Clinical outcome of nutrition-oriented intervention for primary intestinal lymphangiectasia

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Background: **Primary intestinal lymphangiectasia (PIL) is a rare digestive disease and few studies have focused on the therapeutic effect in PIL patients. This study was undertaken to evaluate nutrition-oriented intervention in children with PIL.**

Methods: **Four children with PIL were studied. Their medical records were reviewed. Anthropometric measurements and blood tests were performed during a 8-18 month follow-up.**

Results: **During hospitalization, the 4 patients were subjected to diet intervention. Parenteral nutrition (PN) support was also given to 3 of them. Clinical symptoms and laboratory parameters of the patients were significantly improved at discharge. After discharge, the patients continued diet control, 2 of whom received intermittent PN support. The mean follow-up duration of the 4 patients was 13 months (range, 8-18 months) and they all kept in a stable condition without symptoms relapse. Weight, height and body mass index for age were normal during the follow-up, while total protein, albumin and immunoglobulin concentrations were still slightly below normal level.**

Conclusions: **Nutrition therapy is effective as a valid and safe therapeutic management for PIL patients. No growth retardation was observed in the 4 children after the therapy, but they are still at risk of nutrient malabsorption. Therefore, they need long-term, regular monitoring and intensive nutritional care.**

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Introduction

Intestinal lymphangiectasia (IL) is a rare protein-losing gastroenteropathy, characterized by edema, diarrhea, ascites, lymphocytopenia and malabsorption. The first case of IL was reported by Waldmanin in 1961.[1,2] Intestinal lymphangiectasias can be classified as primary and secondary diseases according to the underlying mechanisms. Primary intestinal lymphangiectasia (PIL) is mainly due to congenital malformation of intestinal lymphatic drainage and often occurs at an early age.[3] Thus, problems such as growth impairment and developmental delay may appear as children grow.[4] Diet intervention is a theoretically established therapy for PIL, while refractory cases are reported frequently.[5] Interests in therapeutic method for this disorder have been increasing recently, but few studies have focused specifically on the assessment of therapeutic effects and nutritional status in the PIL patients. This study was undertaken to evaluate the efficacy of nutrition intervention by investigating clinical symptoms, laboratory parameters and growth status of PIL children.

Methods

We analyzed retrospectively 4 patients with PIL who were admitted to Xin Hua Hospital between June 2007 and August 2008. Biopsy specimens from the small intestine showing marked dilatation of lymphatics or capsule endoscopy revealing edematous aspect of the intestinal mucosa with whitish and swollen villi in the small intestine, corresponding to marked dilatation of lymphatic vessels, confirmed the diagnosis of IL. Information regarding sex, age at onset, date on admission and at discharge, height and weight, clinical characteristics, laboratory parameters, therapeutic methods, treatment duration and clinical outcomes were reviewed in detail. During outpatient visits or telephone interviews once per month, treatments were adjusted according to growth and nutrition assessment including anthropometric measurements and blood tests (lymph-cell count, total protein, serum albumin and immunoglobulin). All patients were treated and followed up by the same physician with the assistance from a

nutrition support team. Anthropometric measurements including height and weight were performed by the same nutritionist qualified for these measurements. Height was measured with a stadiometer to the nearest 1 cm, and weight was assessed by bioelectric impedance analysis to the nearest 10 mg with minimal clothes for which no correction was made. Height for age Z score (a measure of stunting or chronic malnutrition) and weight for age Z score (a measurement of underweight) were calculated by Epi-info 3.5 software for evaluation of growth and nutrition status according to the 2000 Centers for Disease Control and Prevention Growth Charts for the United States. The percentile of height for age and weight for age was defined according to the International WHO Growth Standards for Children and Adolescents. A Z score not exceeding -2 corresponding to ≤3rd percentile (≤P3) was defined as malnutrition, and a score greater than 2 equal to ≥97th percentile (≥P97) was considered as overweight. Total protein and serum albumin were assessed by automated colorimetric method. Immunoglobulin was estimated by nephelometry. Total lymphocyte count was assessed with the Beckman Coulter's automated system.

