Case report of primary intestinal lymphangiectasia diagnosed in an octogenarian by ileal intubation and by push enteroscopy after missed diagnosis by standard colonoscopy and EGD

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Abstract
Rationale: Primary intestinal lymphangiectasia (PIL) is a rare, presumably congenital lesion that is usually diagnosed in patients < 3 years old, is rarely first diagnosed in adulthood, and when first diagnosed in adulthood typically presents with symptoms for many years. Although PIL is often identified by endoscopic abnormalities, it must be emphasized that the jejunoileum/distal duodenum must be intubated for diagnosis because the lesions are present in these regions. This work demonstrates that 1)-PIL can occur in an octogenarian; 2)-shows that the characteristic endoscopic findings are not found at colonoscopy without terminal ileal intubation; and 3)-may be missed at standard EGD without distal duodenal intubation.

Diagnoses: A patient initially presented at age 83 with symptoms of watery diarrhea, abdominal distention, 5-Kg-weight-gain, and weakness for one month, and had typical clinical findings of PIL including chylous ascites, pleural effusions, bilateral pitting leg edema, hypoaalbuminemia, borderline lymphopenia, hypovitaminosis-D, and hypocalcemia. Protein-losing-enteropathy was demonstrated by positive stool tests for alpha-1-antitrypsin. Standard colonoscopy revealed no significant lesions, but terminal ileal intubation during colonoscopy demonstrated creamy-white, punctate, mucosal lesions in terminal ileum, characteristic of lymphangiectasia. EGD with intubation to mid-descending duodenum revealed no significant lesions, but subsequent enteroscopy demonstrated lesions in distal duodenum/proximal jejunum similar to those in terminal ileum characteristic of lymphangiectasia. Histopathologic analysis of lesions of terminal ileum/distal duodenum demonstrated dilated mucosal vessels, confirmed as lymphatic vessels by immunohistochemistry. PIL was diagnosed after excluding secondary causes of intestinal lymphangiectasia.

Interventions/Outcomes: Patient placed on standard PIL diet: oral supplements of medium-chain triglycerides, a high protein diet, supplements of fat-soluble vitamins, and avoiding long-chain fatty acids, with marked clinical improvement.

Lessons: This work shows that: 1)-standard EGD and colonoscopy may miss characteristic lesions of PIL, 2)-enteroscopy or terminal ileal intubation at colonoscopy may be required for the diagnosis because lesions are typically located in distal duodenum/jejunum; and 3)-PIL can first present in the very elderly even with symptoms of short duration.

Abbreviations: BMI = body mass index, CT = computed tomography, EGD = esophagastroduodenoscopy, GI = gastrointestinal, H&E = hematoxylin and eosin, IgM = immunoglobulin M, MRI = magnetic resonance imaging, PCR = polymerase chain reaction, PIL = primary intestinal lymphangiectasia, PLE = protein losing enteropathy, SAAG = serum-ascites albumin gradient.

Keywords: chylous ascites, electron microscopy, enteroscopy, immunohistochemistry, primary intestinal lymphangiectasia, protein losing enteropathy, terminal ileal intubation at colonoscopy

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MSC and AE contributed equally to this work.

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1. Introduction

Primary intestinal lymphangiectasia (PIL) is a rare disease with several hundred reported cases. It is rarely reported in adults because it is presumably a congenital disease and when diagnosed in adults it typically produces a long duration of symptoms such as watery diarrhea, abdominal distention from ascites, and peripheral edema.[1] The clinical spectrum of PIL is extended by reporting a patient who initially presented with PIL as an octogenarian with a short duration of syndromic findings; had nondiagnostic colonoscopy, but had diagnostic ileal intubation during colonoscopy; had nondiagnostic standard esophagogastroduodenoscopy (EGD) to mid-descending duodenum, but had diagnostic push enteroscopy instead of standard EGD to diagnose PIL because the small intestinal lesions may be patchy and localized to jejunulem.

