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CASE REPORT

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Waldmann's disease: Primary intestinal lymphangiectasia diagnosed by 99mTc-labeled albumin macroaggregate scintigraphy—A case report in an adult patient

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Key Clinical Message

Rare yet significant, this case sheds light on the uncommon presentation of Waldmann's disease in adults, showcasing the diagnostic challenges it poses. A multidisciplinary approach, integrating clinical, endoscopic, histological, and radiological evaluations, is crucial for accurate diagnosis and management. Further research is needed to deepen our understanding of this complex disorder.

Abstract

Waldmann's disease, or primary intestinal lymphangiectasia, is a rare disorder characterized by protein-losing enteropathy due to dilation and leakage of intestinal lymphatic vessels. Although typically diagnosed in early childhood, we present a case of a 55-year-old male with a complex medical history. The patient's history included intestinal obstruction, multidrug-resistant pulmonary tuberculosis, and primary antiphospholipid syndrome. He presented with a 2-year history of chronic diarrhea, weight loss, and lower limb edema. Endoscopic and histological examination revealed scattered white spots in the duodenum and terminal ileum, indicative of intestinal lymphangiectasia. Nuclear medicine studies confirmed abnormal protein loss. The rarity of Waldmann's disease in adulthood and its association with other significant medical conditions pose diagnostic challenges. The distinct endoscopic and histological findings, coupled with scintigraphy results, contribute to a comprehensive understanding of this complex case. Differential diagnoses and management considerations are discussed. This case highlights the atypical presentation of Waldmann's disease in adulthood, emphasizing the importance of a multidisciplinary approach for accurate diagnosis and management. Further research is warranted to enhance our understanding of this uncommon disorder and its potential implications for patients with complex medical histories.

KEYWORDS
chronic diarrhea, nuclear medicine scintigraphy, primary intestinal lymphangiectasia, protein-losing enteropathy, Waldmann's disease

1 | INTRODUCTION

Waldmann's disease, or primary intestinal lymphangiectasia, was first described in 1961.[1] It is a rare disorder of unknown etiology that causes protein-losing enteropathy.[2] The condition is characterized by the dilation and leakage of intestinal lymphatic vessels, leading to hypoalbuminemia, hypogammaglobulinemia, and lymphopenia.[3] The symptoms of the disease depend on the severity and location of the affected lymphatic vessels, ranging from mild edema in the lower extremities to generalized edema, ascites, pleural effusion, chronic diarrhea, among others.[1] While it typically develops in early childhood, we present the case of a 55-year-old male.

2 | CASE REPORT

A 55-year-old male with a medical history of intestinal obstruction, multidrug-resistant pulmonary tuberculosis, completing a 2-year course of anti-tuberculosis treatment, and primary antiphospholipid syndrome with a dual risk factor, undergoing daily warfarin therapy, in addition to the amputation of the left upper limb 10, 9, and 6 years ago, respectively. The patient presented a 2-year history of chronic diarrhea with a progressive increase in frequency of liquid stools, associated with approximately 5% weight loss in the last 6 months, and generalized lower limb edema occurring on two occasions.

During the physical examination, the patient exhibited a low normal body mass index (17.4 kg/m^2), xerosis, generalized mucocutaneous pallor, pronounced lines of expression, increased intestinal peristalsis, muscle mass loss, atrophy of the thenar and hypothenar eminences, and hyporeflexia. Additionally, there was pitting edema of ++ severity in the lower limbs, reduced trophism in the examined limbs, and diminished reflexes.

Laboratory examinations revealed: In the complete blood count, absolute lymphopenia was observed. Severe hypoalbuminemia and mild hypokalemia were detected in the blood chemistry panel, along with hypovitaminosis attributed to reduced vitamin B12 levels. The general stool examination showed no abnormalities, and fecal calprotectin was within normal limits. Both the cuproculture and Kinyoun staining were negative. Gen Xpert molecular tests for *Clostridium* and *Mycobacterium tuberculosis* returned negative results. Immunological profiling revealed hypocomplementemia in both C3 and C4, with alterations noted in the quantification of immunoglobulins E, G, and M. These findings are detailed in Table 1.

