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Case Report

Home parenteral nutrition a life-saving therapy in a primary intestinal lymphangiectasia patient affecting the entire GI tract – 3 year follow-up case report

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ABSTRACT

Introduction and Importance: Primary intestinal lymphangiectasia (PIL) is a rare protein-losing gastroenteropathy of unknown etiology, characterized by impaired lymphatic vessels drainage. The pathological changes in PIL result in usually localized or diffuse dilatation of intestinal lacteals, leading to leakage of lymphatic fluid rich of proteins, lymphocytes, and immunoglobulins into the intestinal lumen. PIL may be asymptomatic or mildly symptomatic in moderate forms of the disease. In some patients, though, the outcome may be poor or even life-threatening. This case report demonstrates the severity of protein malnutrition, in some cases, and the extent of GI tract affected, requiring to start PN early and the need for its continuation as home parenteral nutrition (HPN).
Case presentation: We present a case of 39-year-old male with Factor V Leiden deficiency, who presented initially with symptoms of malnutrition and anasarca. The diagnosis was confirmed by histopathological findings pathognomonic for PIL from biopsies of the stomach, small intestine and colon.
Clinical discussion: The patient was started on low fat, high protein parenteral nutrition from the beginning of the treatment and required a long-term HPN for 3 years, because trials of tapering off and discontinuation of PN led to worsening of the biochemical results and recurrence of symptoms. Patient gradually improved and stabilized with persistent nutritional support.
Conclusions: The presented case report shows the magnitude of nutritional support (HPN) needed for severe PIL patients. HPN offers PIL patients with poor outcome and life-threatening complications a chance to improve and lead a normal life.

1. Introduction

Primary Intestinal Lymphangiectasia (PIL), commonly known as Waldmann's disease, was first described in 1961, is a rare protein-losing gastroenteropathy characterized by the impaired drainage of lymphatic vessels [1]. In the clinical setting, the prevalence of late-onset primary intestinal lymphangiectasia cases has increased. Among the main symptoms of PIL, an intermittent diarrhea, nausea, vomiting and bilateral lower limb edema are observed. The intensity of the edema can vary, with pleural or pericardial effusion, chylous ascites up to anasarca. Other clinical manifestations of PIL are malnutrition, weight loss with lack of body weight regain, steatorrhea, malaise, abdominal pain or symptoms associated with fat-soluble vitamin deficiencies [2]. Laboratory tests results are similar to other gastroenteropathies: hypoproteinemia, hypoalbuminemia, decreased serum concentrations of IgG, IgA, IgM, transferrin, and ceruloplasmin. Small bowel contrast studies may show thickened and nodular folds that simulate "stacked coins" [3]. Endoscopic findings show scattered white spots, having a

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"snow-flake-like" appearance over the small intestinal mucosa [4]. Histological analysis is very characteristic and reveals markedly dilated lymphatic vessels that are most apparent on the tips of the small intestine villi. Other examinations such as computed tomography (CT scan), capsule endoscopy, double balloon enteroscopy with biopsy, albumin scynthygraphy and lymphoscynthygraphy could be useful but have limited diagnostic value. Exclusion diagnostic criteria should include: cardiac diseases, intestinal lymphoma, Whipple's disease, sarcoidosis, intestinal tuberculosis, Crohn's disease, infection, toxic substances and systemic sclerosis.

Treatment of PIL is similar to that of other protein losing enteropathies. A low-fat, high-protein and medium-chain triglyceride (MCT) supplemented diet plays a crucial role [5]. In patients with deficiencies in calcium or fat-soluble vitamins (A, D, E, K), a supplementation with mentioned macro-elements and vitamins is necessary along with the long-term nutritional support, such as parenteral nutrition (PN).

We report a comprehensive clinical study of a 39-year old male who was admitted to the hospital because of PIL with an adult onset - a diagnosis made based on the clinical manifestations, laboratory, radiological and pathological findings. We discuss clinical presentation, report patient management with emphasis on parenteral and enteral nutrition. We also show the magnitude of home parenteral nutrition (HPN) crucial for some PIL patients to return to their health. HPN offers PIL patients with poor outcome and life-threatening complications a chance to improve and lead a normal life. The work has been reported in line with the SCARE 2020 criteria [6].