2. Methods

The literature was systematically reviewed by computerized search via PubMed for publications with the following subject headings or keywords: ["primary intestinal lymphangiectasia"] OR ["protein losing enteropathy"]; and by reviewing sections on PIL in pathology textbooks or monographs. Two authors independently reviewed the literature, and decided by consensus which articles to incorporate in this study. The currently reported patient prospectively underwent thorough (noninvasive) academic evaluation by Dr. Cappell, the treating gastroenterologist. This study was approved as a case report/systematic review by William Beaumont Hospital IRB on January 27, 2017.

3. Case report

An 83-year-old Chinese woman living in America for 50 years with no recent foreign travel, no recent antibiotic exposure, and medical history of hypertension treated with carvediol and valsartar, atrial fibrillation treated with warfarin until 1 week before presentation, and status-post emergency laparotomy with oversewing of colonic perforation after colonoscopy 10 years earlier, presented with painless abdominal distention, 5-kg-weight-gain, bilateral leg swelling, watery diarrhea, weakness, and dyspnea for 1 month (Table 1A). On admission, blood pressure = 159/84 mmHg, pulse = 74 beats/min, respiratory rate = 24/minute, temperature = 37.2°C, and BMI (body mass index) = 29.5 kg/m². Physical examination revealed several abnormal signs (Table 1B). Pertinent negatives on abdominal examination included a nontender abdomen, normoactive bowel sounds, and

| Characteristic findings of primary intestinal lymphangiectasia in the currently reported patient. | Pathophysiology of association with PIL or exclusion of other etiologies |
|---|---|
| (A) Symptoms | Ascites from PIL or other causes |
| Increased abdominal girth and weight gain | Likely from bilateral pleural effusions and severe ascites, impinging upon lung volume from PIL or other causes |
| Dyspnea | Subsequently shown to be due to PLE and lymphatic loss from PIL |
| Watery diarrhea | Hypoalbuminemia from PLE or other causes |
| (B) Signs | Hypoalbuminemia from PIL or other causes |
| Bilateral, pitting edema of lower extremities | Ascites from decreased oncotic pressure from hypoalbuminemia from PLE and leaky lymphatics in PIL or other causes |
| Mild bilateral upper extremity edema | Bilateral pleural effusions from decreased oncotic pressure from hypoalbuminemia plus leaky lymphatics in PIL or other causes |
| Abdominal distention with shifting dullness in abdomen | Lymphopenia from leakage of lymphocytes from leaky small intestinal lacteals into bowel lumen |
| Dullness to percussion, absent tactile fremitus, and diminished breath sounds bilaterally over lower lung fields | Protein leakage into gut lumen (PLE) |
| (C) Abnormal routine laboratory tests | Hypovitaminosis D from fat malabsorption from leaky small intestinal lymphatics |
| Borderline lymphopenia: absolute lymphocyte count = 1100/mm³ (normal: 1100–4000/mm³). | Characteristic finding with PLE due to leakage of alpha-1 antitrypsin from bowel wall into bowel lumen |
| Hypoalbuminemia: serum albumin = 1.2 g/dL (normal: 3.5–5.0 g/dL) | Elevated clearance strongly suggests PLE |
| Hypocalcemia: serum calcium = 7.0 mg/dL (normal: 8.4–10.4 mg/dL) | Characteristic of PIL due to leakage of lymphatic fluid from lymphatic vessel hypertension |
| Elevated fecal alpha-1-antitrypsin level: 175 mg/dL (laboratory normal < 54 mg/dL), Elevated alpha-1 antitrypsin clearance = 108 mL/24 h (laboratory normal < 27 mL/24 hr) | Mucosal lacteals are dilated and crammed with creamy lipids in PIL |
| (D) Demonstrating PLE as cause of PIL | Characteristic finding of PIL |
| Chylous ascites | Mucosal lacteals are dilated and crammed with creamy lipids in PIL |
| Terminal ileal intubation during colonoscopy: numerous creamy white, punctate, mucosal lesions | Characteristic pathologic finding of PIL |
| Endoscopic findings at push enteroscopy: numerous creamy white, punctate, macular lesions in distal duodenum and proximal jejunum | Immunohistochemical finding with PIL |
| Histopathology with hematoxylin and eosin stains: dilated mucosal lacteals in terminal ileum and distal duodenum | Immunohistochemical finding with PIL |

CT = computerized tomography, EGD = esophagogastroduodenoscopy, PIL = primary intestinal lymphangiectasia, PLE = protein losing enteropathy.
nonballotable liver. Rectal examination revealed watery, guaiac-negative, brown stool.

