Primary Intestinal Lymphangiectasia: A Case Report

Ridwaan Albeiruti[1]*, MD, Patrick Gleeson[2], MD, Theodore Kelbel[3], MD, Tracy Fausnight, MD[3]

[1]Department of Medicine, West Virginia University, Morgantown, WV; Department of Internal Medicine, College of Human Medicine, Michigan State University, Grand Rapids, MI, USA; [2]Department of Internal Medicine, Temple University, Philadelphia, PA, USA; [3]Helen DeVos Children's Hospital, Spectrum Health, Grand Rapids, MI, USA

Corresponding Author: Ridwaan Albeiruti; albeiru4@msu.edu

Abstract: *Primary intestinal lymphangiectasia (Waldmann's disease) is a rare protein-losing enteropathy which is mostly seen in young children. A 22-month-old male baby presented with a 1-week history of abdominal distension, chronic loose stools, recurrent ear infections, and failure to thrive. He had edematous eyelids and non-pitting edema of his hands and feet. The patient was diagnosed via endoscopic visualization and biopsy of the lymphangiectasia in the small bowel. He was managed through dietary restriction with a high-protein, low-fat diet. The patient subsequently had resolution of the diarrhea and an increase in albumin and total protein on labs. We describe a rare case of primary intestinal lymphangiectasia and highlight its clinical presentation, diagnosis, and treatment.*

Keywords: *primary intestinal lymphangiectasia; Waldmann's disease; protein-losing enteropathy*

INTRODUCTION

Primary intestinal lymphangiectasia, also known as Waldmann's disease, is a rare protein-losing gastroenteropathy which is seen in young children. Its prevalence is unknown. It is believed to be caused by congenital malformation of intestinal lymphatic vessels. Patients will typically present with diarrhea, edema, failure to thrive, and frequent infections. While there is no cure, it is managed through dietary restrictions which include a low-fat, high-protein diet. The following is a case of primary intestinal lymphangiectasia seen in a 22-month-old male baby.

Case Report

A 22-month-old male baby was admitted to the pediatric surgery department with a 1-week history of abdominal distention and concern for bowel obstruction. His symptoms began 2 weeks before presentation with fever and vomiting. Those symptoms resolved over several days, but he subsequently developed abdominal distention. The patient had a history of chronic loose stools exacerbated by dairy products. His mother denied difficulty passing urine, blood or mucus in the stools, abdominal pain, episodes of crying, or respiratory symptoms. He had hypothyroidism but no history of urinary, kidney, or cardiac disease. In addition, he had a history of recurrent ear infections requiring myringotomy tube placement, and the recent history of presumed viral gastroenteritis. Developmentally, he did have delays in gross motor skills having started crawling at 13 months and walking at 19 months. There was no family history of gastrointestinal disease or malabsorption syndromes. His only medication was levothyroxine. All immunizations were up to date. The patient's mother had an unremarkable, term pregnancy with uneventful delivery with no complications. Of note, meconium was passed within the first 12 h after birth.

On physical exam, the patient had normal vital signs with both height and weight between the 25th and 50th percentiles. He had edematous eyelids and non-pitting edema of the hands and feet. His abdomen was soft and distended with diffuse tenderness but no guarding. There were no abdominal masses, hernias, or organomegaly. There was no lymphadenopathy. The rest of the physical exam was normal.

An abdominal ultrasound revealed a dilated, fluid-filled bowel throughout the abdomen with mild bowel wall thickening suggestive of gastroenteritis, small bowel intussusception, and a small amount of free fluid. A Complete Blood Count (CBC) with differential showed lymphopenia with an absolute lymphocyte count of 1.00 K/uL, but was otherwise normal. Liver function testing showed a very low albumin of 1.1 g/dL and a very low total protein of 2.8 g/dL. A stool alpha-1-antitrypsin was very high at 570 mg/dL. Immunoglobulin G (IgG)

Table 1. Pertinent laboratory findings.

Laboratory studies	Patient	Reference ranges
Absolute lymphocyte count	1.00 K/uL	3.0–9.5 K/uL
Albumin	1.1 g/dL	3.5–5.0 g/dL
Total protein	2.8 g/dL	6.3–7.9 g/dL
Stool alpha-1-antitrypsin	570 mg/dL	≤54 mg/dL
IgG	159 mg/dL	313–1170 mg/dL
IgA	22 mg/dL	36–79 mg/dL

and Immunoglobulin A (IgA) were low at 159 and 22 mg/dL, respectively (Table 1).