Imaging examinations: Abdominal computed tomography showed no abnormalities. Upper gastrointestinal endoscopy was unremarkable, and lower gastrointestinal endoscopy revealed dispersed white spots with a 'snowflake' appearance at the level of the terminal ileum were observed (Figure 1). A biopsy was taken, and the report indicates dilation of vessels with a lymphatic appearance in the lamina propria, associated with a moderate amount of plasma cells and distortion of the villi: intestinal lymphangiectasia (Figure 2). A nuclear medicine study was conducted: a scintigram for the detection of intestinal protein loss revealed an abnormal concentration of the radiotracer in the left flank in intestinal projection in the late views, confirming intestinal protein loss (Figure 3).

This disease causes a major loss of proteins owing to intestinal lymphangectasia. Thus, besides albumins (as was the case in our situation), important serum proteins such as immunoglobulins are also reduced, leading to acquired humoral immunodeficiency, which not only predisposes to anasarca but also results in increased susceptibility to infections, thus increasing both morbidity and mortality associated with the condition. Interestingly, these patients show an altered intestinal microbiota, because of chronic severe diarrheal state, favoring growth of bacteria from the fluid phase and from translocation and, probably, yeasts as well. In fact, during the last hospitalization she developed septic shock secondary to bacterial translocation, which ultimately led to their fatal outcome.

2.1 | Methodology

The case presented involves a patient with a complex condition who was ultimately diagnosed with intestinal lymphangiectasia, a rare disease characterized by excessive loss of proteins through the lymphatic vessels of the small intestine. This disorder can lead to serious complications due to protein deficiency and the loss of other important blood components.

The diagnostic approach was meticulous, considering a variety of possible causes for the patient's symptoms, such as extrapulmonary tuberculosis, autoimmune diseases like Crohn's disease and systemic lupus erythematosus, as

TABLE 1 Results table from laboratory tests, clinical and microbiology laboratory, Manolo Morales Peralta Hospital.

Name of test		Name of test		Name of test	
Hb (g/dL)	13.5	Glucose (mg/dL)	78	ASCA	Negative
Hct (%)	39.5	Creatinine (mg/dL)	0.54	Anti-TG2 IgA	Negative
Platelet ($\times 10^9$/L)	370,000	**Protein (g/dL)**	**4.12**	Anti-DPG IgA	Negative
WBC ($\times 10^9$/L) mm^3	5910	**Albumin (g/dL)**	**1.45**	EMA IgA	Negative
Neutrophils ($\times 10^9$/L)	4970	Bilirubin (mg/dL)	0.80	**C3/C4 complement (g/L)**	**0.4/0.2**
Lymphocytes ($\times 10^9$/L)	**537**	AST/ALT (U/L)	27/30	Anti-Smith	12.7
Eosinophils	7	LDH (U/L)	414.30	Anti-dsDNA	11.6
PT/PPT (s)	16/37	Urine protein (mg/24 h)	98	ANA	Negative
INR	2	Procalcitonin (ng/mL)	0.37	**Fecal occult blood**	**Negative**
B12 vitamin (pg/mL)	50	PCR	Negative	**Fecal calprotectin (µg/g)**	**75**
Sodium (mEq/L)	137	**HIV-1/HIV-2**	**Negative**	**Coprocultive**	**Negative**
Potasium (mEq/L)	**3.1**	**IgE (mg/dL)**	**44.7**	**Kinyoun stain**	**Negative**
Corrected calcium (mg/dL)	8.6	**IgG (mg/dL)**	**600**	**Gene Xpert *C. difficile* of stool**	**Negative**
Chlorine (mEq/L)	96.7	**IgM (mg/dL)**	**13.60**	**Gene Xpert MTB/RIFG4 of stool**	**Negative**

Note: Bold values serve as a means of highlighting abnormal test results.

