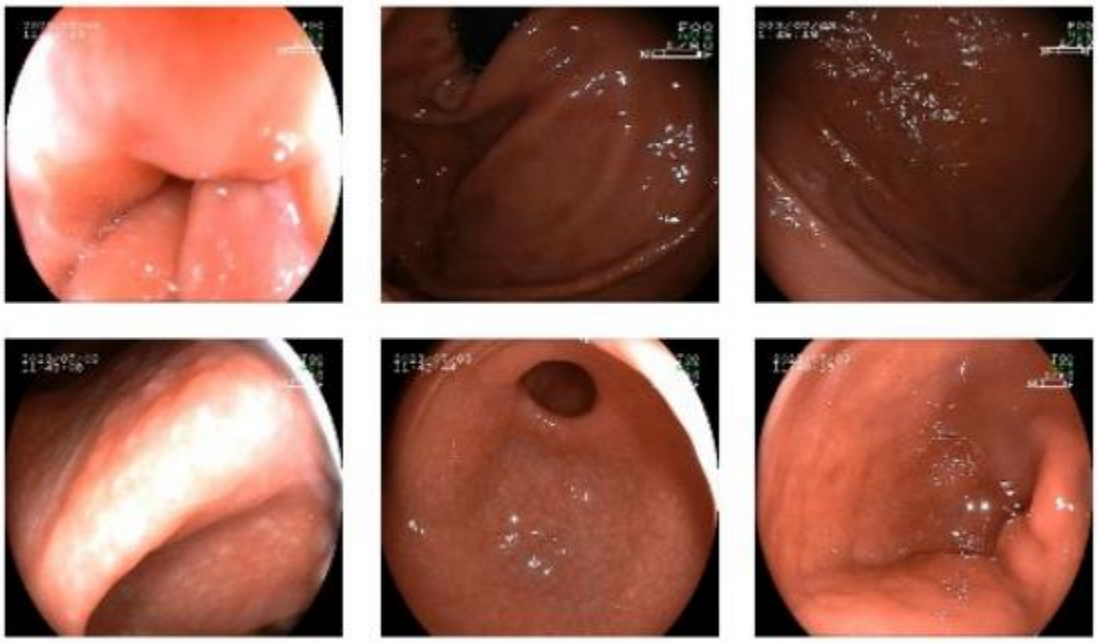

Figure 2: Painless gastroscopy

Enteroscopy pathology: revealed chronic active inflammation in the terminal ileum and mucosal chronic inflammation in the descending colon. (Figure 3 and Figure 4)

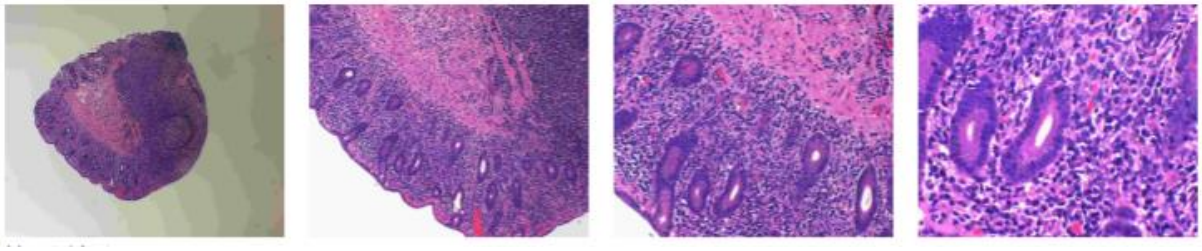

Figure 3: The pathological examination of colonoscopy showed chronic active inflammation in the terminal ileum

Notes : Microscopic examination of intestinal mucosal tissues revealed the following findings: In the terminal ileum, there was no heteromorphism of the crypts, but an increased number of interstitial lymphocytes and plasma cell infiltration, with local lymph follicle formation. Similarly, the ileocecal region showed no crypt heteromorphism, but an increased presence of interstitial lymphocytes and plasma cell infiltration, along with local lymph follicle formation. The ascending colon exhibited crypts without heteromorphism and more interstitial lymphocytes and plasma cell infiltration. The transverse colon displayed similar findings, with crypts without heteromorphism, more interstitial lymphocytes, plasma cell infiltration, and local lymph follicle formation. The descending colon revealed a localized defect in the mucosal surface, alongside crypts without heteromorphism, an increased number of interstitial lymphocytes, and plasma cell infiltration. Lastly, the sigmoid colon also showed crypts without heteromorphism, an increased presence of interstitial lymphocytes, and plasma cell infiltration.