Hospital course

An upper endoscopy was unremarkable. However, a lower endoscopy revealed colonoscopic visualization of lymphangiectasia, and biopsy findings were consistent with the diagnosis. The patient was advised to start a high-protein, low-fat diet with avoidance of dairy products. He subsequently had resolution of the diarrhea and an increase in albumin and total protein on repeat labs.

Final diagnosis

Waldmann's disease (primary intestinal lymphangiectasia).

DISCUSSION

Waldmann's disease or primary intestinal lymphangiectasia is a protein-losing enteropathy caused by dilatation and subsequent rupture of lymphatic channels, or lacteals, in the small intestinal wall. Most cases present before 3 years of age but may be diagnosed in adulthood. The disease is rare and of unknown etiology.[1,2] The pathophysiology is unknown, but a possible mechanism is lymphatic channel malformation in the neonatal period, leading to increased intraluminal pressure within the lacteals, eventually causing dilatation, rupture, and subsequent release of lymphatic contents into the bowel.[3] The consequent loss into the bowel of albumin, immunoglobulins, lymphocytes, and chylomicrons – containing triglycerides and fat-soluble vitamins – account for the observed clinical manifestations of this disease.

Clinical manifestations of Waldmann's disease are mostly due to the protein-losing enteropathy. Peripheral edema due to hypoproteinemia is the most common clinical characteristic. The edema is pitting and often found in the lower extremities bilaterally, but edema in the face and external genitalia may be observed in severe cases. Patients may have serous effusions into the pleural, pericardial, or peritoneal cavities. Anasarca is rare but has been reported. Less commonly, lymphedema is observed, resulting in a non-pitting edema usually in the distal lower extremities bilaterally.[1] Persistent, moderate, watery diarrhea is another common presenting feature. Abdominal complications are due to hypoproteinemia or bowel wall edema due to dilated lymphatic vessels. Hypoproteinemia can cause ascites, leading to abdominal distention. Bowel wall edema may lead to mechanical ileus due to decreased lumen size, an abdominal mass, or intussusception.[4]

Nonspecific systemic symptoms, failure to thrive, and developmental delay may be observed as a result of diarrhea, hypoproteinemia, and malabsorption of fat-soluble vitamins. Recurrent and opportunistic infections are seen in patients with significant hypogammaglobulinemia and lymphopenia. Cases of cryptococcal meningitis, cryptococcal osteomyelitis, cryptosporidium or viral gastroenteritis, necrotic enterocolitis, and necrolytic migratory erythema have been reported.[5]

The diagnosis requires endoscopic visualization of lymphangiectasia in the small bowel followed by characteristic pathologic findings on biopsy. Pathologic findings include the presence of lacteal contents, dilated lymphatic vessels, and an absence of villous atrophy or microorganisms. Laboratory investigation may strongly suggest the diagnosis. Decreased total protein and albumin, hypogammaglobulinemia, and lymphopenia are frequent findings. The humoral defect manifests as decreased levels of IgG, IgA, and Immunoglobulin M (IgM), whereas cellular immunity defect is frequently observed as CD4+ lymphopenia. A highly suggestive finding is high 24-h stool α1-antitrypsin due to enteric protein loss. Stool α1-antitrypsin has replaced albumin scintigraphy as the preferred test for protein loss. Abdominal ultrasound may show nonspecific features, such as bowel wall thickening, dilated bowel loops, ascites, intussusception, and plical hypertrophy. Abdominal computed tomography (CT) shows small bowel wall thickening and edema. CT may be particularly helpful in localizing the area of lymphangiectasia in the small bowel. Capsule endoscopy can also describe the extent of lymphangiectasia as it traverses the entirety of the small bowel.[6]

The differential diagnosis includes many conditions that have intestinal lymphangiectasia and protein-losing enteropathy as a secondary feature. These include constrictive pericarditis, sarcoidosis, surgical repair of congenital heart disease, Crohn's disease, Whipple's disease, intestinal lymphoma, intestinal tuberculosis,

and radiation or chemotherapy with retroperitoneal fibrosis.[6] A thorough history and physical exam are usually sufficient for ruling out secondary causes, and a small bowel biopsy is helpful in some cases.