2. Case Presentation

A 39-year-old male was admitted to the Gastroenterology Department at Poznan University of Medical Sciences, Heliodor Swiecicki Clinical Hospital with facial edema, bilateral upper and lower extremity edema, ascites, limited pleural effusion, Terry's nails (Fig. 1a–c) and fatigue. Symptoms have gradually appeared and intensified over the past month before admission. Laboratory evaluation confirmed low serum concentration of protein, hypoalbuminemia, hypogammaglobulinemia, hyperfibrinogenemia, high levels of platelets as well as vitamin B12, vitamin D and iron deficiencies (Table 1). Prior to admission, the patient had right subclavian and jugular vein thrombosis and was diagnosed with Factor V Leiden thrombophilia. Myeloproliferative disorders, lymphomas, and other neoplasms were excluded. He was treated with acenocoumarol with optimization of INR in therapeutic range between 2.0 and 3.0 with resolution of thrombotic symptoms.

Patient was generally in a good health before the symptoms of anasarca started, he had no allergies to food or medication and his family history was unremarkable. He was a nonsmoker, only occasionally drunk alcohol and did not use recreational drugs. Patient was married, had two healthy children and worked as a typesetter in a printing company. He did not have any previous interventions or surgeries.

Table 1
Patient's biochemical parameters at the diagnosis and after 3 years of HPN.

BIOCHEMICAL PARAMETERS	HOME PARENTERAL NUTRITION		NORMS
	BASELINE	AFTER 3-YEARS	
Total protein level [g/dl]	2.84	5.8	6.4–8.3
Albumins [g/dl]	0.73	2.9	3.5–5.2
Gammaglobulins [g/dl]	0.18	0.5	0.6–1.2
Hemoglobin [g/dl]	10.6	12.1	13.5–17.2
Red blood cells [x10^6/μl]	3.2	3.9	4.2–5.8
Iron [μg/dl]	31	66	59–158
Ferritin [ng/ml]	46	107	30–400
Platelets [x10^3/μl]	750	550	140–400
Creatinin [mg/dl]	0.4	0.38	0.7–1.2
HDL [mg/dl]	18	25	>35
Alanine Transaminase [U/l]	22	16	10–41
Aspartate Aminotransferase [U/l]	26	11	10–37
Bilirubin [mg/dl]	0.01	0.09	<1.2
Alkaline phosphatase [U/l]	45	147	40–130
Gamma-glutamyl transpeptidase [U/l]	21	113	8–61
CRP [mg/l]	74	6.1	<5
Fibrinogen [mg/dl]	>1275	1284	200–393
Vitamin B12 [pg/ml]	163	243	191–663
Vitamin D - 25 OH [ng/ml]	6	32	30–80

Endoscopic evaluation of the upper GI revealed an edematous mucosa within the stomach and duodenum (Fig. 2). Histopathology revealed edematous stroma, covering 2/3 of the mucosa with dilated lacteals, evidence of intestinal lymphangiectasia both in the stomach (Fig. 3a) and duodenum (Fig. 3b–c). Colonoscopy revealed numerous

