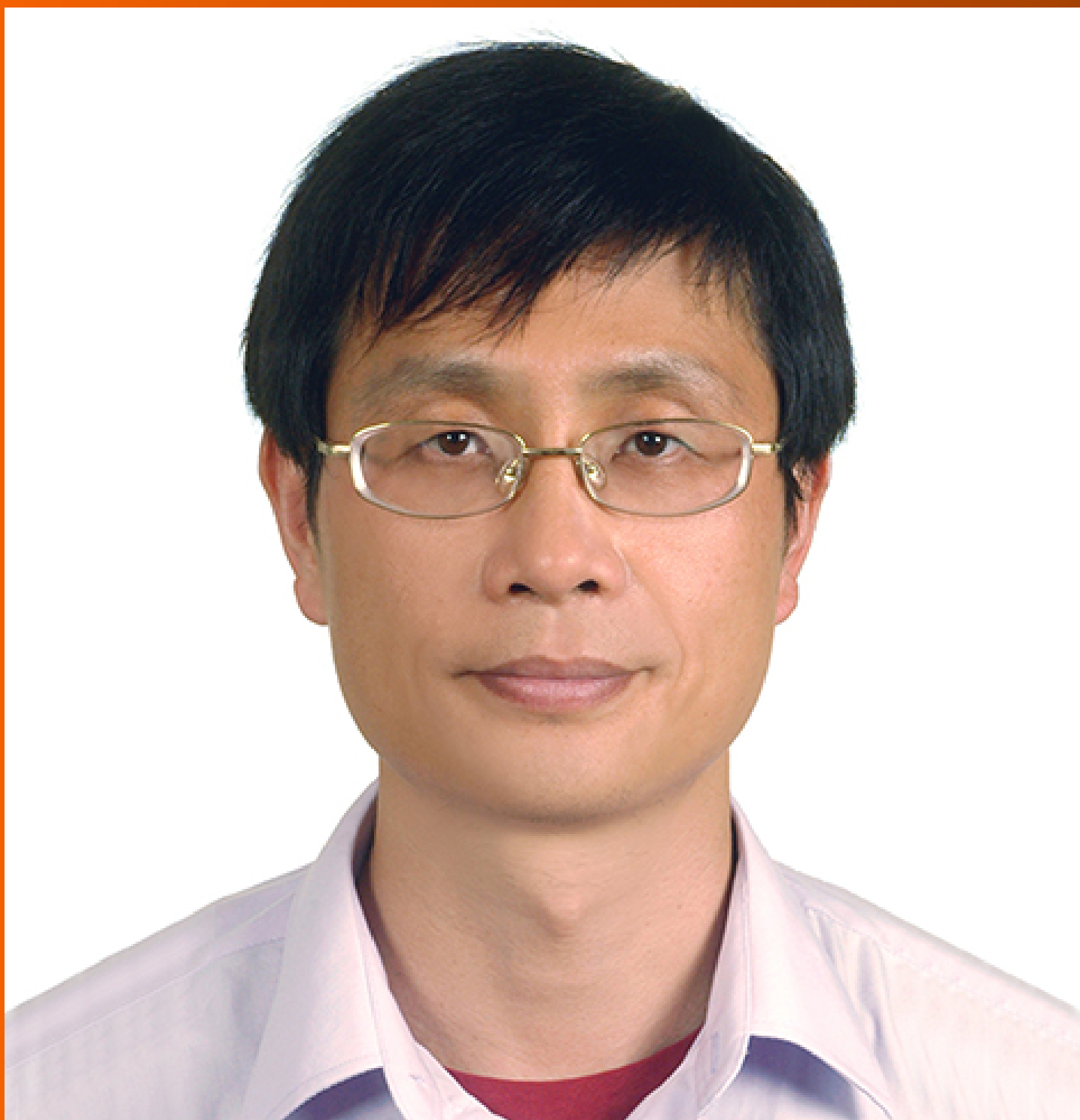


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ABOUT COVER

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Retrospective Study

Experience of primary intestinal lymphangiectasia in adults: Twelve case series from a tertiary referral hospital

Ji Eun Na, Ji Eun Kim, Sujin Park, Eun Ran Kim, Sung Noh Hong, Young-Ho Kim, Dong Kyung Chang

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Abstract

BACKGROUND

While primary intestinal lymphangiectasia (PIL) is considered a rare condition, there have been several reported cases in adults. Nevertheless, the absence of clear guidance from diagnosis to treatment and prognosis poses challenges for both physicians and patients.

AIM

To enhance understanding by investigating clinical presentation, diagnosis, treatment, complications, and prognoses in adult PIL cases.

METHODS

We enrolled adult patients diagnosed with PIL between March 2016 and September 2021. The primary outcome involved examining the diagnosis and treatment process of these patients. The secondary outcomes included identifying complications (infections, thromboembolism) and assessing prognoses (frequency of hospitalization and mortality) during the follow-up period.