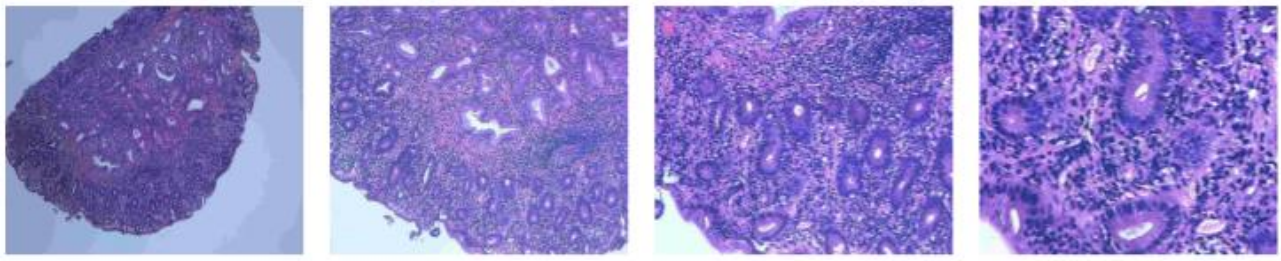

Figure 4: The pathological examination of colonoscopy showed mucosal chronic inflammation in the descending colon

Notes: Microscopic examination of intestinal mucosal tissue from different segments of the jejunum revealed the following findings: In the jejunal polyp, there were polypoid lesions with submucosal hyperplasia of mucous glands and interstitial lymphocyte infiltration. In the proximal jejunum, the mucosa showed widening of the intestinal villi, hyperplasia of interstitial lymphoid tissue, lymph follicle formation, small granulomas, and infiltration by numerous lymphocytes, plasma cells, and scattered neutrophils, with no malformed crypts. Similar findings were observed in the middle and distal

jejunum, where there was widening of the small intestinal villi, hyperplasia of interstitial lymphoid tissue, lymph follicle formation, small granulomas, and infiltration by lymphocytes, plasma cells, and scattered neutrophils, with no abnormal crypts noted.

Gastroscopic pathology: Microscopic examination revealed chronic active inflammation with erosion in the descending duodenum mucosa, and some glands exhibited low-grade adenomatous hyperplasia. Special staining showed positive results for AB and PAS. In the gastric antrum, chronic gastritis with mild inflammation was observed, and immunohistochemistry showed Helicobacter pylori negative. (Figure 5)

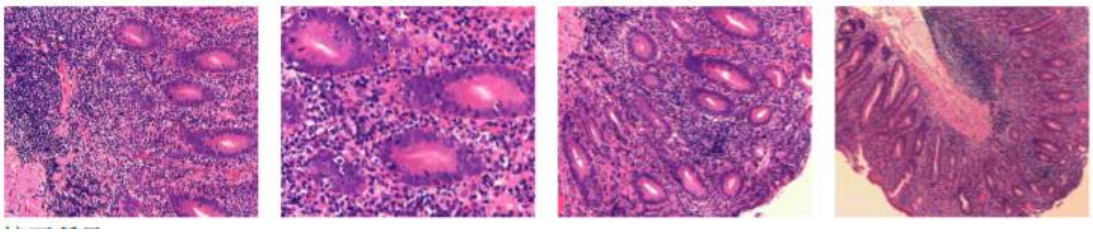

Figure 5: Gastroscopic pathology

Notes: Naked eye observation revealed two gray-white lesions in the descending duodenum, each with a maximum diameter of 0.2 cm, and two similar lesions in the gastric antrum, with diameters ranging from 0.2 to 0.3 cm. Microscopic examination of the descending duodenum showed intestinal mucosal tissue with surface epithelium featuring long, rod-shaped nuclei, and extensive interstitial infiltration of both acute and chronic inflammatory cells. In the gastric antrum, the mucosal structure was preserved, with epithelial hyperplasia of the gastric pits and minimal interstitial infiltration of lymphocytes.