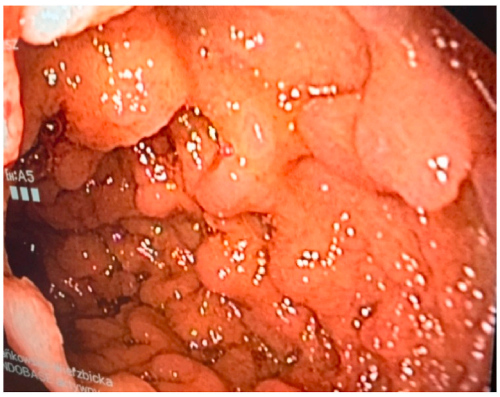
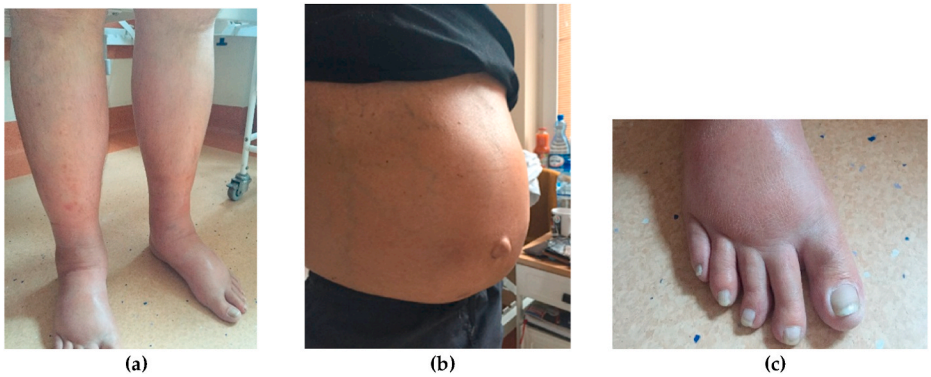


Fig. 2. Endoscopic view of lymphangiectasia in the duodenum with edematous and cobblestone mucosa.



(a) (b) (c)

Fig. 1. Bilateral lower extremity edema (a), ascites (b), Terry's nails (c).

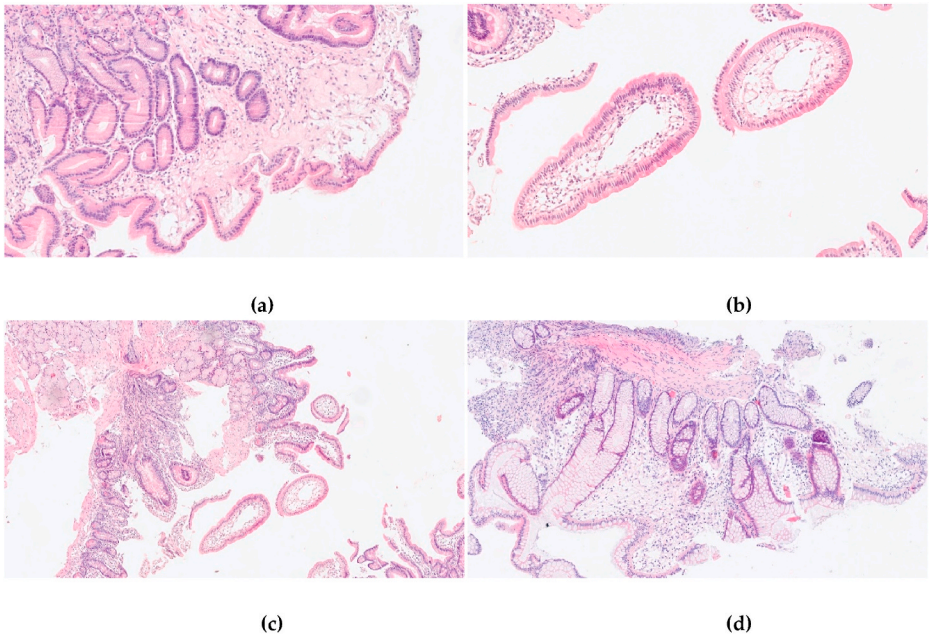


Fig. 3. Biopsy samples - hematoxylin and eosin (H&E) staining method: gastric mucosa revealing marked submucosal lymphangiectasia with edema, magnification 10× (a), duodenal mucosa with dilated lymphatics in intestinal lymphangiectasia, magnification 16× (b), duodenal mucosa with dilated lymphatics involving mucosa and submucosa, magnification 6× (c), colonic mucosa with disturbed architecture and edema of mucosal stroma, magnification 10× (d).

polyps around the splenic flexure and transverse colon. Biopsy of the polyps, suggested hyperplasia with moderate edema of the mucosal stroma and histopathology confirmed PIL in the colon (Fig. 3d). Magnetic resonance (MR) enterography revealed enhanced outer layer of jejunum and ileum showing continuous involvement of the whole small intestine and thickening of the colonic wall (Fig. 4a–b). Echocardiography, QuantiFERON test and Flow Cytometry-FCM were performed to rule out secondary causes of lymphangiectasia.