RESULTS

Among the 12 included patients, peripheral edema (100%) and diarrhea (75%) were the main presenting complaints. Laboratory tests showed that all the patients exhibited symptoms of hypoalbuminemia and hypogammaglobulinemia. Radiologically, the predominant findings were edema of the small intestine (67%) and ascites (58%). The typical endoscopic finding with a snowflake appearance was observed in 75% of patients. Among the 12 patients, two responded positively to octreotide and sirolimus, and eight who could undergo maintenance therapy

discontinued subsequently. Complications due to PIL led to infection in half of the patients, thromboembolism in three patients, and one death.

CONCLUSION

PIL can be diagnosed in adults across various age groups, with different severity and treatment responses among patients, leading to diverse complications and prognoses. Consequently, tailored treatments will be necessary. We anticipate that our findings will contribute to the management of PIL, an etiology of protein-losing enteropathy.

Key Words: Primary intestinal lymphangiectasia in adults; Protein-losing enteropathy; Diagnosis; Treatment; Prognosis

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Core Tip: We reviewed the diagnosis, treatment, and prognosis of adult patients diagnosed with primary intestinal lymphangiectasia and found varying severities. Hence, tailored treatments are essential for adult patients with primary intestinal lymphangiectasia given the diverse presentations and responses.

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INTRODUCTION

Primary intestinal lymphangiectasia (PIL), or Waldmann's disease, is a rare lymphatic system disorder that predominantly affects the gastrointestinal tract[1]. Lymphatic capillaries exist within the intestinal villi, following the submucosal lymphatic vessels, and ultimately converging into lymphatic vessels or lymph nodes within the mesentery. This gathered lymph drains into the thoracic duct and enters the venous circulation at the same as the left subclavian vein[2]. The lymphatic system of the gut plays a significant role in regulating interstitial fluid, absorbing long-chain fatty acids through chylomicrons, and housing T and B cell lymphocytes, thus serving an essential function within the immune system[3]. In the PIL, the dilation or rupture of the lymphatic system of the gut results in the leakage of lymph, leading to lymphopenia and hypogammaglobulinemia. Furthermore, increased protein excretion in the stool causes hypoproteinemia[1]. Clinical manifestations of this condition encompass various symptoms, including peripheral edema, diarrhea, and abdominal pain[4]. Pathological diagnosis serves as the confirmation method, yet the absence of guidance regarding the diagnostic process and treatment poses challenges for clinicians and patients, even given the rare nature of the PIL.

Although PIL has been reported in children[5,6], its mechanisms and prevalence remain poorly understood, with some reports suggesting possible genetic alterations. Moreover, several cases with detailed PIL occurrences in adults have also been documented[4,7-11].

Thus, this study aims to elucidate the clinical presentation, diagnosis, treatment strategies, complications, and prognoses associated with PIL cases diagnosed in adults. By sharing these experiences, we aim to provide valuable insights for the effective management of this condition.

MATERIALS AND METHODS

Patients and diagnosis

A retrospective screening was conducted on patients aged 18 and above diagnosed with PIL (I89.0) based on medical records from March 2016 to September 2021. A medical fee reduction policy in South Korea is accessible specifically for extremely rare diseases. PIL falls within this category, allowing for the utilization of the disease code for screening purposes. Exclusions were made for patients who lacked treatment records at our institution or were followed up for less than six months.

Applying the criteria for special coding of extremely rare diseases and following the diagnostic criteria utilized at our institution required meeting all three of the following criteria: First, distinct clinical symptoms must be present, including hypoproteinemia, peripheral edema, lymphocytopenia, chronic diarrhea, steatorrhea, abdominal pain, nausea, vomiting, chyle ascites or chylothorax, or alpha-1 antitrypsin (AAT) clearance exceeding 27 mL/24 h. Second, relevant findings must be verified through imaging tests [endoscopy, ultrasonography, abdominopelvic computed tomography (CT), *etc.*]. Such findings encompassed a snowflake appearance, low attenuation thickening of the small bowel wall, or ascites. Third, histological confirmation of dilated lymphatics within the intestine was required, observed in the mucosa, submucosa, serosa, subserosa, or mesentery.

Following the diagnostic criteria, basic blood tests were conducted, including complete blood count, chemistry profile, electrolyte levels, lipid profile, immunoglobulin (Ig) A/G/M/E, prothrombin time/activated partial thromboplastin time, fibrinogen, ferritin, and C-reactive protein (CRP). For confirming protein-losing enteropathy, serum AAT (mg/dL) was assessed, along with stool concentration of AAT (mg/dL) and AAT clearance calculated following a 24-h stool collection (grams). Radiologically, chest X-rays and abdominopelvic CT scans were performed as standard imaging procedures. Endoscopically, esophagogastroduodenoscopy (EGD), colonoscopy, and capsule endoscopy were performed. Depending on the physician's assessment, oral or anal enteroscopy could be chosen instead of EGD and colonoscopy. A corresponding diagnosis code was assigned based on the comprehensive results of these tests and their alignment with the specified diagnostic criteria.