Informed consent was obtained from the parents of the 4 children, and the study protocol was approved by the Ethics Committee of Xin Hua Hospital.

Results

The 4 patients had a relatively early onset of the disease with a mean age of 4 months (range, 0-9 months), and the mean duration from the first onset of symptoms to diagnosis was 4.5 years (range, 2-8 years). All patients showed hypoproteinemia and decreased immunoglobin except for IgE. The mean duration of hospitalization was 23.5 days (range, 12-40 days). Patients 1, 2 and 4 were confirmed with a diagnosis of IL by the presence of intestinal lymphangiectasia based on both endoscopic and histological findings of intestinal biopsy. Videocapsule endoscopy revealed edema of the intestinal mucosa with whitish and swollen villi in the whole small intestine, corresponding to marked dilatation of lymphatic vessels. Patient 3 with negative histology of biopsy specimens was finally diagnosed with IL by capsule endoscopy, showing typical characteristics of IL from the upper jejunum to the end of the ileum. Scintigraphy was also suggested to detect gastrointestinal protein loss, but it was denied by their parents. Excluding secondary causes of lymphatic obstruction and other underlying diseases, the 4 children were diagnosed with PIL. Only in patients with segmental lesions or complications such as intestinal obstruction, local bowel resections were reported successfully. In the 4 patients with extensive lesions, nutrition therapy was an option of treatment. A low long-chain triglycerides (LCT), high-protein diet supplemented with medium-chain triglyceride (MCT), was prescribed in all patients after the diagnosis of IL. Parenteral nutrition (PN) support was also given to patients 1, 2 and 4 with symptoms such as severe diarrhea associated with dehydration and electrolyte disturbance for an average of 22.7 days (range: 13-31 days). Edema, diarrhea and ascites were alleviated, and

Table 1. Clinical characteristics and nutrition intervention during the hospitalization

Case	Sex	Age at onset (mon)	Age on admission (y)	Edema	Diarrhea	Ascites	Lymphocyte ↓	TP ↓	ALB ↓	Immuno globulin ↓	Diet therapy (d)	PN duration (d)
1	M	3	7	+	+	+	+	+	+	+	40	24
2	M	9	3	+	+	+	+	+	+	+	31	31
3	F	0	8	+	–	–	–	+	+	+	15	0
4	F	4	2	+	+	+	–	+	+	+	12	13

+: positive; –: negative; TP: total protein; ALB: albumin; PN: parenteral nutrition.

Table 2. Main laboratory parameters on admission, at discharge and during follow-up

Parameters (reference range)	Group	Case 1	Case 2	Case 3	Case 4	Mean value
Total protein (g/L) (60-80 g/L)	A	31.4	33.6	37.7	38.1	35.20
	D	46.3	50.7	48.5	66.3	52.95
	F_1	45.5	51.0	50.8	53.0	50.08
	F_2	47.7	49.0	52.5	47.9	49.28
Albumin (g/L) (35-50 g/L)	A	20.0	21.4	26.1	25.1	23.15
	D	26.7	33.3	31.5	43.8	33.83
	F_1	27.2	32.9	30.5	36.0	31.65
	F_2	27.3	31.2	32.0	30.7	30.30
Immunoglobulin (g/L) (35-50 g/L)	A	11.4	12.2	11.6	13.0	12.05
	D	19.6	17.4	17.0	22.5	19.13
	F_1	18.3	18.1	20.3	17.0	18.43
	F_2	20.4	17.8	20.5	17.2	18.98

Goup A: on admission; goup D: at discharge; goup F_1: at the first follow-up; goup F_2: at the last follow-up.