After diagnosis of PIL, high protein, low-fat and low-triglyceride enteral nutrition (EN) was initiated; semi-elemental formula in combination with parenteral nutrition (PN), in the „All in One" (AIO) system according to individually prepared admixtures. Single admixture was prepared based on the ESPEN Guidelines [7]. The composition of AIO bag included proteins, fats (20% from MCT/LCT), carbohydrates (glucose), water- and fat-soluble vitamins, trace elements, as well as omega-3 fatty acids supplement with a 10–20% ratio of fatty acids. Protein requirement was assessed individually based on a formal nutritional assessment. Our patient's prescription provided 1.2–1.5g of protein 0.19–0.24g of nitrogen/kg/day. Additionally, the oral diet was enriched with semi - elemental formula (Nutrison Advanced Peptisorb Powder - Nutricia, Milupa Gmbh, Fulda, Germany). The patient had shown gradual improvement with persistent nutritional support when hospitalized and was discharged with HPN. During 3 years of HPN patient was followed-up at regular visits in the outpatient nutritional therapy clinic every three months and was admitted to the hospital every year during the three-year follow-up period for more thorough evaluations. No metabolic complications were observed, patient symptoms gradually improved and stabilized which allowed him to return to his daily routine and work.

3. Discussion

In patients with the diagnosis of PIL prognosis varies. PIL may be asymptomatic or mildly symptomatic in moderate forms of the disease

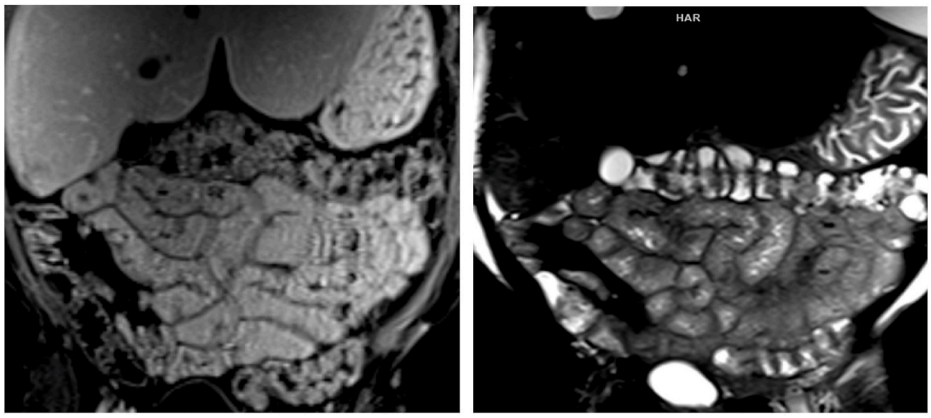


Fig. 4. MR enterography T1 weighted image with contrast enhancement, feathery thickening with enhancement of the small intestinal mucosa (a), MR enterography T2 weighted image (HASTE), thickening of the folds of the stomach, duodenum, jejunum and the colonic wall with features of swelling (b).

or in patients who follow a low-fat diet. In some patients, though, the outcome may be poor or even life-threatening when voluminous serous effusion (pleural, pericardial), ascitis or anasarca spontaneously recure, after low-fat diet withdrawal.

In regards to treatment options, diet therapy remains the cornerstone. A lifelong diet therapy of low-fat, high MCT, high protein content and vitamin supplements has to be implemented. The oral diet is the mainstay of treatment, based on high protein content due to enteric protein loss from leaky lymphatics and MCT as they are directly absorbed into the portal venous system and avoids lacteal overloading. Enriched in fatty soluble vitamins diet should be followed with limited content of long-chain fatty acids that are absorbed by damaged lacteals leading to the chyli engorgement, rupture of malformed lymphatic vessels and worsening of lymphatic hypertension [8]. A diet with MCT improves the symptoms of PIL and reduces mortality rate [9]. Aoyagi et al. [10] reviewed nine patients with intestinal lymphangiectasia; patients who did not respond to a low-fat diet, were treated with TPN or EN with elemental diet and polymeric diet. EN could be as effective as TPN providing a safe alternative therapy for patients with PIL but not in our case - due to chronic intestinal failure EN was not sufficient enough, therefore we had to combine EN + PN. If an improvement is not observed, partial or TPN should be considered to re-establish a basic nutritional status. PN allows to restore nutritional macro and microelement deficiencies.

