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Case Report

Efficacy of Sirolimus in a 17-Month Old Patient with Primary Intestinal Lymphangiectasia

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Abstract

Primary intestinal lymphangiectasia (PIL) is an uncommon condition characterized by the dilation of lymphatic vessels that supply the small intestinal wall, leading to the leakage of lymph into the small-bowel cavity. This causes a protein-losing enteropathy, resulting in decreased lymphocytes, low albumin levels, and reduced gamma globulin levels 1. Typically diagnosed before the age of three, PIL rarely occurs in adults. Here, we describe the case of a severely affected one-year-old Saudi girl with PIL, showing poor response to standard treatments. Initially diagnosed at four months of age through lymph scintigraphy, endoscopy, and histopathology. she experiences recurring swelling in her upper and lower limbs, ascites, genital swelling, and diarrhea. She requires frequent albumin transfusions every two weeks to manage her symptoms, despite most standard therapies proving ineffective in maintaining remission. Interventions like monogen formula alone have been insufficient. However, the introduction of sirolimus has significantly reduced her hospital admissions and need for albumin transfusions to once every four to six weeks. She is presently undergoing sirolimus therapy along with fat-soluble vitamins (ADEK) and a low-fat diet supplemented with medium-chain triglycerides.

Keywords: ***Sirolimus, Lymphangiectasia, efficacy, paediatrics, albumin.***

Introduction

In 1961, Waldmann et al. first identified Primary Intestinal Lymphangiectasia (PIL), a rare disorder causing protein loss in the intestine [1]. This condition arises from congenital malformation or lymphatic obstruction. Lymphangiectasia involves the dilation and excessive growth of lymphatic channels in the mucosa, submucosa, or subserosa, resulting in the loss of protein and lymph into the gut, causing hypoproteinemia, hypogammaglobulinemia, hypoalbuminemia, and lymphopenia 1. Sirolimus has emerged as a novel approach for PIL management. As an immunosuppressant, sirolimus inhibits the mTOR pathway, crucial for cell growth and lymphatic vessel formation. This inhibition helps regulate lymphatic function, potentially easing PIL symptoms [2].

Case Report

17 months old girl known to have Primary intestinal lymphangiectasia which was diagnose at age of 4 months based on lymphscintigraphy endoscopy and histopathology results. At just two days old, she exhibited non-pitting edema in her right upper limb, initially thought to be lymphedema. Within a month, she developed edema in her scalp, lower limbs, and genitalia, leading to investigations revealing low serum albumin and a suspected condition induced by cow's milk protein. Subsequent visits abdomen US showed mild free fluid. Consequently, we opted for an endoscopy, revealing distinctive snowflake-like lesions. albumin transfusions along with a low-fat diet supplemented and medium-chain triglycerides were started. Despite these measures, her condition worsened with increased edema in her eyes, hands, and abdominal distention, confirmed by ultrasound displaying bowel loop wall thickening. Multiple readmissions followed, marked by low albumin levels requiring frequent transfusions until Sirolimus was initiated at daily dose of 0.5 mg due to the severe form of PIL and malabsorption. Following Sirolimus treatment initiation, the frequency and severity of admissions decreased significantly, with fewer instances of abdominal distension and improvement of albumin levels. This remarkable improvement in symptoms coincided with the introduction of Sirolimus. Currently, our patient has completed six months of Sirolimus treatment and has shown significant improvement. Currently, she continues with regular follow up and undergoes repeated lab tests, including assessment for albumin level, lymphocyte, total protein, liver function test and lipid profile.

Discussion

Our patient who was diagnose at age of 4 months based on lymph scintigraphy endoscopy and histopathology, we started him on special formula including MCT put she did not show any improvement, and still requiring albumin transfusion every two to three weeks to manage her symptoms, despite most standard therapies proving ineffective in maintaining remission.

Various publications discuss treatment options. The primary approach in PIL involve lifelong dietary adjustment, focusing on high protein, limiting fat intake, substituting with MCT formula, and supplementing with vitamins [3]. A report of Wen et al. showed that all four children examined responded well to nutrition therapy with low long-chain triglycerides and high- protein diet supplemented with MCT formula [4]. Exclusion of long-chain fatty acids prevents the engorgement and rupture of malformed lymphatics while MCTs get directly absorbed into the portal venous circulation [5]. In case of poor response to this treatment, partial or total parenteral nutrition should be considered. Other treatment modalities described in the literature with variable efficacy include antiplasmin therapy, octreotide, corticosteroids and albumin infusions [6-8].