By combining with age, family history, clinical manifestations and laboratory examination, the patient was finally highly suspected with adult autoimmune enteropathy. In order to confirm the diagnosis, the gastrointestinal autoantibody spectrum was further examined, and multiple pathological specimens were sent to Peking Union Medical College Hospital for pathological consultation, and the results returned the consideration of adult autoimmune enteropathy.

Treatment: Following the confirmed diagnosis, the patient was administered 40 mg of intravenous methylprednisolone once daily for 2 weeks. To support intestinal health, compound glutamine enteric-coated capsules were prescribed to nourish the intestinal mucosa, and bacillus subtilis enteric-coated capsules were used to regulate the intestinal flora. Entecavir capsules were given for anti-hepatitis B virus therapy. Additionally, calcium supplementation, a proton pump inhibitor (PPI) for gastric protection, and nutritional support were provided as part of the symptomatic treatment. The diarrhea of the patient was significantly reduced, and the stool was improved from 5-9 times of watery stools to 2-3 times of loose stools, and the appetite was improved. After discharge, the above medication regimen was switched to take 40 mg of prednisone tablet once a day for 2 weeks, with the instruction to reduce prednisone dose by 5mg every 2-4 weeks.

Follow-up: After 3 months, the dose of prednisone was reduced to 20 mg once a day for maintenance treatment, and the patient had loose stools 2-3 times a day and slight body weight gain of 5kg, with body weight maintained at about 55kg. After half a year, the patient tried to stop the use of hormone drug, but the diarrhea was repeated. After 8 months, the patient received a flora transplantation in the other hospital, but he still had repeated diarrhea after the transplantation, and his body weight decreased by 5kg, and he continued to maintain 20 mg of prednisone tablet. After 1 year of follow-up, he was still given 15mg of hormone maintenance, with loose stools once or twice a day, and mesenteric vein thrombosis was found on reexamination abdominal CT, and anticoagulant therapy with rivaroxaban tablet was added. The patient is still under regular follow-up.

Discussion

Adult autoimmune enteropathy (AIE) is primarily diagnosed using the criteria established by Mayo Medical Center in 2007 [6], which include the following: 1) adult chronic diarrhea (duration >6 weeks); 2) malabsorption syndrome; 3) specific small intestinal pathological findings such as partial or complete villus atrophy, increased deep crypt lymphocytes, increased crypt apoptosis, and elevated intraepithelial lymphocytes; 4) exclusion of other causes of villus atrophy, such as Crohn's disease, stomatitis diarrhea, and intestinal lymphoma; 5) positive anti-enterocyte and/or anti-goblet cell antibodies; 6) items 1–4 are essential for diagnosing AIE. The presence of AE or AG antibodies is a crucial diagnostic criterion, but the absence of these antibodies does not rule out AIE. The patient in this case was a 32-year-old male who presented with intractable diarrhea that did not improve after multiple visits to another hospital, where he received acid suppression, stomach protection, and antidiarrheal treatments. Given the positive results of multiple laboratory tests for food intolerance, multidisciplinary consultation was requested for further clinical evaluation. Following this, the gastrointestinal autoantibody spectrum was tested, returning positive results. Additionally, further pathological confirmation was recommended, and the results from an authoritative hospital confirmed the diagnosis.