On admission, laboratory findings included: hemoglobin = 8.2 g/dL, serum iron = 40 mg/dL, and iron saturation = 17%, indicating borderline iron-deficiency anemia. The platelet count = 140,000/mm³, leukocyte count = 4700/mm³, absolute neutrophil count = 2900/mm³, and absolute lymphocyte count = 1100/ mm³ (borderline lymphopenia; normal: 1100–4000/mm³). The international normalized ratio (INR) = 1.0, and partial thromboplastin time = 28.7 seconds (normal: 23.0–30.0 seconds). Serum sodium = 128 mmol/L (laboratory normal: 135–145 mmol/L), and creatinine = 0.7 mg/dL. Liver function tests were within normal limits, except for albumin = 1.2 g/dL (laboratory normal: 3.5–5.1 g/dL), and globulin = 1.6 g/dL (laboratory normal: 2.2–4.0 g/dL) (Table 1C). The troponin level was <0.03 mg/mL (negative for myocardial infarction), and brain type natriuretic peptide = 163 pg/mL (laboratory normal: <450 pg/mL in patients >75 years old).

Chest roentgenogram revealed large, bilateral, pleural effusions. Abdominal ultrasound revealed massive ascites and a 10.1 × 4.9 cm right adnexal mass, which on abdominopelvic computerized tomography (CT) had an attenuation of 60 Hounsfield units, characteristic of a hematoma (Fig. 1). The only risk factor for hematomas was receiving warfarin until 1 week earlier, but the patient denied recent abdominal trauma, only risk factor for hematomas was receiving warfarin until 1 week earlier for atrial fibrillation, but had no history of malnutrition. A nutritional consultant reported a normal dietary history without malnutrition.

The patient’s breathing improved after undergoing therapeutic paracentesis, with evacuation of 4.3 L of fluid, while simultaneously transfusing 8 g of human albumin. Ascitic fluid analysis revealed chyleous fluid containing 100 cells/µL, with a differential of neutrophils = 4%, lymphocytes = 32%, and monocytes = 44%. The ascitic fluid albumin = 1.0 g/dL, and SAAG (serum-ascites albumin gradient) = 0.2 g/dL. Ascitic fluid cytology was negative for malignancy. Serum antinuclear antigen was positive at low titer (1:16, lab normal: <1:160 titer). Vitamin B12 level = 227 pg/mL (normal: 271–870 pg/mL), and vitamin D level = 7.2 pg/mL (normal: 19.9–79.3 pg/mL). Serum C-reactive protein = 0.7 mg/dL (normal: <0.8 mg/dL). Patient was seronegative for human immunodeficiency virus, hepatitis B virus, and hepatitis C virus. Interferon gamma release (quantiferon) assay was negative. Fecal alpha-1 antitrypsin level and serum clearance were elevated (Table 1D), findings indicating protein losing enteropathy (PLE).[2]

To evaluate the diarrhea, 3 stool examinations for ova and parasites were negative. Stool cultures were negative for routine enteric pathogens. PCR (polymerase chain reaction) test of stool for Clostridium difficile toxin B was negative. For evaluation of (borderline) iron deficiency anemia, EGD with standard intubation to mid-descending duodenum revealed a normal examination with normal gastric rugae and normal appearing duodenum to mid-descending duodenum. Histopathologic examination of endoscopic biopsies of normal appearing, duodenal mucosa did not reveal celiac disease or Whipple disease. Colonoscopy showed normal appearing colonic mucosa and diverticulosis. Histologic examination of random colonoscopic biopsies of colonic mucosa did not reveal microscopic colitis. Terminal ileal intubation during colonoscopy revealed numerous, creamy white, punctate (“snowflake”) mucosal lesions, highly consistent with intestinal lymphangiectasia (Fig. 2A). Push enteroscopy performed by the same endoscopist (MSC) also demonstrated numerous similar mucosal lesions in distal duodenum/proximal jejunum, without visible lesions in proximal duodenum (Fig. 2B and C). Histologic analysis of colonoscopic biopsies of terminal ileum and of enteroscopic biopsies of distal duodenum demonstrated dilated lacteals within tips of intestinal villi (Fig. 3A), confirmed as dilated lacteals by 2 immunohistochemical markers for lacteal endothelium (Fig. 3B and C). Ultrastructural analysis of one of the dilated lymphatic channels (seen in Fig. 3A) contained multiple structures with shape, size, and structure consistent with chylomicrons (Fig. 4). Pathologic analysis of a duodenal aspirate revealed no giardia. Serum immunoglobulin M (IgM) level = 28 mg/dL (laboratory normal: 47–206 mg/dL), IgG = 542 mg/dL (laboratory normal: 520–1500 mg/dL), and IgA = 86 mg/dL (laboratory normal: 88–374 mg/dL). A monoclonal IgM spike was not present on serum protein electrophoresis.