Outcomes and data

The primary outcome was to disseminate diagnostic findings and the treatment course for adult PIL. The secondary outcome was to convey experiences regarding complications and prognoses encountered during the follow-up period.

The study data were retrospectively acquired through the review of medical records. Demographic information included age, gender, body mass index, and comorbidities at diagnosis. Diagnostic findings were categorized into symptoms (peripheral edema, diarrhea, abdominal pain, nausea/vomiting), laboratory results (leukocyte count, lymphocyte count, hemoglobin, albumin, IgG, ferritin, CRP, AAT clearance), radiological findings (small bowel wall edema, ascites, pleural effusion, ileus), endoscopic observations (snowflake appearance), and pathological findings. Treatment was classified into medical treatment and interventions. Medical treatment includes diet therapy, albumin administration, octreotide, tranexamic acid, steroids, sirolimus, and everolimus. The sequence of drug selection, treatment continuation status, and reasons for discontinuation were outlined for each case. The execution and reasons for interventions [such as lung mediastinum magnetic resonance imaging (MRI), lymphangiography, or lymphatic embolization] were documented. Throughout the follow-up period, complications and prognoses were defined by the annual frequency of hospitalization, infections, thromboembolism, and mortality. Patients included in the case series were tracked from the date of diagnosis until their last outpatient visit or date of death.

RESULTS

Patients' characteristics

A total of 18 patients aged 18 and above diagnosed with PIL were screened. Among them, 12 patients were included in the case series, following the exclusion of those with no treatment records or a follow-up period of fewer than six months (6 patients). The age range was from 28 yr to 76 yr, with a median age of 48 yr. The gender distribution was well-balanced, with seven males and five females. Among the existing comorbidities, cerebrovascular disease, diabetes mellitus, and cancer were the most prevalent, each accounting for 3 cases out of 12 (25%) (Table 1).

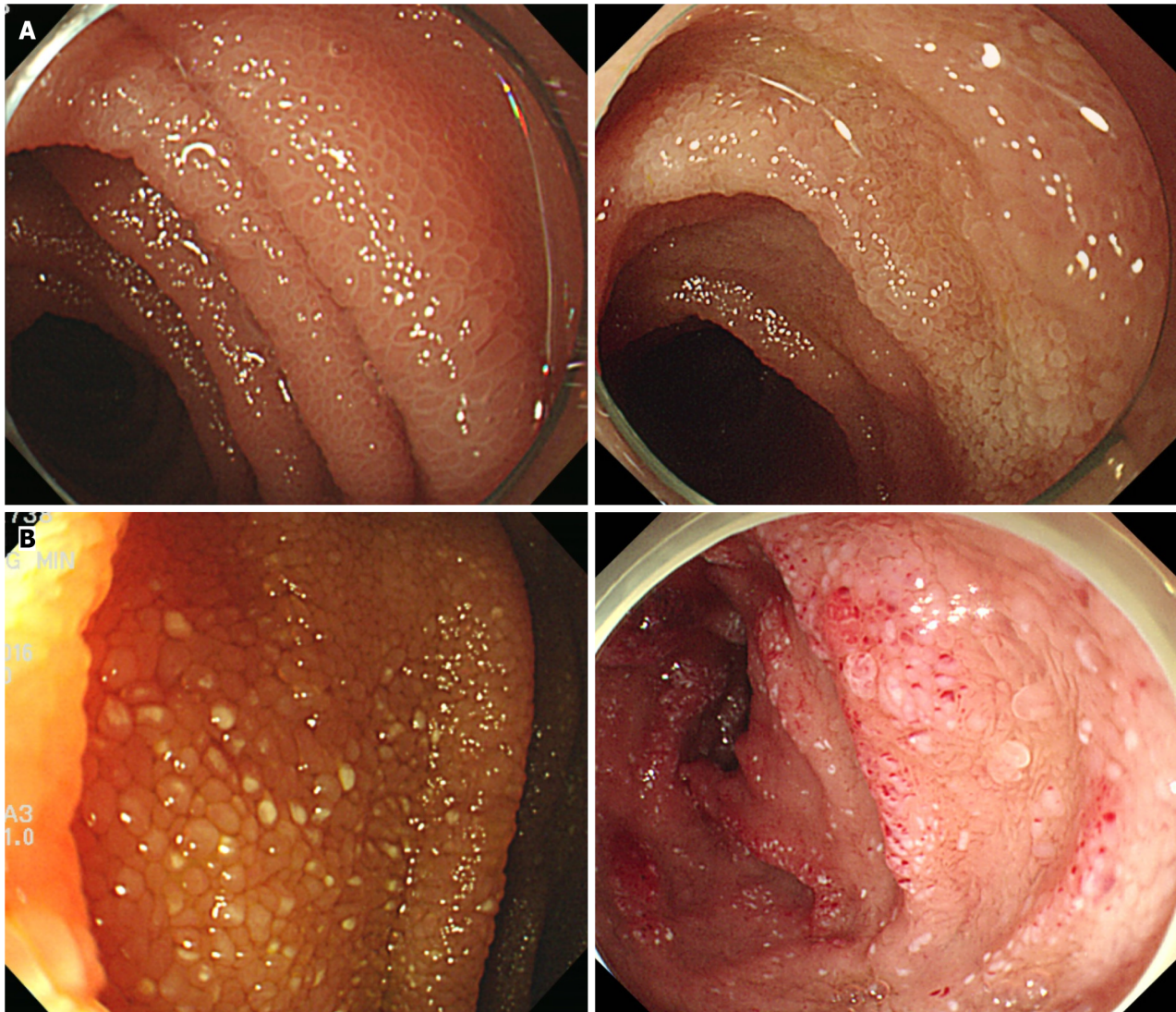
Table 1 Demographic information in patients with primary intestinal lymphangiectasia	
Demographic information	
Total number of patients	12
Age, yr	48 (32, 63)
Male/female	7/5 (58/42)
BMI	22 (21, 23)
Comorbidities	
Cerebrovascular disease	3 (25)
Hypertension	2 (17)
Cardiovascular disease (unstable angina, MI, CHF)	1 (8)
Chronic obstructive pulmonary disease	0 (0)
Diabetes mellitus	3 (25)
Chronic kidney disease	1 (8)
Cancer	3 (25)
Follow-up duration, mo	30 (24, 37)