The patient presented with typical refractory diarrhea and had received treatment at several hospitals before being referred to our institution, but his symptoms showed minimal improvement despite treatments involving diarrhea relief, intestinal flora regulation, stomach protection, spasmolysis, and gastric motility promotion. Upon admission, further tests, including autoantibody screening, gastrointestinal endoscopy, and pathology, were conducted to explore the underlying cause of the diarrhea. Based on the diagnostic criteria for adult autoimmune enteropathy, and by integrating the clinical data with test results, AIE was highly suspected. The condition was differentiated from other causes of small intestinal villus atrophy, including celiac disease, Whipple's disease, small intestinal bacterial overgrowth, acquired immune deficiency syndrome (AIDS), lymphoma, and others. The diagnosis was ultimately confirmed through pathological examination and genetic testing. This diagnosis clarified the cause of the patient's refractory diarrhea, and after symptomatic supportive treatments such as glucocorticoid anti-inflammation, entecavir for hepatitis B virus, digestive enzyme supplementation, correction of electrolyte imbalances, mucosal repair

promotion, and acid suppression for stomach protection, the patient's condition remained stable.

AIE is a rare and unexplained intestinal disease caused by abnormal expression of X chromosome FOXP3 gene coding and loss of regulations of regulatory T cells and effector T cells, leading to excessive immune stress [7]. The incidence rate of AIE is less than 1/100,000, which is more common in infants under 6 months of age [3]. In recent years, it has also been found in adults, but all of them are case reports or case summaries [3-4,6,8]. AIE mainly involves the small intestine, with the proximal small intestine obviously involved, and the colon may also be involved. Patients with AIE are often complicated with severe malabsorption and hypoalbuminemia, and they have chronic refractory diarrhea, electrolyte disorder and severe malnutrition, with endoscopic manifestation of small intestinal villus shortening, histopathological changes such as villus atrophy, lamina propria inflammatory cell infiltration, goblet cell reduction, visible apoptotic bodies and so on [2,9]. Therefore, in clinical work, it is necessary to pay attention to the significance of multi-point biopsy of duodenal mucosa by gastroscopy.

AIE is a rare disease and its diagnosis needs to be made with caution, with the exception of other diseases that can cause small intestinal villus atrophy, especially celiac disease and intestinal lymphoma. Celiac disease is often characterized by a positive celiac disease-associated antibody spectrum, and it can be endoscopically manifested as small intestinal villi shortening, and it is mostly pathologically manifested as markedly increased mucosal intraepithelial lymphocytes, with the presence of goblet cells and Paneth cells [10]. Intestinal lymphoma often shows multiple deep ulcers under endoscopy, but it can present with only minor changes, and the diagnosis is pathologically dependent [1]. Currently, AIE-related autoantibodies tests have been increasingly emphasized by scholars, and it is hoped that more convenient and accurate serum detection methods can be introduced and promoted to help diagnose the disease more conveniently and quickly in clinical practice.

In summary, AIE is rare and a heterogeneous disease characterized by severe refractory diarrhea and immune-mediated gastrointestinal injury in combination with other autoimmune-related diseases. Although anti-intestinal epithelial cell antibodies and anti-cup cell antibodies have been found in most cases, their presences are non-specific and cannot be used for the diagnosis of AIE. The histological manifestations of AIE are very different, and there are many similarities with other immune-related diseases. Therefore, the diagnosis of AIE is difficult, which must be considered in conjunction with medical history, clinical symptoms, endoscopic changes, histological and serological examinations.

Conclusion

Adult AIE is a rare and complex disease characterized by chronic, refractory diarrhea and immune-mediated gastrointestinal damage, often accompanied by other autoimmune conditions. Despite its clinical similarities with other diseases causing small intestinal villus atrophy, such as celiac disease and intestinal lymphoma, AIE can be differentiated through careful evaluation of medical history, clinical symptoms, endoscopic findings, histological changes, and serological tests, particularly the presence of specific autoantibodies. This case highlights the challenges of diagnosing AIE, as the patient presented with significant weight loss and refractory diarrhea over six months, along with abnormal autoantibody levels and food intolerance, which were crucial in guiding the diagnosis. Comprehensive testing, including pathological examination and genetic testing, was essential to rule out other potential causes, ultimately confirming the diagnosis of AIE. This case underscores the importance of a multidisciplinary approach in diagnosing and managing this rare condition, and emphasizes the need for increased awareness and diagnostic methods to improve patient outcomes in clinical practice.

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