The patient was treated with a diet low in long-chain fatty acids, supplements of oral medium-chain triglycerides (MCTs), a high protein diet, and supplements of fat-soluble vitamins, under supervision by a dietician. She received bilateral leg support stockings to reduce leg edema. Follow-up abdominal CT 1 month later revealed marked shrinking of adnexal mass to 5.4 × 2.9 cm, consistent with partial hematoma resorption. The patient clinically improved at 2 months follow-up on this therapeutic regimen, with markedly decreased ascites, decreased leg edema, and increased serum albumin level.

4. Discussion

The reported patient presented with profound ascites and hypoalbuminemia. Comprehensive evaluation excluded the following common causes of ascites and hypoalbuminemia: portal hypertension/cirrhosis was excluded by normal liver function tests except for hypoalbuminemia, absent peripheral stigmata of chronic liver disease, no hepatosplenomegaly at abdominal CT, no esophagogastric varices at EGD, and SAAG = 0.2 g/dL (<1.1 g/dL indicates noncirrhotic ascites); congestive
heart failure/cardiac disease was excluded by physical examination, low troponin level, normal ejection fraction and no valvular disease at echocardiography, and brain type natriuretic peptide = 163 pg/mL (laboratory normal: <450 pg/mL in patients >75 years old); nephrotic syndrome was excluded by lack of proteinuria on a 24-hour urine collection; and malnutrition was excluded by dietary history obtained by a nutritional consultant, and elevated BMI.

Figure 2. Endoscopic findings in a female octogenarian with primary intestinal lymphangiectasia. (A) Close-up view with ileal intubation during colonoscopy demonstrates numerous, small, creamy white, punctae consisting of dilated lymphatic vessels filled with lymphatic fluid throughout the terminal ileum. (B and C) Far-away (B) and close-up (C) views at push enteroscopy demonstrate numerous, small, creamy white, punctae consisting of dilated lymphatic vessels filled with lymphatic fluid throughout distal duodenum and proximal jejunum.

Figure 3. Histopathology and immunohistochemistry of lymphangiectasia. (A) Conventional hematoxylin and eosin stain. Medium-power photomicrograph of terminal ileal biopsy taken during ileal intubation at colonoscopy demonstrating a single villus on the mucosal surface containing an extremely dilated vascular space lined by unifoliated epithelium, with histology highly consistent with a lacteal vessel. (B and C) Immunohistochemistry of lymphangiectasia. High-power photomicrographs of terminal ileal biopsy taken during ileal intubation shows immunohistochemical staining with antibodies to D2–40 (podoplanin) avidly binding in cytoplasm of lymphatic endothelium (B), and immunohistochemical staining with antibodies to ERG avidly binding to the nucleus of lymphatic endothelium (C), demonstrating that the vessels are lacteals. Neither antibody demonstrates affinity to ileal epithelial glands.
The current work-up excluded other causes of PLE or secondary intestinal lymphangiectasia before diagnosing PIL. Crohn disease and Menetrier disease were excluded as gastrointestinal (GI) causes of PLE by colonoscopy with ileoscopy, and by EGD with biopsies, respectively. Genetic syndromes causing intestinal lymphangiectasia were excluded by lack of gross congenital anomalies (e.g., unilateral lower extremity hypertrophy with Klippel–Trenauney syndrome). Lymphangiectasia secondary to intraabdominal lymphoma or lymphatic obstruction were excluded by no abdominal tumor or abdominal lymphadenopathy detected on CT examination. Waldenstrom macroglobulinemia, a prominent cause of secondary lymphangiectasia in adults, was excluded by absence of a monoclonal IgM spike on serum protein electrophoresis and an abnormally low serum IgM level; the IgM level should be elevated in Waldenstrom macroglobulinemia because of synthesis of IgM macroglobulins, whereas the IgM level is reduced in PIL due to PLE.

