

Intestinal lymphangiectasia associated with chylothorax and multiple lower extremity arteriovenous malformation: A case report and literature review*

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Abstract

Intestinal lymphangiectasia (IL) is an uncommon protein losing enteropathy, characterized by small intestinal mucosa or serosa lymphangiectasia and intestine lymph loss. Currently, IL is a very rare disease in children or adults, with typical clinical symptoms including hypoalbuminemia, absolute lymphocyte reduction, ascites, edema, etc. We report a case of an adult with intestinal lymphatic ectasia accompanied by chylothorax and multiply arteriovenous malformations of the hip and lower extremity. CT and MRI revealed diffuse edema and thickening of the small intestine, accompanied by splenomegaly and pleural effusion. Extensive nodularity of lower ileum and the ileocecal region could be seen during intestinal endoscopy. Finally, small intestinal lamina propria lymphangiectasis was confirmed by pathological examination. To raise awareness of the disease, here we compare our case and those previously reported, and discuss the diagnosis and management of IL.

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Intestinal lymphangiectasia (IL) is clinically uncommon protein losing enteropathy that often is caused by lymphatic malformation in the small intestine. The disease occurs more commonly in children than in adults. We report a 46-year-old male patient suffering from IL, accompanied by chylothorax and lower extremity arteriovenous malformation, which has been reported rarely in the literature previously.

Case report

The patient was a 46-year-old man who had experienced chest tightness and fatigue, which were aggravated by exercise, for a month with no obvious cause; he also reported melena, 3 times per day. In addition, he had a history of inguinal hernia surgery and hemorrhoids. He had no history of tumor, trauma or other medical problems. He presented with an anemic appearance and poor

mental condition. Arteriovenous malformation could be seen on the hip and low extremity. Initial laboratory values were: WBC 2.97×10^9 /L, N 79.8%, L 11.4%, Hb 52.0 g/L, serum calcium 2.01 mmol/L, serum protein quantification: total protein 43.2 g/L, albumin 24.9 g/L, globulin 18.3 g/L, serum IGG 4.2 g/L, IGA 0.66 g/L, IGM 0.21 g/L; T-sport (-). Examination of the pleural fluid revealed pale pink chylous fluid. Liver and kidney function were normal. Tumor markers (CEA, CA-199, and CA-125) were within normal limits. Chest CT revealed bilateral pleural effusion (Fig. 1), small intestine dual-phase CT revealed diffuse edema of intestinal wall with localized nodular mucosa, increased mesenteric lymph nodes and splenomegaly (Fig. 2); T2-weighted fat suppression MRI of intestine revealed small mesenteric edema, thickening and edema of small bowel wall, and a small amount of ascites (Fig. 3); endoscopy revealed edema of the mucosa of the small intestinal and ileum and extensive nodularity

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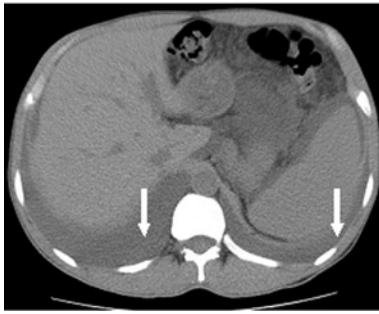


Fig. 1 Chest CT scan. A small pleural effusion (white arrow) bilaterally

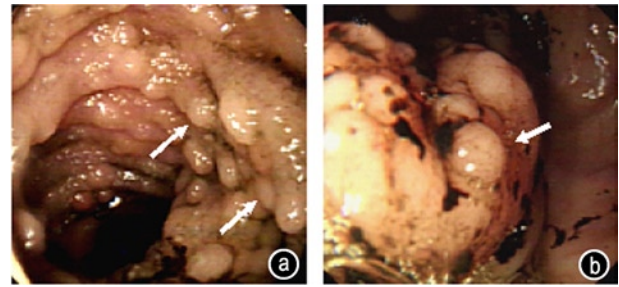


Fig. 4 Endoscopy revealed mucosal edema of the small intestinal and ileum (a) and ileocecal (b) extensive nodularity (white arrow)