Categorical variables were presented as numbers and percentages, whereas continuous variables were represented as median and interquartile range. BMI: Body mass index; CHF: Congestive heart failure; MI: Myocardial infarction.

Diagnostic findings

Peripheral edema was observed in all 12 patients, diarrhea diagnosed in 9 patients (75%), and abdominal pain in 4 patients (33%) (Table 2). No patients reported feeling nausea or vomiting. Lymphocytopenia was observed in 5 patients (42%). The median albumin level was 1.8 g/dL, highlighting hypoalbuminemia across all patients. IgG levels were also low, with a median level of 391 mg/dL (normal range 600-1600 mg/dL). Except for two missing values, AAT clearance exceeding 27 mL/24 h was confirmed in all ten patients.

Radiologically, bowel wall thickening and edema were observed in 8 patients (67%), and ascites were detected in 7 patients (58%). Pleural effusion was present in 3 cases (25%). Endoscopic findings revealed edematous and whitish delineated villi observed in all patients (Figure 1). The snowflake appearance (whitish spots) was noted in 9 patients (75%). Pathological confirmation was observed in all patients, illustrating lymphangiectasia in the mucosa and submucosal layers (Figure 2).



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Figure 1 Endoscopic image of the small intestine. A: Edematous or whitish delineated villi; B: A snowflake appearance.

Treatment and complications

Dietary education was provided to all patients, focusing on a low-fat and high-protein diet incorporating medium-chain triglycerides (MCT) oil. Tailored to individual symptoms, periodic albumin replacement was recommended, and most patients underwent albumin infusion within the outpatient hospital setting. Over a median follow-up duration of 30 mo, in conjunction with foundational dietary education and albumin replacement, the subsequent medications were used for treatment: octreotide, tranexamic acid, steroids, sirolimus, and everolimus. In each case, the drug selection sequence and the concurrent administration periods were delineated using the numbers 1 to 5 (Table 3). Among the 12 patients, eight (#2, 4, 5, 6, 8, 10, 11, and 12) continued long-term treatment with octreotide or sirolimus, either as monotherapy or in combination. However, two patients (#1 and #9) exhibited enhanced albumin levels and ameliorated clinical symptoms during maintenance treatment with octreotide (#1) and sirolimus (#9), allowing them to maintain regular follow-ups after

Table 2 Diagnostic findings in patients with primary intestinal lymphangiectasia

Diagnostic findings	
Symptoms	
Peripheral edema	12/12 (100)
Diarrhea	9/12 (75)
Abdominal pain	4/12 (33)
Nausea/vomiting	0 (0)
Laboratory findings	
Leukocyte, $10^9/L$	4.8 (3.9, 6.6)
Lymphocyte, $10^9/L$	1.1 (0.7, 1.4)
Lymphocytopenia, $< 1.0 \times 10^9/L$	5/12 (42)
Hemoglobin, g/dL	11.9 (10.7, 13.4)
Albumin, g/dL	1.8 (1.7, 2.4)
IgG, mg/dL	391 (343, 474)
Ferritin, ng/mL	130 (54, 256)
Ferritin < 30 (male) or 13 (female) ng/mL (two missing value)	1/10 (10)
CRP, mg/dL	0.16 (0.08, 0.49)
Alpha-1 antitrypsin clearance, mL/24 h	566 (211, 704)
Alpha-1 antitrypsin clearance > 27 mL/24 h (two missing value)	10/10 (100)
Radiologic findings	
Small bowel wall thickening and edema	8/12 (67)
Ascites	7/12 (58)
Pleural effusion	3/12 (25)
Ileus	0/12 (0)
Endoscopic findings	
Snowflake appearance	9/12 (75)
Pathological findings	
Dilation of the lymphatics in mucosa or submucosa	12/12 (100)

Categorical variables were presented as numbers and percentages, whereas continuous variables were represented as median and interquartile range. CRP: C-reactive protein.

discontinuing the medications. One patient (#7) had mild clinical symptoms and was only monitored using diet and albumin replacement. Patient (#3) was ineligible for PIL treatment due to concurrent cancer treatment.