Clues that the patient might have PIL, rather than more common causes of ascites and hypoalbuminemia, include: finding of chylous ascites on paracentesis, and presentation with persistent watery diarrhea, leg edema, pleural effusions, hypogammaglobulinemia, and fat soluble vitamin deficiencies including hypovitaminosis-D. PIL is a rare form of PLE characterized by localized or diffuse dilation of enteric lacteals. Leakage of intestinal lymph into small bowel lumen results in hypoalbuminemia, lymphopenia, PLE, and chylous ascites, as well as the other observed features in this patient (Table 1).

Patients with PIL are moderately predisposed to opportunistic infections, such as viral warts, and to lymphomas secondary to mildly attenuated humoral and cellular immunity from intestinal loss of lymphocytes, lymphatic fluid, and immunoglobulins; and decreased immunoglobulin synthesis due to decreased B-lymphocyte levels, but opportunistic infections are relatively uncommon, attributed to relatively well-preserved memory and effector CD4+T cells. The reported patient had no opportunistic infections or lymphomas.

In the current patient, lymphangiectasia were not identified by standard colonoscopy because the colon lacks lacteals, but were identified by intubation of terminal ileum at colonoscopy, and were not identified by standard EGD, presumably because lymphangiectasia are not prominent in proximal duodenum, but were identified by intubation of distal duodenum at push enteroscopy (Table 1E). Moreover, lymphangiectasia were not identified in proximal descending duodenum even at push enteroscopy. Notably, the diagnosis of PIL would have been missed in this patient without ileal intubation at colonoscopy and without enteroscopy after a nondiagnostic EGD. Wen et al reported PIL may be missed “because the intestinal abnormalities often occur at the jejunoileum and may be slight or the lesions segmental.” Capsule endoscopy generally visualizes the entire...
small intestine, which is useful to assess extent of lymphangiectasia, but lacks capability to perform biopsies for pathologic diagnosis.[11] Double balloon endoscopy is preferred over capsule endoscopy because of higher sensitivity from better endoscopic visualization, and higher specificity due to ability to perform biopsies for pathologic diagnosis.[12] Endoscopic appearance is characteristic: numerous, creamy white, discrete, punctate, (“snowflake”) lesions on small intestinal mucosa, as currently reported.[13,14] Histopathologic demonstration of dilated lacteals in endoscopic biopsies of intestinal mucosa is diagnostic. In this study, traditional demonstration of dilated lacteals by hematoxylin and eosin stains (Fig. 3A), was supplemented by highly specific immunohistochemical markers of lacteals (Fig. 3B and C). However, an expert GI pathologist can diagnose lymphangiectasia without immunohistochemistry. This vascular space was also confirmed to be a lymphatic lumen on electron microscopy due to absence of erythrocytes in the lumen and the presence of multiple rounded structures with the size, shape, and internal structure compatible with chylomicrosomes.[15]

Technetium-labeled human serum albumin (99mTc-HSA) scintigraphy can demonstrate local protein leakage as bowel enhancement, but this procedure is costly, time-consuming, and has been superseded by alpha-1 antitrypsin determination.[16,17] Alpha-1 antitrypsin is a marker of PLE because this protein resists degradation by intraluminal digestive enzymes.[2,17] Radiologic examinations, including abdominal ultrasound, CT, and MRI (magnetic resonance imaging), are typically nondiagnostic because lymphangiectasia are punctate, macular mucosal lesions; but these examinations may show nonspecific findings of ascites and diffuse small bowel thickening and edema, or demonstrate secondary causes of lymphangiectasia, such as lymphoma.[1,5,18]

Conventional treatment is by a special diet: low in long-chain fatty acids because these fatty acids are absorbed only by the (malformed) lacteals to avoid lymphatic hypertension, lacteal dilation, and proteinaceous and lymphatic fluid loss; high in medium chain triglycerides (MCTs) to circumvent malformed lacteals because MCTs are directly absorbed via portal vein into the circulation[19]; high in proteins to counter enteric protein loss from leaky lymphatics; and supplements of fat soluble vitamins, because to counter steatorrhea. These dietary measures reduce symptoms and mortality.[20] Leg support stockings help reduce leg edema. The currently reported patient responded well, at 2 months follow-up, to these therapies.