The primary treatment is a high-protein, low-fat diet rich in medium chain triglycerides. Medium chain triglycerides are absorbed directly into the portal venous circulation, bypassing chylomicron transport and thereby avoiding lacteal engorgement. This diet provides protein and fat while limiting dilatation and rupture of the lacteals. Patients may have clinical and laboratory recovery within several weeks of initiating the diet. The need for this dietary control appears to be lifelong.[6,7] Other treatment suggestions have not been highly validated. Antiplasmin and octreotide may alter lymphatic permeability or absorption to attenuate lacteal engorgement, but are not well-supported therapies. Surgery may be effective for removing bowel with localized lymphangiectasia but is only indicated in rare cases. Albumin infusion is sometimes used for symptomatic relief of edema caused by hypoproteinemia.[1] Antimicrobial prophylaxis may be considered in patients with recurrent infections, although dietary control usually improves clinical immunologic function in these patients.[5]

CONCLUSION

Primary intestinal lymphangiectasia or Waldmann's disease is a rare protein-losing gastroenteropathy seen in young children, likely caused by congenital malformation of intestinal lymphatic vessels. Clinical manifestations include edema, persistent diarrhea, failure to thrive, developmental delay, and recurrent infections. A detailed history and physical exam are essential as there are numerous secondary causes of intestinal lymphangiectasia. A targeted laboratory investigation may be highly suggestive of the disease, although diagnosis requires endoscopic visualization and biopsy of the small bowel. Treatment consists of a low-fat, high-protein diet rich in medium chain triglycerides.

Learning Points

- Primary intestinal lymphangiectasia (Waldmann's disease) is a rare protein-losing gastroenteropathy seen in young children caused by congenital malformation of intestinal lymphatic vessels.
- Symptoms include edema, persistent diarrhea, failure to thrive, developmental delay, and recurrent infections.
- To diagnose, endoscopic visualization and biopsy of the small bowel is required.
- Treatment consists of lifelong low-fat, high-protein diet that is rich in medium chain triglycerides.

Conflict of interest and funding

The material presented is original, has not been previously published, and has not been submitted for publication elsewhere. All authors have no conflicts of interest. Authors R.A. and P.G. contributed equally to this article. The authors have not received any funding or benefits from industry or elsewhere to conduct this study.

References

1. Vignes S, Bellanger J. Primary intestinal lymphangiectasia (Waldmann's disease). Orphanet J Rare Dis 2008; 3: 5. doi: 10.1186/1750-1172-3-5

2. Wen J, Tang Q, Wu J, Wang Y, Cai W. Primary intestinal lymphangiectasia: four case reports and a review of the literature. Dig Dis Sci 2010; 55(12): 3466–72. doi: 10.1007/s10620-010-1161-1

3. Hokari R, Kitagawa N, Watanabe C, Komoto S, Kurihara C, Okada Y, et al. Changes in regulatory molecules for lymphangiogenesis in intestinal lymphangiectasia with enteric protein loss. J Gastroenterol Hepatol 2008; 23(7 Pt 2): e88–95. doi: 10.1111/j.1440-1746.2007.05225.x

4. Katoch P, Bhardwaj S. Lymphangiectasia of small intestine presenting as intussusception. Indian J Pathol Microbiol 2008; 51(3): 411–12.

5. Dierselhuis MP, Boelens JJ, Versteegh FG, Weemaes C, Wulffraat NM. Recurrent and opportunistic infections in children with primary intestinal lymphangiectasia. J Pediatr Gastroenterol Nutr 2007; 44(3): 382–5. doi: 10.1097/01.mpg.0000233192.77521.2f

6. Ingle SB, Hinge Ingle CR. Primary intestinal lymphangiectasia: minireview. World J Clin Cases 2014; 2(10): 528–33. doi: 10.12998/wjcc.v2.i10.528

7. Xinias I, Mavroudi A, Sapountzi E, Thomaidou A, Fotoulaki M, Kalambakas A, et al. Primary intestinal lymphangiectasia: is it always bad? Two cases with different outcome. Case Rep Gastroenterol 2013; 7(1): 153–63. doi: 10.1159/000348763