Three patients (#6, 9, and 10) exhibited pleural effusion and underwent lung mediastinal MRI. Among these cases, two patients (#6 and #10) underwent lymphangiography to validate the presence of lymphatic leakage. Within this subset, one patient (#6) received confirmation of lymphatic leakage and consequently underwent embolization.

The yearly frequency of hospitalizations ranged from 0 to as high as 14 occurrences (Table 4). Infections were identified in 6 patients (#1, 3, 6, 9, 10, and 12), encompassing bacterial infections such as urinary tract infections, pneumonia, spontaneous bacterial peritonitis, cellulitis, and catheter-related infections. Furthermore, a diverse array of infections, including tuberculosis, herpes zoster, and invasive pulmonary aspergillosis, were observed. Symptoms of thromboembolism were observed in 3 cases involving pulmonary thromboembolism in patients #1 and #10 and cerebral infarction in patients #6. Mortality was witnessed in 2 cases, specifically in patients #3 and #6. Among these cases, patient #6 encountered a deteriorating course attributed to uncontrolled PIL, resulting in their death.

DISCUSSION

This study observed that PIL can be diagnosed across a range of age groups in adults, between the twenties the seventies, with most of the patients primarily presenting with peripheral edema and diarrhea. Hypoalbuminemia and hypogamma-

Table 3 Medical treatment and interventions during the follow-up of adult patients with primary intestinal lymphangiectasia

Case number	Age/sex	Albumin	Octreotide	Tranexamic acid	Steroid	Sirolimus	Everolimus	Outcome of treatment	Lng medias-tinum MRI (reason)	Lymphangiography	Lymphatic embolization
		Periodic injection intravenously	Subcutaneous; Dose; Frequency; Duration	Oral; Dose; Frequency; Duration	Oral; Dose; Frequency; Duration	Oral; Dose; Frequency; Duration	Oral; Dose; Frequency; Duration		No/yes (reason)	No/yes (reason)	No/yes (reason)
1	30/M	Yes	(5) 100-200 mcg qd-bid for 6 month	(4) 500 mg tid for 3 month	(2) 40 mg tapered for 2 month	(3)-(4) 1-2 mg qd for 6 month	(1) 2.5 mg qd for 2 month	Improvement and observation after stopping medical treatment			
2	70/M	Yes	(1)-(3) 50-100 mcg qd-bid for continuously	(2) 500 mg tid for 3 month		(3) 1 mg qd for 6 month		Octreotide continuously			
3	63/F	Yes						Unable to treat appropriately due to underlying colon cancer			
4	54/M	Yes				(1) 2-3 mg qd for continuously		Sirolimus continuously			
5	28/F	Yes	(1)-(2) 100 mcg qd for 6 month			(2) 1-2 mg qd for continuously		Sirolimus continuously			
6	67/F	Yes	(1) 100 mcg bid for 3 month	(2) 250 mg tid for continuously		(2) 2 mg qd for continuously		Tranexamic acid and sirolimus continuously	Yes (pleural effusion)	Yes (pleural effusion)	Yes (pleural effusion)
7	32/M	Yes						Regular albumin replacement	No	No	No
8	65/M	Yes				(1) 1-2 mg qd for continuously		Sirolimus continuously	No	No	No
9	41/F	Yes			(1) 40 mg tapered for 4 wk	(2) 1-2 mg qd for 1.5 yr		Improvement and observation after stopping medical treatment	Yes (pleural effusion)	No	No
10	35/M	Yes	(1)-(2) 50-200 mcg qd-bid for 2 yr	(4) 250 mg tid for 6 month	(3) 30 mg tapered for 1 month	(2)-(4) 1 mg qd for continuously		Sirolimus continuously	Yes (pleural effusion)	Yes (pleural effusion)	No
11	32/M	Yes	(2) 100 mcg qd-bid for continuously			(1)-(2) 1-4 mg qd for continuously		Octreotide and sirolimus continuously	No	No	No
12	76/F	Yes	(2) 100 mcg qd-bid for continuously			(1) 1 mg qd-bid for 6 month		Octreotide continuously	No	No	No

bid: Bis in die (two times a day); F: Female; M: Male; tid: Ter in die (three times a day); qd: Quaque die (once a day); qid: Quarter in die (four times a day).