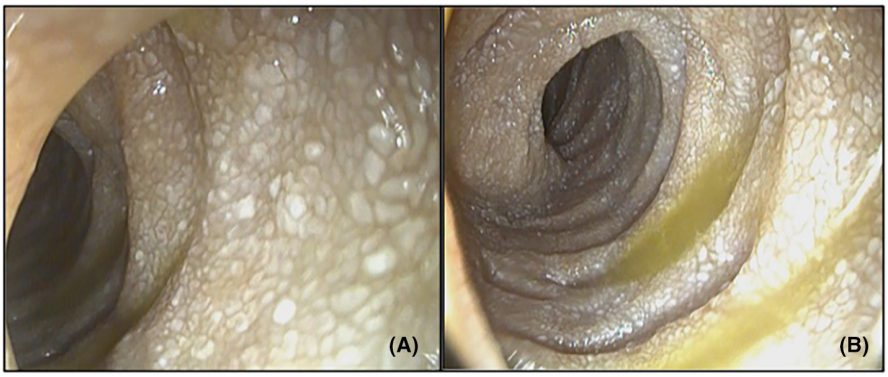

FIGURE 1 (A, B) Mucosa of the second portion of the duodenum with scattered white spots resembling "snowflakes" at the level of the terminal ileum. Endoscopy Department, Manolo Morales Peralta Hospital, Managua, Nicaragua.

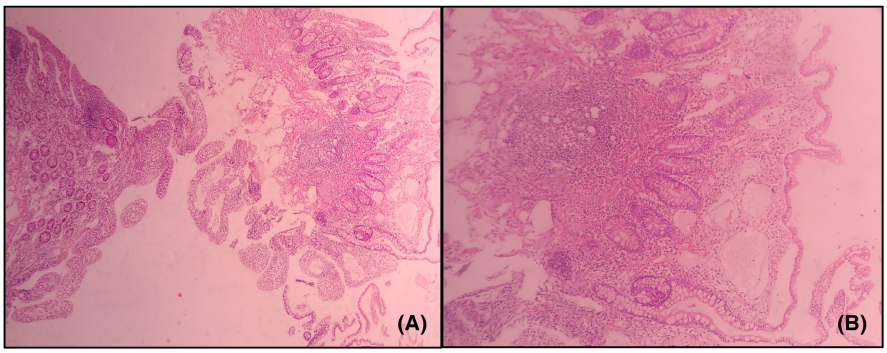

FIGURE 2 (A) H&E 10×. Distorted intestinal villi. (B) H&E 40×. Dilation of lymphatic vessels. Pathology Department, Manolo Morales Peralta Hospital—Q 5635-22. Managua, Nicaragua.

well as primary immunological disorders. The observation of characteristic lesions in the small intestine, resembling "snowflake-like flakes," during endoscopic evaluation was crucial in reaching the diagnosis.

Once the histopathological diagnosis of intestinal lymphangiectasia was established, it was necessary to confirm the abnormal protein loss at the intestinal level. Therefore, "99mTc-labeled Albumin Macroaggregate Scintigraphy" was performed, which not only confirmed the losses but also localized the sites of greatest leakage, mainly in the terminal ileum, where snowflake-like lesions were found.

Patient management focused on symptomatic treatment, as there is no specific therapy for this disease. A