Our patient was on Monogen formula without improvement, which require multiple admission every two to three weeks to receive albumin transfusion, with increasing in symptoms. The next step in the management plan was to start Sirolimus. After starting Sirolimus, the patient showed dramatic improvement in form of symptoms improving, decreasing number of admissions, and increasing level of Albumin as showed in (Table 1). No side effects were detected after a six-months completion of Sirolimus at a daily dosage of 0.5 mg.

Table 1: Investigations

Before starting Sirolimus								**After starting Sirolimus**				
Admission number	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**Ref. Range**
Albumin	19	20	17	21	19	16	21	18	25	35	20	38-54 g/L
Lymphocytes	3.25	2.78		0.29	1.80	2.10	1.29	4.81	1.54	1.32	1.35	3.7-7.5
Total Protein	33	34	34		31	31	32	32	42	45	38	56-75 g/L
ALT/AST	30/52	36/46	54/61	68/81	119/122	63/79	103/90	33/42	40/54	26/36	24/49	<55/5-34 U/L
Cholesterol	-	-	-	-	-	-	-	3.6	3.2	2.62	3.72	<4.4
Triglycerides	-	-	-	-	-	-	-	1.04	1.04	0.75	1.40	<1.7
LDL	-	-	-	-	-	-	-	-	2.06	1.75	2.46	<2.59
HDL	-	-	-	-	-	-	-	-	0.67	0.53	0.63	>1.55

The exact mechanism of Sirolimus is not fully known, but it is believed to directly affect lymphatic endothelial cell. It alters the signaling of the mammalian target of rapamycin, leading to suppression of lymphatic sprouting, proliferation, and inducing apoptosis 9.

Histopathological Study

1. Duodenum, first part, biopsy:

- Duodenal mucosa with foci showing mild lymphangiectasia and regenerative changes
- No villous blunting or increased intrepithelial lymphocytes

2. Duodenum, second part, biopsy:

- Duodenal mucosa with foci showing mild lymphangiectasia and focal surface vacuolation
- No villous blunting or increased intraepithelial lymphocytes

3. Stomach, biopsy:

- Oxyntic -type mucosa with no significant pathologic changes
- No H.pylori infection identified
- Negative for intestinal metaplasia, dysplasia, or carcinoma

Conclusions

The Conclusions section should clearly explain the main findings and implications of the work, highlighting its importance and relevance.

Ethics approval and consent to participate

Not applicable

List of abbreviations

Primary intestinal lymphangiectasia (PIL)
Medium Chain Triglycerides (MCT)

Data Availability

A data availability statement is compulsory for research articles and clinical trials. Here, authors must describe how readers can access the data underlying the findings of the study, giving links to online repositories and providing deposition codes where applicable.

Conflicts of Interest

There is no conflict of interest regarding the publication of this paper."

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No funds were applied in this case report

Authors' contributions

Saleh Alsuqayhi is the first author of this case report
Azhar Swaidi, Ammar Alyousef, Homoud Alhebbi were the co-authors
Mohammed Alamrani is the supervisor

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Not applicable

References:

[1] Waldmann TA, Steinfeld JL, Dutcher TF, Davidson JD, Gordon RS. The role of the gastrointestinal system in "idiopathic hypoproteinemia". Gastroenterology. 1961;41:197–207.
[2] Tak W. Mak, Mary E. Saunders, inThe Immune Response, 2006
[3] 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.

[4] Wen J, Tang Q, Wu J, Wang Y, Cai W: Primary intestinal lymphangiectasia: four case reports and a review of the literature. Dig Dis Sci 2010;55:3466–3472.
[5] Alfano V, Tritto G, Alfonsi L, Cella A, Pasanisi F, Contaldo F: Stable reversal of pathologic signs of primitive intestinal lymphangiectasia with a hypolipidic, MCT-enriched diet. Nutrition 2000, 16:303–304.
[6] MacLean JE, Cohen E, Weinstein M. Primary intestinal and thoracic lymphangiectasia: a response to antiplasmin therapy. Pediatrics. 2002 Jun. 109(6):1177-80.
[7] Al Sinani S, Rawahi YA, Abdoon H. Octreotide in Hennekam syndrome-associated intestinal lymphangiectasia. World J Gastroenterol. 2012 Nov 21.18(43):6333-7.
[8] Freeman HJ, Nimmo M. Intestinal lymphangiectasia in adults. World J Gastrointest Oncol. 2011 Feb 15. 3(2):19-23.
[9] Baluk P, Yao LC, Flores JC, Choi D, Hong YK, McDonald DM. Rapamycin reversal of VEGF-C-driven lymphatic anomalies in the respiratory tract. JCI Insight. 2017;2:e90103