globulinemia were observed in blood tests, often accompanied by lymphopenia of less than half. These findings are consistent with previous reports[4]. Protein-losing enteropathy was confirmed in all patients, excluding those with missing data, based on AAT clearance. Radiologic images showed frequent small bowel wall edema, aligning with prior studies[12,13]. Over half of the patients presented moderate to significant amounts of ascites. Of all 12 patients, four patients underwent enteroscopy instead of EGD and colonoscopy. A characteristic snowflake appearance was observed in 75% of cases. Edematous villi and whitish delineated villi were observed in all patients. It is important to be aware that such distinctive findings can be observed, and histological examination is necessary to distinguish them from normal features. Pathological confirmation was possible in all patients using biopsies targeting suspicious lesions and random biopsies. All PIL patients received fundamental dietary education about the low-fat, high-protein, and MCT diet. Octreotide and sirolimus demonstrated the most promising treatment persistence effects. However, the occurrence of complications and treatment outcomes varied significantly among patients. While two patients displayed improvement and were ready to discontinue treatment, one patient experienced complications that ultimately led to death. This emphasizes that even in cases of PIL diagnosed in adults; however, prognosis can vary greatly depending on the severity of the condition and the response to treatment.

This study has significant importance as it provides the first insights into the diagnosis, treatment, complications, and prognosis of adult patients with PIL. Given the rare nature of PIL and the limited number of case reports in adults, there was a lack of guidance for diagnosis and treatment. This study presented the institutional protocols for diagnosing PIL, a cause of protein-losing enteropathy, among patients exhibiting clinical symptoms and blood test results. Sharing such protocols has the potential to aid physicians encountering similar patients, offering them a valuable point of reference.

The low-fat, high-protein, MCT oil diet has been reported to contribute to the recovery of PIL by lowering lymphatic pressure through bypassing absorption *via* the gut lymphatic system[14,15]. Therefore, dietary education on this approach is considered fundamental for initiating treatment. The potential efficacy of drugs such as octreotide, sirolimus, everolimus, tranexamic acid, and steroids has been suggested, but studies regarding their long-term maintenance treatment effects are limited[16]. Octreotide is believed to exhibit therapeutic effects by targeting gut lymphatics flow to reduce fat absorption in the intestine[17-19]. One case report observed sustained treatment effects for over six months [19]. In our study, among seven patients who received octreotide treatment, three patients showed no effect and discontinued, one patient improved and subsequently stopped, and among the remaining three patients who received consistent therapy, one continued octreotide monotherapy for four years (#2), and another patient received combination treatment with sirolimus for two years (#11). This suggests that long-term treatment might also be anticipated in patients with a favorable response. Sirolimus acts on lymphatic endothelial cells by inhibiting the mammalian target of rapamycin signaling, thereby suppressing lymphatic proliferation. This mechanism has been utilized in the treatment of lymphangiectasia and lymphangiomyomatosis[20,21]. Among four pediatric patients, two patients with lymphangiectasia confined to the intestine reported an effect after 3-4 mo of treatment, though there has been no report in adults[22]. In our case series, among the ten patients who received sirolimus treatment, three patients experienced limited efficacy and discontinued, one improved and subsequently discontinued, and six patients showed sustained effects lasting from around 1 yr to 4 yr, leading to maintenance treatment. This suggests that long-term therapy may also yield effectiveness in patients who respond well to sirolimus. Considering the mechanistic distinctions, where octreotide predominantly impacts the flow within the lymphatic system, and sirolimus acts on lymphatic endothelial cells, it is conceivable that patients who did not respond well to octreotide might respond to sirolimus and vice versa.

Table 4 Complications and prognosis during the follow-up of adult patients with primary intestinal lymphangiectasia

Case number	Age/sex	Hospitalization after diagnosis, frequency per year	Any infection, no/yes (disease)	Any thromboembolism, no/yes (disease)	Mortality, no/yes (cause)
1	30/M	14	Yes (invasive pulmonary aspergillosis, zoster, tuberculosis)	Yes (pulmonary thromboembolism)	No
2	70/M	2	No	No	No
3	63/F	6	Yes (pneumonia, cellulitis, urinary tract infection)	No	Yes (underlying cancer)
4	54/M	1	No	No	No
5	28/F	1	No	No	No
6	67/F	6	Yes (pneumonia)	Yes (cerebral infarction)	Yes (primary intestinal lymphangiectasia)
7	32/M	2	No	No	No
8	65/M	1	No	No	No
9	41/F	2	Yes (zoster)	No	No
10	35/M	7	Yes (catheter-related infection)	Yes (pulmonary thromboembolism)	No
11	32/M	0	No	No	No
12	76/F	3	Yes (spontaneous bacterial peritonitis, pneumonia)	No	No