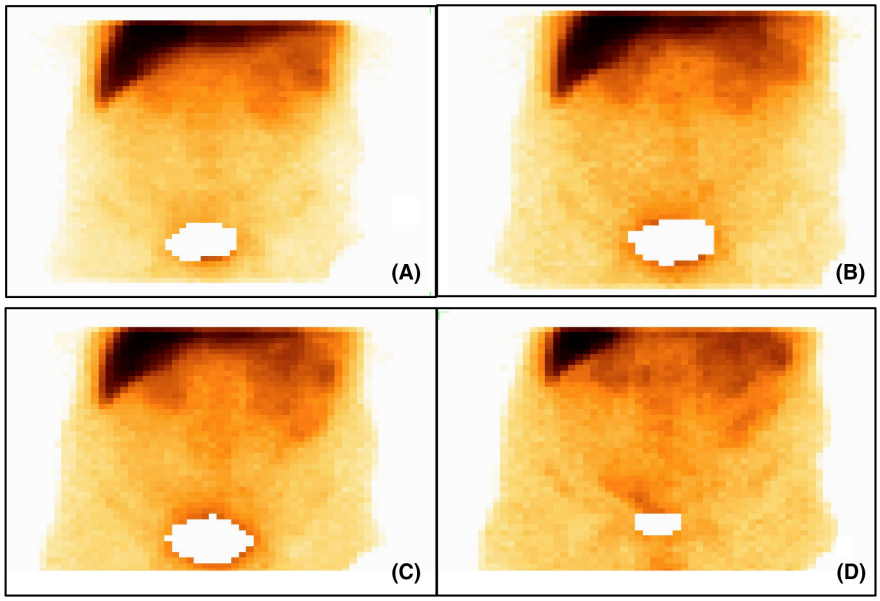

FIGURE 3 Scintigram with 99mTc-labeled albumin macroaggregate. (A) Hour 1, early phase, physiological uptake in the liver and spleen. (B) Hour 2. (C) Hour 3. (D) Hour 4, late phase, abnormal concentration of the radiotracer in the left flank in intestinal projection. Nuclear Medicine Department, National Center of Radiotherapy—Managua, Nicaragua.

high-protein diet was implemented, and human albumin was administered to address protein deficiency. However, despite these efforts, the patient experienced progressive deterioration and developed infectious complications that contributed to a fatal outcome.[6]

It is crucial to highlight that intestinal lymphangiectasia is a disease with a variable but potentially severe prognosis that can limit the patient's life expectancy. Management focuses on relieving symptoms and preventing complications, but it is not always effective in halting disease progression. In some cases, such as this one, a fatal outcome is unfortunately a possibility, especially when severe complications occur.[6]

3 | DISCUSSION

The rarity of Waldmann's disease in adulthood and its association with other significant medical conditions pose diagnostic challenges. The distinct endoscopic and histological findings, coupled with scintigraphy results, contribute to a comprehensive understanding of this complex case. Currently, the sensitivity and negative predictive value of HSA scintigraphy labeled with 99mTc make it superior to Alpha 1 antitrypsin clearance in the diagnosis of protein-losing enteropathy (PLE). In view of the easy application, lack of adverse effects, wide availability, and rapid results, we recommend 99m Tc-labeled HSA scintigraphy as a method initial diagnostic tool for patients with PLE. Finally, it is necessary to integrate clinical evaluation, endoscopic, histological, and radiological characteristics, to make an accurate diagnosis of PLE case.[4,5] Differential diagnoses and management considerations are discussed.

4 | CONCLUSION

This case highlights the atypical presentation of Waldmann's disease in adulthood, emphasizing the importance of a multidisciplinary approach for accurate diagnosis and management. Further research is warranted to enhance our understanding of this uncommon disorder and its potential implications for patients with complex medical histories.

AUTHOR CONTRIBUTIONS

Alex José Castellón Méndez: Conceptualization; data curation; funding acquisition; writing – original draft. **Allan Bodán Campbell:** Conceptualization; investigation; resources; supervision. **Victor Rosales Obregón:** Conceptualization; data curation; investigation; project administration; resources; writing – review and editing. **Mohammed Zahran:** Conceptualization; methodology; project administration; resources; supervision; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflicts of interest with any organization regarding the article submitted for publication.

DATA AVAILABILITY STATEMENT

We commit to ensuring the availability and confidentiality of the information related to the presented clinical case. Our priority is to safeguard patient privacy and adhere to the highest ethical standards in handling medical information. All clinical documentation will be protected and used solely for educational and academic discussion purposes.

ETHICS STATEMENT

This involves the description of a clinical case. It is not a clinical trial, and no experimentation has been conducted on animals or humans. The authors of this manuscript have adhered to the protocols of our workplace (Manolo Morales Peralta Hospital) for the publication of clinical cases, and patient anonymity has been preserved.

CONSENT

Written informed consent was obtained from the patient and their family to publish this report in accordance with the journal's patient consent policy.

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