Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Medicine

Exudative Enteropathy Revealing Waldmann's Disease: A Rare Case Report

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DOI: 10.36347/sjmcr.2024.v12i04.008 | **Received:** 28.02.2024 | **Accepted:** 07.04.2024 | **Published:** 09.04.2024

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Abstract **Case Report**

Introduction: Waldmann's disease, or primary intestinal lymphangiectasia (PIL), is an uncommon condition characterized by digestive lymphatic dilatations, predominantly observed in the pediatric population and rarely in adults. First described in 1961, its etiology remains unknown, and it presents with diverse manifestations, from chronic diarrhea to ascites. Diagnosis involves intestinal biopsies and radiological assessments, with treatment primarily focused on dietary modifications and, in exceptional cases, surgery. ***Observation***: This report details a unique case of Waldmann's disease diagnosed in a 52-year-old man with a history of type 2 diabetes. Presenting with a complex clinical picture including generalized edematous syndrome, chronic diarrhea, and ascitic manifestations, the patient underwent a comprehensive diagnostic evaluation ruling out renal, hepatic, and cardiac causes. Endoscopic examinations revealed multiple duodenal lymphangiectasias, supporting the diagnosis of exudative gastroenteropathy. The patient responded positively to dietary interventions with medium-chain triglycerides, showing a significant regression of symptoms. ***Discussion***: Waldmann's disease, a rare pathology with unknown prevalence, typically manifests in early childhood. However, the case presented here highlights the atypical onset in adulthood, emphasizing the importance of considering this diagnosis in cases of exudative enteropathy with an early onset. Clinical signs, including lower limb edema, chronic diarrhea, and visceral effusions, may vary, making a definitive diagnosis challenging. Diagnostic modalities such as imaging, biopsies, and specialized tests like Alpha-1 antitrypsin clearance play a crucial role in confirming the condition. Complications, including the risk of neoplasia and immunological abnormalities, require vigilant follow-up. Treatment primarily involves medical and dietary approaches, with encouraging results. Surgical resection may be considered in limited forms, and management failure could necessitate parenteral nutrition or alternative pharmacological interventions. ***Conclusion***: Waldmann's disease, though rare, should be considered in adults presenting with exudative enteropathy, especially given the potential risk of B-type non-Hodgkin's lymphoma. This case underscores the importance of recognizing atypical presentations and implementing tailored therapeutic strategies for improved patient outcomes. Regular monitoring is essential to detect and manage potential complications effectively.

Keywords: Exudative enteropathy, Waldmann, Lymphangiectasia, Diarrhea, Hypoproteinemia.

INTRODUCTION

Waldmann's disease or primary intestinal lymphangiectasia (PIL) is a rare condition in the pediatric population, very rare in adults, of unknown etiology, characterized by digestive lymphatic dilatations. Waldmann *et al*., first described 18 cases of "idiopathic hypercatabolic hypoproteinemia" in 1961 [1]. The prevalence of clinically relevant PIL is not known [2, 3].

It can be presented in a variety of forms, from chronic diarrhea to ascites or undernutrition. Intestinal biopsies and radiology have an important role in the diagnosis of this pathology. Treatment is based on the administration of medium-chain triglycerides and, exceptionally, surgery.

We report the case of a patient diagnosed with Waldmann's disease at the age of 52.

OBSERVATION

This is a 52-year-old man with a history of type 2 diabetes on insulin. He presented with a generalized edematous syndrome consisting of bilateral, soft, painless, bucketing edema of the lower limbs, moderate ascites and scrotal edema, associated with chronic watery

diarrhea evolving for 6 years. Biological tests revealed significant hypoproteinemia at 35g/l with hypoalbuminemia at 18 g/l, lymphopenia at 700 elements/mm3 and hypogammaglobulinemia.

Radiologically, abdominal ultrasound and thoracoabdominal CT scan with injection revealed moderate ascites and pleurisy.

As part of the etiological assessment of the edematous syndrome causes by the hypoproteinemia and hypoalbunemia, we ruled out an exhaustive assessment to eliminate the 3 main causes: renal, hepatic and cardiac.

To rule out loss of renal origin, we carried out a 24-hour proteinuria test, which came back normal.

We also eliminated hepatocellular insufficiency since the liver was normal in the abdominal ultrasound, and the liver biological work-up was normal.

For the cardiac cause, we performed a trans-thoracic echocardiography, which revealed a small pericardial effusion with good cardiac function.