Table 3. Percentile and Z score references of height for age and weight for age on admission and during follow-up

Group	Case	Age (y)	Height (cm)	Weight (kg)	BMI	WAZ	HAZ
A	1	6.7	102 (<P1)	16.7 (P1-P3)	15.77	-2.41	-3.24
	2	2.7	85 (P1-P3)	13.5 (P25-P50)	17.42	-0.85	-2.08
	3	7.5	119 (P15-P25)	23.2 (P25-P50)	16.33	-0.25	-0.99
	4	2.1	84 (P15-P25)	11.5 (P25-P50)	16.3	-1.01	-0.95
F	1	8.2	120 (P5-P15)	24.8 (P25-P50)	17.26	-0.36	-1.60
	2	3.4	92 (P3-P5)	15.0 (P50-P75)	17.75	-0.02	-1.55
	3	8.2	129 (P50-P75)	29.1 (P75-P85)	17.41	0.54	0.05
	4	3.6	102 (P50-P75)	15.5 (P50-P75)	14.88	0.28	0.99

Group A: on admission; group F: during follow-up; BMI: body mass index; WAZ: weight for age Z score; HAZ: height for age Z score.

laboratory parameters showed a great improvement (Table 1). After discharge, the patients were followed up for an average of 13 months (range: 8-18 months). All the children continued diet control, and PN was administered to patients 1 and 2 in a gradually decreasing frequency. No complications of PN were observed, and there was no symptom relapse (Table 2).

Table 3 shows percentile and Z score references of height for age and weight for age in the 4 patients. On admission, patients 3 and 4 had normal weight and height for age while patient 1 was stunting and underweight with a weight for age Z score of -3.24 (<P1) and a height for age Z score of -2.41 (P1-P3), and patient 2 had a height for age Z score of -2.08 (P1-P3), showing chronic malnutrition. During follow-up, anthropometric assessments showed normal results in the 4 patients.

Discussion

As PIL primarily affects children, treatment aims to alleviate symptoms, maintain plasma protein level, and optimize weight gain and linear growth through diet intervention with minimizing parenteral support.[5,6] A low-LCT diet supplemented with MCT is the cornerstone of PIL management.[7] The absence of LCT in the diet prevents engorgement of intestinal lymphatics, thereby preventing their rupture.[8] MCT as a substitute for LCT is directly absorbed into the portal venous circulation, thus providing nutrient fat but avoiding lacteal engorgement.[9,10] When patients are refractory to diet intervention or symptoms are severe, PN as a complementary therapy for PIL provides effective nutrition support and reduces oral fat intake.[11] Lee and Kong[2] reported that a high-fat diet before endoscopic examination leads to more prominent abnormal lymphatics and facilitates the endoscopic and histological diagnosis of intestinal lymphangiectasia. Their study provided indirect evidence to the effects of diet control. By reviewing individual cases, Desai et al[12] found that although MCT diet is not completely curative in all cases, it does improve the symptoms of PIL and reduces the mortality. However, the need for diet intervention is considered permanent, as clinical symptoms relapse is frequent upon relaxation of the regimen.

For segmental lesions, surgery is a quite useful method, and some cases have been reported successfully treated by local bowel resection. Other forms of medical therapy have been proposed to treat PIL recently. For instance, octreotide was successfully used in some cases,[13,14] but there were also cases with no improvement after octreotide therapy.[15] The effect of octreotide on intestinal lymphangiectasia remains to be elucidated.

In our study, the 4 children were given a low-LCT, high-protein diet supplemented with MCT after the diagnosis of PIL. Their daily diet with 75-80 kcal/kg per day (Calorie intake was adjusted in accordance with weight) consisted of 60% carbohydrates, 20% proteins and 20% lipids. The parents recorded their children's daily diet, including the varieties and quantities of food. The results of diet investigations were analyzed by the Nutritional Analysis and Consultation System, and the treatments were adjusted accordingly. Our children had diet intervention at a mean age of 5 years (range: 2-8 years), they were tolerable to the low-fat diet. During hospitalization, PN was also prescribed in 3 of the 4 children whose symptoms were severe, from once per day to twice per week. The 4 children had a good response to nutrition therapy. Edema, diarrhea and ascites were alleviated and laboratory parameters were also improved. After discharge, these children continued diet control, and PN was given to 2 of them from twice per week at discharge to once per three weeks. During follow-up, the 4 children showed no symptoms relapse, although the levels of total protein, albumin and immunoglobulin were slightly below the normal levels. In two children with malnutrition on admission, anthropometric assessment showed normal results during follow-up.