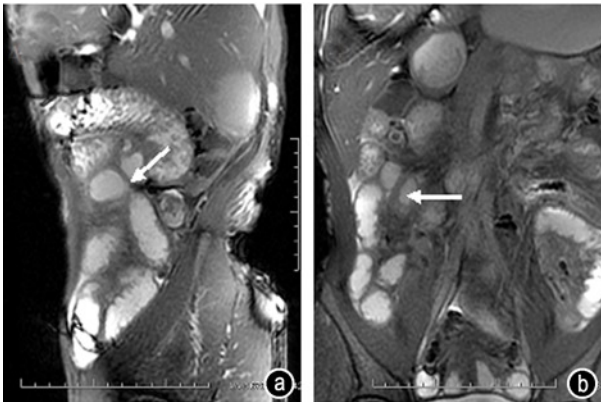


Fig. 3 T2 weighted MRI revealed diffuse edema of small bowel and mesentery (white arrow). (a) Sagittal image; (b) Coronal image

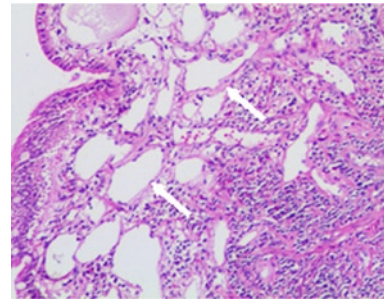


Fig. 5 Histology of the small intestinal biopsy: small intestinal lamina propria lymphatic dilation (white arrow), consistent with intestinal lymphangiectasia (HE, original magnification $\times 40$)

of the ileocecal region (Fig. 4). Biopsy revealed lymphatic dilation of the small intestinal lamina propria, consistent with IL (Fig. 5). Based on these findings the patient was treated with blood transfusions, albumin and other nutritional symptomatic treatments, with which he improved to a stable condition.

Discussion

Intestinal lymphangiectasia is a relatively uncommon disorder of the small intestine, caused by lymphatic flow obstruction, resulting in intestinal lymphatic expansion and rupture. The formation of chylous diarrhea, steatorrhea and chylous ascites result from lymph leakage into the intestine or abdominal cavity. IL was first proposed by Waldman in 1968^[1]. According to the causes, IL could be divided into primary and secondary; primary small intestinal lymphangiectasia (PSIL) is a relatively rare disorder

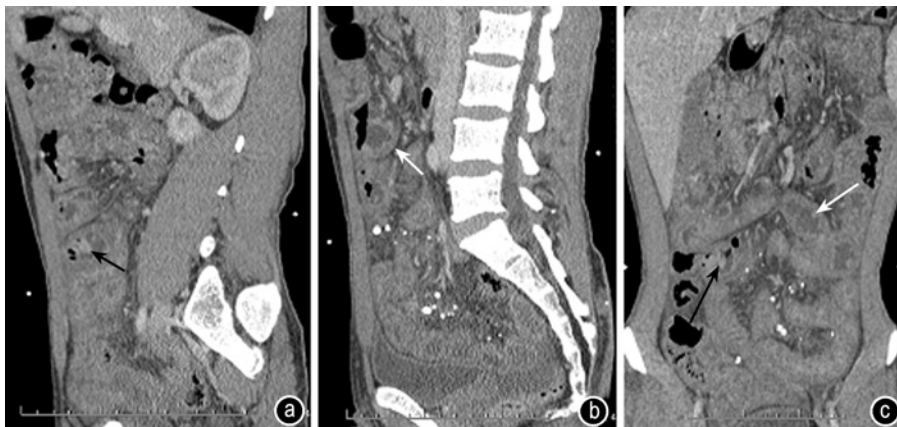


Fig. 2 Abdominal contrast-enhanced CT revealed diffuse edema of intestinal wall (white arrow), with localized mucosal nodularity (black arrow) and arteriovenous malformation of hip (white arrow head). (a and b) Sagittal images; (c) Coronal image

and the cause is unknown. In recent years, immune factors have been suggested to be associated with disease. PSIL is common occurrence in children and adolescents [1], and ninety percent of the patients present before 30 years of age, and the average age of onset is 11 years old. IL may be secondary to other disease states, such as systemic lupus erythematosus (SLE) [2], constrictive pericarditis, repeated parasitic infection [3], post-radiation effects [4], hepatic cirrhosis [5], abdominal trauma or surgical injury, resulting in inflammation and narrowing of the lymphatic vessels and surrounding tissue, leading to poor return of lymphatic circulation with leakage of lymph into the intestine or abdominal cavity.