Other treatments include corticosteroids, octreotide, and antiplasmin (traxenemacid).[4,9] Corticosteroids demonstrate efficacy in intestinal lymphangiectasia secondary to inflammatory diseases causing PLE, particularly lupus and Crohn disease, because corticosteroids are antiinflammatory, but have a limited role in PIL, a noninflammatory disorder.[4,21] The currently reported patient had a normal CRP level, indicating no active inflammation. Octreotide decreases absorption of triglycerides; induces transient splanchic vasoconstriction; and reduces clinical manifestations of PLE.[4,22] Antiplasmin may improve lymphatic permeability to proteins by promoting fibrinolysis.[21,24] Small bowel resection may be necessary for uncontrollable GI bleeding from intestinal ulcers or refractory mechanical obstruction from severe focal bowel wall edema from PIL.[25] Segmental bowel resection was not an option in this patient because the PIL was diffuse.

This work has limitations: it is retrospective and reports only 1 case; currently reported finding of initial appearance and diagnosis of PIL in old age lacks definitive pathophysiologic mechanism for delayed presentation; reported short duration of symptoms is not necessarily equivalent to short duration of disease; and lymphangiectasia secondary to colonic surgery 10 years earlier could not be entirely excluded as an alternative etiology for lymphangiectasia from lymphatic obstruction. However, abdominal CT did not demonstrate large abdominal lymphatic duct obstruction. The recent hematoma was an unlikely cause of the symptoms and signs because among other reasons it was too recent.

This patient presented at age 83 with PIL. Comprehensive literature review revealed intestinal lymphangiectasia is rarely reported in patients > 65 years old, and nearly all cases in the elderly occurred in intestinal lymphangiectasia secondary to Waldenström macroglobulinemia,[26] or genetic syndromes.[27] This case appears to be the oldest reported case of PIL, with another case reported in a 73-year-old patient.[28] This report extends the maximal age of presentation of PIL; this old age is notable because PIL generally presents in infants as a presumed congenital defect.

In conclusion, this work demonstrates a case of PIL with notable findings illustrating that standard colonoscopy and standard EGD to mid-descending duodenum may be nondiagnostic; PIL may clinically first manifest in an octogenarian, extending the maximal age for diagnosis; and immunohistochemistry may strengthen the pathologic diagnosis determined by routine H&E.