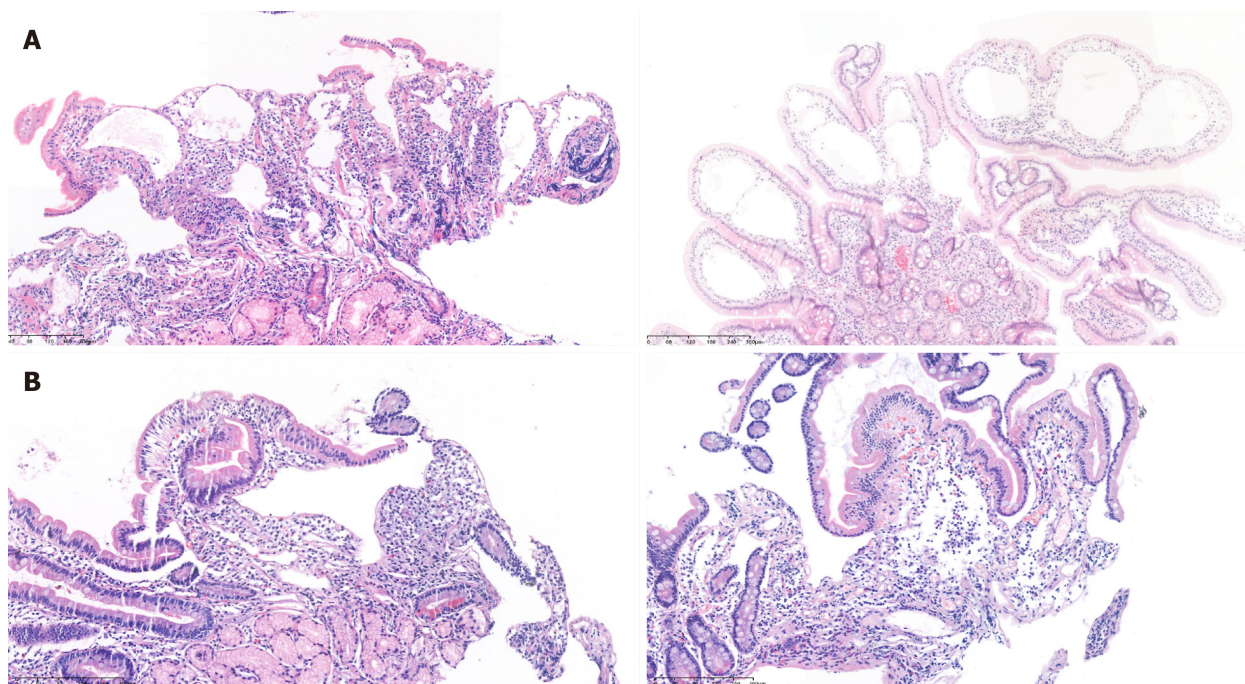
F: Female; M: Male.

This suggests that the efficacy of these two drugs could differ based on the primary pathology of each patient, and combination therapy could also be considered an option. Everolimus[23], as the 2nd generation of sirolimus, and tranexamic acid[24,25], which aims to reduce intestinal protein loss by decreasing plasma fibrinolytic activity, did not demonstrate long-term efficacy in this study.

In cases where chyle ascites or chylothorax is identified, non-invasive tests such as lymphatic scintigraphy[26,27] or MR lymphangiography[28] can be conducted to assess problems within the lymphatic drainage system. However, their role in PIL is limited. At our institution, lung mediastinal MRI can be utilized to examine potential leakage or rupture in thoracic lymphatics. Consequently, we conducted this examination in three cases. While lymphangiography is an invasive procedure, it was performed for two patients in this study based on the outcomes of preceding non-invasive tests and consultation with specialized radiologists, leading to embolization in one case. While the available tests might vary among different medical facilities, it is worth considering the flow of the lymphatic system, where lymphatic capillaries connect to lymphatic vessels and nodes within the submucosal and mesentery regions that ultimately drain into the thoracic duct². This investigation could help illuminate whether chyle ascites or chylothorax is linked to structural abnormalities within the subserosal lymphatics[29].

Mechanistically, PIL can induce changes in the immune system due to lymphatic loss, leading to lymphocytopenia and hypogammaglobulinemia[1]. Although reports on infections in adult PIL are limited, this study observed that half of the patients experienced various infections. One patient suffered from a severe fungal infection, such as invasive pulmonary aspergillosis. Therefore, it is necessary to exercise caution regarding infectious complications in adult patients with PIL. Venous thromboembolism was observed in 2 out of 12 patients. Prior research has established an association between hypoalbuminemia and venous thromboembolism in various conditions, such as nephrotic syndrome, hospitalized patients, and inflammatory bowel disease[30-34]. This connection is linked to the anticoagulant properties of albumin[35, 36], its role as a negative acute-phase reactant indicating a hyperinflammatory state[37,38], and the compensatory hepatic synthesis of coagulation factors[39]. Similarly, caution is warranted concerning the potential association between hypoalbuminemia and venous thromboembolism within the context of PIL.