In summary, diet intervention with adequate PN is an option for PIL in children, and diet control can prevent symptoms relapse. There is no growth

retardation in such children after nutrition therapy, but they are still at risk of nutrient malabsorption. Therefore they need long-term, regular monitoring and intensive nutritional care.

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References

1 Vignes S, Bellanger J. Primary intestinal lymphangiectasia (Waldmann's disease). Orphanet J Rare Dis 2008;3:5.
2 Lee J, Kong MS. Primary intestinal lymphangiectasia diagnosed by endoscopy following the intake of a high-fat meal. Eur J Pediatr 2008;167:237-239.
3 Moller A, Kalhoff H, Reuter T, Friedrichs N, Wagner N. Congenital intestinal lymphangiectasia: a rare differential diagnosis in hypoproteinemia in infants. Klin Padiatr 2006;218:224-225.
4 Diaz N, Khoury A, Taboada M, Isava I, Calderon A, Lopez C, et al. Primary intestinal lymphangiectasia in children: report of 3 cases. G.E.N 1995;49:307-309.
5 Kuroiwa G, Takayama T, Sato Y, Takahashi Y, Fujita T, Nobuoka A, et al. Primary intestinal lymphangiectasia successfully treated with octreotide. J Gastroenterol 2001;36:129-132.
6 Takahashi H, Imai K. What are the objectives of treatment for intestinal lymphangiectasia. J Gastroenterol 2001;36:137-138.
7 Martin CC, Garcia AF, Restrepo JM, Perez AS. Successful dietetic-therapy in primary intestinal lymphangiectasia and recurrent chylous ascites: a case report. Nutr Hosp 2007;22:723-725.
8 Andersen UM, Lund HT. Primary intestinal lymphangiectasis. Ugeskr Laeger 1996;158:1840-1841.
9 Koo NH, Lee HJ, Jung JW, Hwan Kim S, Lee KM, Hwang JS. Intestinal lymphangiectasia: a response to medium-chain triglyceride formula. Acta Paediatr 2005;94:982-983.
10 Greco F, Piccolo G, Sorge A, Pavone P, Triglia T, Spina M, et al. Early-onset of primary intestinal lymphangiectasia: a case report and diet treatment. Minerva Pediatr 2003;55:615-619.
11 Aoyagi K, Iida M, Matsumoto T, Sakisaka S. Enteral nutrition as a primary therapy for intestinal lymphangiectasia: value of elemental diet and polymeric diet compared with total parenteral nutrition. Dig Dis Sci 2005;50:1467-1470.
12 Desai AP, Guvenc BH, Carachi R. Evidence for medium chain triglycerides in the treatment of primary intestinal lymphangiectasia. Eur J Pediatr Surg 2009;19:241-245.
13 Kuroiwa G, Takayama T, Sato Y, Takahashi Y, Fujita T, Nobuoka A, et al. Primary intestinal lymphangiectasia successfully treated with octreotide. J Gastroenterol 2001;36:129-132.
14 Filik L, Oguz P, Koksal A, Koklu S, Sahin B. A case with intestinal lymphangiectasia successfully treated with slow-release octreotide. Dig Liver Dis 2004;36:687-690.
15 Lynn J, Knight AK, Kamoun M, Levinson AI. A 55-year-old man with hypogammaglobulinemia, lymphopenia, and unrelenting cutaneous warts. J Allergy Clin Immunol 2004;114:409-414.

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