We also performed an exhaustive assessment of chronic diarrhea including anti-endomisium anti-transglutaminase autoantibodies which were negative, as well as anti-retroviral serology and phtisiology tests. The endoscopic workup consisted of colonoscopy and EOGD. EOGD revealed a gastritis with pre-pyloric ulceration and multiple bulbar and duodenal lymphangiectasias (Fig1.); biopsies were free of abnormalities. Colonoscopy was without abnormalitie

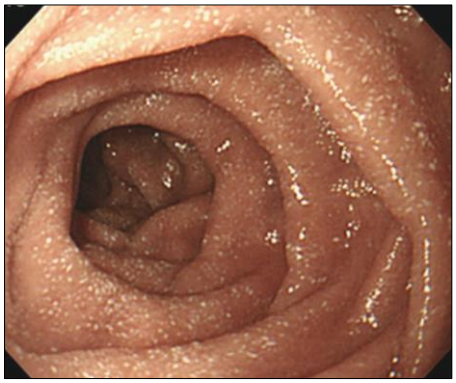
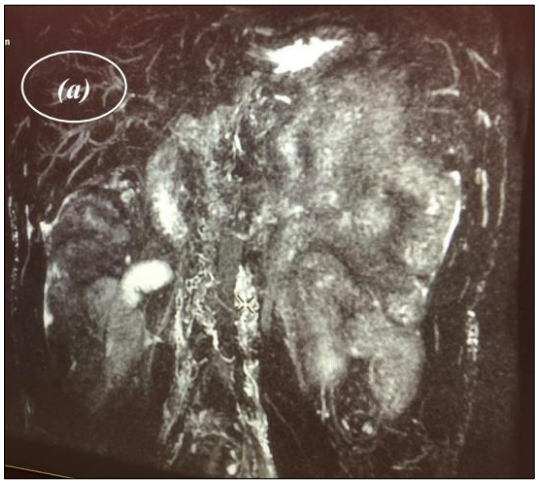


Fig. 1: **Endoscopic image showing lymphangiectasias in D2**

At this stage, the diagnosis of exudative gastroenteropathy was strongly suggested in view of the digestive loss of protein, after eliminating other causes of protein loss.

In order to confirm the diagnosis of exudative gastroenteropathy, we performed the determination of Alpha-1 antitrypsin clearance which was very high (>2206, 08mg/24h).

As part of the etiological assessment of entero exudative gastropathy, we performed a lympho-MRI, especially in the presence of duodenal lymphangiectasia on EOGD. The lympho-MRI showed significant lymphatic ectasia, most marked in the retroperitoneal area, with no obstruction to the lymphatic pathway, which primarily evokes Waldmann's disease (Fig 2).



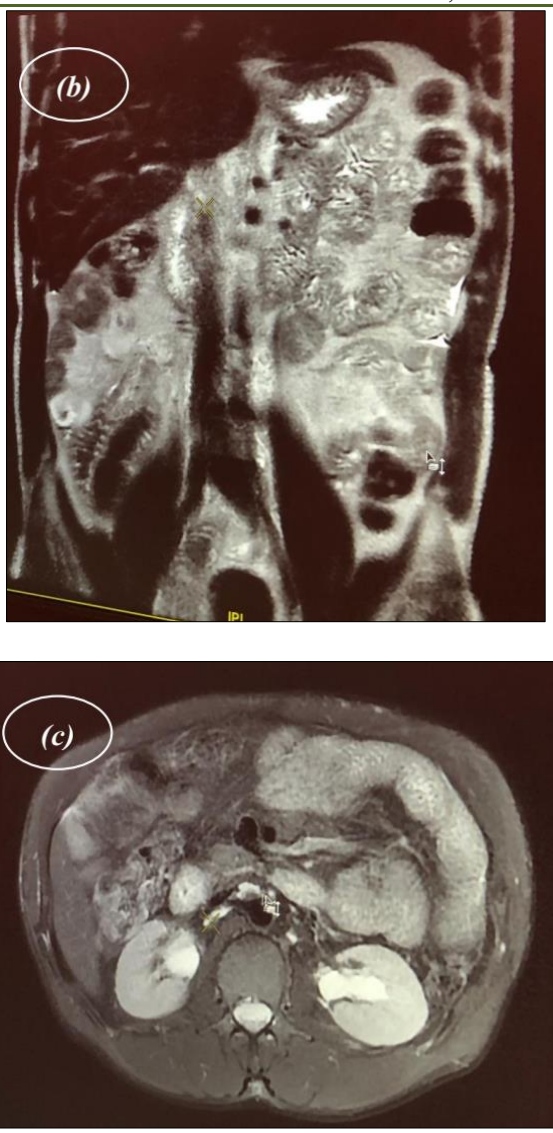


Fig. 2: Lympho-MRI showing significant lymphatic ectasia, most marked in the retroperitoneal area, in coronal (a, b) and transverse (c) sections

The patient was put on a diet low in long-chain fats, with the addition of medium-chain triglycerides.

The evolution was marked by a clear regression of oedema after 8 weeks of diet. We plan to keep a close clinical, biological and endoscopic monitoring, especially given the risk of lymphomatous complications such as digestive or extradigestive B lymphomas

DISCUSSION

Waldmann's disease, or primary intestinal lymphangiectasia (PIL), is a very rare pathology of unknown etiology, characterized by digestive lymphatic dilatations leading to intraluminal lymphatic leakage responsible for exudative gastroenteropathy with hypoalbuminemia, lymphopenia and hypo-gammaglobulinemia [4].

The prevalence of Waldmann's disease is unknown. It is a rare disease. More than 300 cases have been described in the literature, but it would appear that the prevalence is increasing as diagnostic methods become more refined, enabling the diagnosis of frustrating presentations [5]. The cause of PIL remains unknown to this day. Abnormalities in the regulation of genes involved in the development of the lymphatic system have been reported: VEGFR3 (vascular endothelial growth factor receptor 3), PROX1 (prospero-related homeobox-transcriptional factor), FOXC2 (forkhead transcriptional factor), SOX18 (sex-determining region Y-box) [6].