The present study had several limitations. Firstly, owing to the rare nature of the disease, the number of patients included in this study was constrained. Nonetheless, as a tertiary referral center, the primary objective was to share comprehensive experience spanning from diagnosis to prognosis of PIL. Secondly, we did not provide guidance on which treatment approach to choose first, how long to observe, or the appropriate dosage. However, we described the dosages and durations of medications in detail with their treatment effects. Thirdly, the details of albumin replacement, including dosage and frequency, were not fully available for all patients. Fourthly, lymphatic scintigraphy was not feasible within this institution, and consequently, it was not incorporated into this study.



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Figure 2 Pathological image of lymphangiectasia in mucosa and submucosa. A: Marked dilated lymphatics in the tips of villi; B: Lymphangioma involving mucosa and submucosa.

CONCLUSION

While the clinical presentation and laboratory findings in adults diagnosed with PIL were like previous reports, considerable variability exists in the severity of the disease, treatment response, and prognosis among patients. This suggests the need for individually tailored and proactive treatment approaches in adult PIL.

ARTICLE HIGHLIGHTS

Research background

This thesis explores Primary Intestinal Lymphangiectasia (PIL), a rare disorder affecting the gastrointestinal tract. PIL involves the dilation or rupture of the gut's lymphatic system, leading to lymph leakage, lymphopenia, hypogammaglobulinemia, and other symptoms like peripheral edema and abdominal pain. Despite its rarity, PIL has been reported in both children and adults, with unclear mechanisms and prevalence.

Research motivation

The research seeks to fill gaps in knowledge, offering insights for more effective management of adult PIL patients.

Research objectives

The study aims to enhance understanding by investigating clinical presentation, diagnosis, treatment, complications, and prognoses in adult PIL cases.

Research methods

The research employed a retrospective screening of adult patients diagnosed with PIL from March 2016 to September 2021. Utilizing the specific disease code for extremely rare diseases in South Korea, medical records were examined, excluding those with insufficient treatment history or follow-up less than six months. Diagnosis criteria involved clinical symptoms, imaging tests, and histological confirmation. Various tests, including blood, radiological, and endoscopic examinations, were conducted to confirm the diagnosis. Data collected included demographic information, diagnostic findings, treatment details, and outcomes. Treatment options ranged from medical therapies (diet, albumin administration, octreotide, *etc.*) to interventions (magnetic resonance imaging, lymphangiography, embolization). Complications and prognoses were tracked through annual hospitalization frequency, infections, thromboembolism, and mortality. Patients were followed from diagnosis to the last outpatient visit or date of death.

Research results

In this study, 12 out of 18 adult patients diagnosed with PIL were included in the case series. The patients, aged 28 yr to 76 yr, exhibited a well-balanced gender distribution, with prevalent comorbidities such as cerebrovascular disease, diabetes mellitus, and cancer. Diagnostic findings revealed common symptoms of PIL, including peripheral edema in all patients, diarrhea in 75%, and abdominal pain in 33%. Lymphocytopenia was observed in 42% of patients. Radiological and endoscopic examinations consistently confirmed features of PIL, such as bowel wall thickening, ascites, pleural effusion, and a distinctive snowflake appearance. Treatment involved dietary education focusing on a low-fat, high-protein diet with medium-chain triglycerides, along with periodic albumin replacement. Medications like octreotide, tranexamic acid, steroids, sirolimus, and everolimus were employed, with individualized sequences and durations. Eight patients continued long-term treatment, while some achieved symptom improvement and discontinued medication. Complications included infections in six patients, thromboembolism in three cases, and mortality in two patients. Pleural effusion cases underwent lung mediastinal magnetic resonance imaging and lymphangiography, with one patient undergoing embolization. The study contributes valuable insights into the clinical presentation, treatment, and outcomes of adult PIL cases, highlighting the challenges and complexities associated with the management of this rare disorder. Remaining issues include optimizing treatment strategies, addressing complications, and improving long-term prognoses.

Research conclusions

The study enhances our understanding of adult PIL, emphasizing the need for personalized treatment approaches and proactive management strategies. The findings contribute valuable knowledge to the limited existing literature on this rare condition, offering insights that can guide clinicians in the diagnosis and treatment of adult patients with PIL.

Research perspectives

Future research in PIL should focus on refining treatment protocols, exploring combination therapies, conducting larger multi-center studies, investigating the role of diet, and addressing immune system changes. These efforts will contribute to improving the management and outcomes of adult PIL patients.

FOOTNOTES

Author contributions: Na JE and Kim JE contributed study concept and design; Na JE and Kim JE contributed acquisition, analysis, or interpretation of the data; Na JE and Kim JE contributed writing and drafting of the manuscript; Kim JE, Hong SN, Kim ER, Kim YH, Chang DK and Park S contributed critical revision of the manuscript for important intellectual content; Na JE contributed statistical analysis; all authors approved the final submission.

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