Patient's severity of protein malnutrition, TPL 2.84 g/dl, albumins 0.73 g/dl and the extent of affected GI tract, required a start of PN from the beginning and it had to be continued as HPN over the next 3 years after discharge, because trials of tappering off and discontinuation of PN led to worsening of the biochamical results and recurrence of symptoms.

In such protein deficiency, the oral nutrition, even with a semi-elemental diet was not sufficient enough to cover energy and protein demand. Hence, an EN was treated as trophic nutrition, while PN was the main source of nutrients, vitamins and trace elements. PN was conducted in the AIO system according to individually prepared admixtrues. Aggressive management of the disease, in combination with early start of PN, restored patient's proper nutritional status.

Other forms of therapy include antiplasmin therapy, corticosteroids, small bowel resection, peritoneovenous (Levine) shunt, octreotide and intestinal transplant are of limited efficacy.

This report has limitations, since there has not been such severe PIL case reported in publications, affecting the entire GI tract, further studies are needed to know if the diet and long-term HPN treatment we chose for our patient was as effective in other severe cases of PIL and if it would also resolve their clinical symptoms, improve quality of life and cause return to their general health. It would also be good to go into further clinical observation of amino acid and organic acid profile tests which could possibly clarify and allow to get to the bottom of what was the cause of PIL in the first place and be able to better treat such patients.

4. Conclusions

Our patient with factor V Leiden deficiency and PIL present in the entire GI tract after continuous 3 years of HPN treatment and oral diet supplemented with enteral semi-elemental diet, gradually improved and stabilized. The parameters of nutritional status have also significantly improved with near complete resolution of ascites and extremitie edema. We observed a dramatic improvement of patient's clinical state and quality of life, which allowed him to return to his daily routine and work. Such severe PIL case affecting the entrie GI tract has never been previously reported in literature and has never been successfully treated with resolution of all symptoms. With diet and customized HPN therapy we were able to normalize such severe protein, albumin and vitamin deficiencies with no adverse effects or metabolic complications. HPN offers PIL patients with poor outcome and life-threatening complications a chance to improve and lead a normal life.

4.1. Patient perspective

The life-long diet therapy of low-fat, high MCT, high protein content and vitamin supplementation, as well as, advantages and possible complications of long term home parenteral nutrition were explained to the patient. He agreed to that treatment option. The patient had shown gradual improvement with persistent nutritional support during hospitalization and continued to improve while at home on HPN. He was educated and trained by a gastroenterologist involved in initiation and treatment of enteral and parenteral nutrition, as well as HPN. He was ecstatic that he was feeling good and especially from the fact that he was able to return to his daily routine and work. Because of the fact, he was feeling well again, and his anasarca symptoms resolved with HPN, he was adherent and compliant with the diet and long-term HPN therapy.

Ethical approval

N/a.

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Author contribution

Conceptualization, D.M-W.; methodology, K.I. and K·K-K.; investigation, D.M.W. and K·K.; resources, D.M-W. A.W. and M.K.; writing—original draft preparation, D.M-W., M.K., M.A.K. and A.W.; writing—review and editing, D.M-W., M.S-M., M.A.K.; visualization, D. M-W. and M.S-M.; supervision, A.D. All authors have read and agreed to the published version of the manuscript.

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3. Hyperlink to your specific registration (must be publicly accessible and will be checked): **N/a.**

Guarantor

Marcin A. Kucharski and Dorota Mańkowska-Wierzbicka.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Provenance and peer review

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Declaration of competing interest

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2021.102483.

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