The disease is usually diagnosed before the age of 3, with occasional widespread and lethal digestive forms [7-9].

Clinical data are not always specific, and may be labile over time, in a disease that evolves in relapses [10, 11], hence the delay in diagnosis of this polymorphous clinical entity, particularly in less severe

forms. In our patient, the diagnosis was made in adulthood, at the age of 52, which means 6 years after the onset of the initial symptomatology, essentially chronic diarrhea followed by the appearance of an edematous and ascitic syndrome. The discovery of the disease at the age of 52 makes our case unique, and leads us to consider this diagnosis in the face of a clinical and biological picture of exudative enteropathy with a very early onset, given the risk of lymphomatous complications such as digestive or extradigestive B lymphomas.

The most suggestive triad of the disease is the combination of lower limb edema, chronic diarrhea and visceral effusions. However, any combination of clinical signs is possible. Edema is by far the most frequent sign, and can in itself summarize the clinical picture. They are present in almost 80% of cases [12-10]. According to Waldmann and al. their severity depends more on the extent of lymphatic involvement than on the depth of hypoproteinemia [12]. Edema can range from isolated limb edema to hydrops. Lymphedema due to lymphatic involvement is less frequent. Typically, they are asymmetrical, affecting a single limb in most cases, often the lower limb. On clinical examination, it is not always easy to distinguish hypoproteinemia-related edema from lymphedema. Stemmer's sign, which is almost pathognomonic, confirms the diagnosis of lymphedema (if it affects the foot) by showing an inability to pinch the skin on the dorsal surface of the second toe [13]. This sign is very important to be aware of, so as to enable early diagnosis and begin specific management to avoid complications of the disease.

Biologically, hypoproteinemia is constant, global and non-selective. Hypocholesterolemia is often present. Lymph leakage through the gastrointestinal tract is responsible for hypo-albuminemia, hypogammaglobulinemia, hypocalcemia and lymphopenia of TD4 lymphocytes, responsible for immunological disturbances that explain the risk of infection [14]. The severity of the disease is probably due to the extension of lymphangiectasia into the digestive tract. This is confirmed by increased alpha-1 antitrypsin clearance and normal xylose tests. Intestinal or duodenal biopsies confirm the diagnosis, showing dilatation of intestinal lymphatics from the submucosa and mucosa to the apex of the villi. There is no villous atrophy or inflammatory infiltrate. Occasionally, the macroscopic appearance may be suggestive of a whitish, puffy appearance of the digestive villi. This macroscopic appearance was found in our patient. Biopsies may be negative, as lesions may be highly localized and segmental, as in our patient's case [4-15].

Video-capsule enteroscopy can help diagnose primary or secondary digestive lymphangiectasia, particularly when unguided systematic duodenal biopsies are negative. It can individualize more distal forms of Waldmann's disease or secondary intestinal lymphangiectasias. Histological confirmation of these distal forms is provided by biopsies taken during double balloon enteroscopy [16]. Ultrasound and CT scans are useful for eliminating secondary lymphangiectasia [15]. Ultrasound provides indirect data in children and adults: dilatation of a digestive loop, regular and diffuse thickening of the intestinal wall, thickening of the folds, mesenteric edema, ascites [17]. In adults and children, abdominopelvic CT with contrast injection may show diffuse or sometimes nodular parietal thickening of the small bowel wall due to edema. Digestive dilatation may be visible, giving rise to the halo sign [18, 19].

Complications of Waldmann's disease are essentially represented by the occurrence of neoplasia, mainly lymphoid. On average, cancerous processes appear 10 to 15 years after the onset of enteropathy [20]. This type of complication requires regular follow-up of the patient, even when the disease is relatively stable. Our patient will be scheduled for six-monthly follow-up consultations.

The second complication is immunological abnormalities affecting the B and T cell lineages. Damage to the B cell line is characterized by a decrease in immunoglobulins (IgG, A, M) and a reduced antibody response to antigenic stimuli, with a major risk of infection [21]. Treatment of Waldmann's disease is essentially medical and dietary, based on a diet low in long-chain fats. The addition of medium-chain triglycerides and enrichment with proteins and fat-soluble vitamins provide the essential organic requirements [22]. Results on the diet are generally excellent.

In our case, our patient's profession made the task easier, as he is a chef, and so he was able to follow the diet without difficulty, which produced good results with the regression of edema after 8 weeks on the diet.

In the event of failure, exclusive parenteral nutrition may be used [22], or treatment with octreotide (200 mg-2/d) or antiplasmins, whose efficacy is inconsistent [23].

In limited forms of the disease, surgical resection may be indicated with a favorable outcome [16].

CONCLUSION

Waldmann's disease is a rare exudative enteropathy of lymphatic origin, the majority of cases detected having started in early childhood. This diagnosis should be considered in adults, given the risk of B-type non-Hodgkin's lymphoma.

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