The main clinical symptoms of IL include hypoalbuminemia, reduced lymphocytes, edema, abdominal effusion, chronic diarrhea and low-fat hyperlipidemia. Abnormal laboratory values reveal non-selective protein loss, with decreased serum total protein, albumin and immune globulin (including IgG, IgA, IgM, and especially IgG, due to its long half life), lymphopenia, decreased serum calcium, increased α 1-antitrypsin clearance. In the past, the diagnosis of IL relied mainly on lymphangiography and lymphatic isotope imaging. While lymphatic malformations may be observed on angiography, there may be a high false negative rate. ^{99m}Tc isotope lymphatic imaging method may isolate the protein to leak to specific parts of the intestine, aiding the diagnosis and guiding the surgery, but it is only effective for 30% of patients, has low sensitivity, and takes a long time to check [6]. Typical radiological manifestations could be seen on imaging, Holzknicht [7] summarized the CT findings: diffuse thickening and edema of small bowel wall, with mild dilatation of the small intestine, and mesangial edema, ascites and pleural effusion, usually without hepatosplenomegaly. In our case, imaging revealed diffuse thickening and edema of the small intestine wall, with a typical halo, increased mesenteric lymph nodes, abdominal and pelvic ascites, similar to the findings reported in previously [6-7]. There are only few reports regarding MRI findings of IL. MRI has a higher soft tissue resolution and multi-dimensional imaging capability, which may make MRI a better imaging method to display pathological evidence of small mesenteric edema, bowel wall thickening and lymphangiectasia [7-8]. On the coronal and sagittal T2-weighted fat suppression sequences, diffuse edema of small bowel and mesenteric, intramural lymphatic fluid and a small amount of high signal ascites could be observed. Radiologic assessments can aid in the interpretation of endoscopy findings, and in follow-up after treatment response.

Further, it is important to exclude other diseases such as cancer, tuberculosis, CD, Whipple's disease and celiac disease. It is very important for us to differentiate IL from intestinal tuberculosis, CD, and SLE enteritis. The incu-

bation period of intestinal tuberculosis is very long, and most patients have a history of pulmonary tuberculosis. In addition, the thickening or stenosis of intestinal wall and ring enhancement of mesenteric lymph nodes were visible on CT [9]. The patients often have ascites. Crohn's disease often presents with segmental bowel wall thickening, thickening of the mesenteric vasculature and the comb sign, which is created by engorged vasa recta, vessels that penetrate the bowel wall perpendicular to the bowel lumen [10]. Focal or diffuse thickening of the bowel wall and the swelling of the mesenteric vasculature often is found in lupus enteritis [11]; associated with clinical features, the diagnosis is usually not difficult. In our case, the patient had typical clinical manifestations of IL, as well as the expected laboratory tests and imaging findings. Due to the expansion of intestinal lymphatics and the accumulation lymph in the intestinal mucosa, which were confirmed by pathological examination, low-density or high signal area could be found on CT and MRI. With the accumulation of lymph fluid in the intestinal lymphatics, the pressure is too high, resulting in localized nodularity and intestinal bleeding, resulting in melena. Since the patient also may have had thoracic lymphatic duct dilatation, bilateral pleural effusion occurred (chylothorax was confirmed by pleural effusion experiments). In addition, the patient presented with multiple arteriovenous malformation of hip and low extremity, which was rarely mentioned in previous cases. We did not find any secondary causes of IL, so a diagnosis of primary IL was established. After admission, the patient was treated with albumin, blood transfusion and low-fat long-chain fatty acids. With this treatment, the patient's clinical condition and nutritional status were improved.

Early diagnosis of IL is critical, because clinical symptoms of 50% of patients, including hypoalbuminemia and edema, can be relieved and improved from medium chain triglycerides low-fat diet (MCT) therapy. Treatment of intestinal lymphangiectasia may vary depending on the cause. Currently the most common therapy recommended is a low-fat, high-protein diet supplemented with medium-chain triglyceride (MCT) [12-14], which is effective both for PSIL and secondary IL. In addition, some patients may benefit from anti-fibrinolytic therapy and internal jugular vein or intrahepatic door bypass surgery. In conclusion, when patients present with typical clinical manifestations, combined with laboratory tests and imaging findings, IL should be considered. Eventually, the clear diagnosis of IL needs colonoscopy, biopsy and pathological examination.

Conflicts of interest

The authors indicated no potential conflicts of interest.

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