References

[1] Wen J, Tang Q, Wu J, et al. Primary intestinal lymphangiectasia: four case reports and a review of the literature. Dig Dis Sci 2010;55:1466–72.
[2] Perrault J, Markowitz H. Protein-losing gastroenteropathy and the intestinal clearance of serum-alpha-1-antitrypsin. Mayo Clin Proc 1984;59:278–9.
[3] Hennekam RC, Geerdink RA, Hamel BC, et al. Autosomal recessive intestinal lymphangiectasia and lymphedema with facial anomalies and mental retardation. Am J Med Genet 1989;34:593–600.
[4] Troskot R, Jurčič D, Bilić A, et al. How to treat an extensive form of primary intestinal lymphangiectasia? World J Gastroenterol 2015;21:7320–5.
[5] Vignes S, Bellanger J. Primary intestinal lymphangiectasia (Waldmann’s disease). Orphanet J Rare Dis 2008;3:5.
[6] Lee SJ, Song HJ, Boo SJ, et al. Primary intestinal lymphangiectasia with generalized warm. World J Gastroenterol 2015;21:8467–72.
[7] Bouhnik Y, Etennaïy I, Nemeth J, et al. Very late onset small intestinal B cell lymphoma associated with primary intestinal lymphangiectasia and diffuse cutaneous warts. Gut 2000;47:296–300.
[8] Fuss IJ, Strombl W, Cuccherini BA, et al. Intestinal lymphangiectasia, a disease characterized by selective loss of naive CD45RA+ lymphocytes into the gastrointestinal tract. Eur J Immunol 1998;28:4725–85.
[9] Lynn J, Knight AK, Kamoun M, et al. A 55-year-old man with hypogammaglobulinemia, lymphopenia, and unrelenting cutaneous warts. J Allergy Clin Immunol 2004;114:409–14.
[10] Chamouard P, Nehme-Schuster H, Simler JM, et al. Videcapsule endoscopy is useful for the diagnosis of intestinal lymphangiectasia. Dig Liver Dis 2006;38:699–703.
[11] Oh TG, Chung JW, Kim HM, et al. Primary intestinal lymphangiectasia diagnosed by capsule endoscopy and double balloon endoscopy. World J Gastrointest Endosc 2011;3:235–40.
[12] Takenaka H, Ohmiya N, Hirooka Y, et al. Endoscopic and imaging findings in protein-losing enteropathy. J Clin Gastroenterol 2012;46:575–80.
[13] Abramowsky C, Hupert ZV, Kilbridge P, et al. Intestinal lymphangiectasia in children: a study of upper gastrointestinal endoscopic biopsies. Pediatric Pathol 1989;9:823–34.
[14] Akaskara H, Muca SM, Morshita T, et al. Endoscopic and histopathological study on primary and secondary intestinal lymphangiectasia. Dig Dis Sci 1981;26:312–20.
[15] Akaskara H, Tsuchiya M, Enomoto Y, et al. Electron microscopic study of the small intestine in intestinal lymphangiectasia and constructive pericarditis [Article in German]. Leber Magen Darm 1977;7:14–20.
[16] Chiu NT, Lee BF, Hwang SJ, et al. Protein-losing enteropathy: diagnosis with 99mTc-labeled human serum albumin scintigraphy. Radiology 2001;219:86–90.
[17] Ingle SB, Chitra RH. Primary intestinal lymphangiectasia: minireview. World J Clin Cases 2014;2:528–33.
[18] Fakhri A, Fishman EK, Jones B, et al. Primary intestinal lymphangiectasia: clinical and CT findings. J Comput Assisted Tomogr 1984;9:767–70.
[19] Suresh N, Ganesh R, Sankar J, et al. Primary intestinal lymphangiectasia. Indian Pediatr 2009;46:903–6.
[20] Desai AP, Guvenc BH, Carachi R. Evidence for medium chain triglycerides in the treatment of primary intestinal lymphangiectasia. Eur J Pediatr Surg 2009;19:241–5.
[21] Fleisher TA, Strober W, Muchmore AV, et al. Corticosteroid-responsive intestinal lymphangiectasia secondary to an inflammatory process. N Engl J Med 1979;300:605–6.
[22] Suehiro K, Morikage N, Murakami M, et al. Late-onset primary intestinal lymphangiectasia successfully managed with octreotide: a case report. Ann Vasc Dis 2012;5:96–9.
[23] Mine K, Matsuyayashi S, Nakai Y, et al. Intestinal lymphangiectasia markedly improved with antiplasmin therapy. Gastroenterology 1989;96:1596–9.
[24] MacLean JE, Cohen E, Weinstein M. Primary intestinal and thoracic lymphangiectasia: a response to antiplasmin therapy. Pediatrics 2002;109:1177–80.
[25] Zhu LH, Cai XJ, Mou YP, et al. Partial enterectomy: treatment for primary intestinal lymphangiectasia in four cases. Chin Med J 2010;123:760–4.
[26] Pratz KW, Dingli D, Smyrk TC, et al. Intestinal lymphangiectasia with protein-losing enteropathy in Waldenstrom macroglobulinemia. Medicine (Baltimore) 2007;86:210–4. Review.
[27] Christu KA, Pastaka C, Papadopoulos D, et al. Yellow nail syndrome or diffuse lymphatic network disease. Acta Medica (Hradec Kralove) 2002;45:181–2.
[28] Huber X, Degen L, Muenst S, et al. Primary intestinal lymphangiectasia in an elderly female patient: a case report on a rare cause of secondary immunodeficiency. Medicine (Baltimore) 2017;96:e7729.