

SUPPLEMENTARY MATERIAL

Supplementary Table 1. All case reports reporting on adult patients (diagnosis after the 18th birthday) with Primary Intestinal Lymphangiectasia (PIL).

Reference	Year	Gender	Duration of symptoms	Age at diagnosis (years)	Symptoms						Laboratory findings							Imaging		Diagnosis					Therapy ± response	Complications			
					Edema	Abdominal pain	Effusion	Diarrhea	Weight	Others	Anemia	Lymphocytopenia	Hypoproteinemia	Hypoalbuminemia	Hypogammaglobulinemia	Electrolytes	A1AT (fecal)	Others	CT/US	Others	Upper GI Endoscopy	Colonoscopy	Enteroscopy	VCE			Surgery		
[1]	2020	M	6y	30	U+L							1		1					CT - diffusely thickened mucosal outline of small bowel Lymphoscintigraphy		1	1					MCT diet – good		
[2]	2020	F		54	L		0	0		Loss of appetite, fatigue						Na↓ electrolytic troubles			CECT – circumferential partial thickening of the proximal duodenum 99mTc-HSA		1							Cystic lymphangioma (8 years later)	
[3]	2020	M	8y	29	L		Pneumonia with PE + PL						1	1	IgG↓			CD4↓				1				MCT diet - good			
[4]	2019	F	9y	59	L	1		1		Nausea	1		1		1 + IgG↓	Ca↓	Clearance ↑	IgM↓ IgA↓			0	0	1	1			MCT diet - good		
[5]	2019	F	2d	30		1				Nausea, vomiting, Hematochezia									CECT - pancolitis and a small bowel intussusception with proximal distention			0 (IBD)		1	1		Resection of jejunal lesion - PIL		
[6]	2018	F	1m	83	1	Abdominal distension	PL + A	1	↑	General weakness		1		1		Ca↓	Clearance ↑	Vit D ↓	CT – adnexal mass (DD hematoma through warfarin intake)		0	0	1				MCT diet - good		
[7]	2018	F	28y	34	U+L		PL, PE, A	0		Dyspnea	1			1		Na↓ Ca↓ Mg↓ alkalosis		ANA+, Iron↓			?	?					MCT diet + Octreotide – good (recurrence after discontinuation)		
[8]	2017	F		60	0		0	0			0	1	1	1	1		↑		CT/MRI - Diffuse thickening jejunum				1				MCT diet - good		
[9]	2017	F	Infancy	26	1			1		Occasional tetany																	MCT diet - good	Complications during pregnancy (abortion due to hypothyroidism; cesarean section due to clinical worsening in second pregnancy)	
[10]	2017	F	1m	75	L	0		0		inappetence, confusion, disorientation, and depression		1	1		IgG↓			CD3↓, CD3/C D4↓C D3/CD 8↓	CT -prominent duodenal papilla		1							No	
[11]	2015	M					PL + A – only on imaging			Pallor	1	1		1	1	Ca↓		Cholesterol↓, Iron↓	CT – edema small bowel wall, nodular infiltration of the mesentery		1	1	1				Octreotide – unsuccessful Tranexamic acid for anemia	Anemia/Hypoalbuminemia persisted; bleeding from angiodysplasia of first jejunal artery branch → embolization + resection	

[12]	2015	M	3m	36	L			1	↓	generalized warts		1	1	1	IgG↓		Clearance ↑	CD4↓	CT – diffuse thickening small bowel		1		1		MCT diet - good		
[13]	2015	F	5y	32	L					Pallor	1	1		1			Clearance ↑	Iron↓			0	0	1		MCT diet + octreotide 200müg/twice a day	8 months later: ascites + pleural effusion, multiple cysts small bowel - resection	
[14]	2015	M	20y	51	L			1		Lymphedema lower limb			1					General protein deficiency in gel electrophoresis			0	0	1		Surgery - good		
[15]	2015	F		26	L	1	A	1		Vomiting bile, recurrent tympanites,	1	1			IgG↓	Electrolyte deficiencies		Vitamin deficiencies	US – increased wall thickness small bowel		1	0	1			After 20y: stenosis in jejunum, aspiration and resuscitation → adenocarcinoma of jejunum – died in the course	
[16]	2015	M	6m	42	L (10y)			1 (6m)	↓	grand mal seizure	1	1	1	1	IgG↓	Ca↓ Mg↓		Hypoglycemia	CT – normal US – normal 99mTc-HAS		0	0	1		MCT – unsuccessful Octreotide – moderate (relapse when discontinued)		
[17]	2014	F		52	L		PL + A			Hypoparathyroidism,	1		1	1	IgG↓			Iron↓	CT – hepatomegaly + splenomegaly; high liver stiffness		1				MCT diet - good		
[18]	2013	F	3y	51	L		A	0		Swelling of abdomen, dyspnea		1	1	1	IgG↓			IgA↓	Lymphoscintigraphy		1	0		1	MCT diet		
[19]	2012	F	7m	30	L		PL + A - only on imaging			Pallor, severe headache, bilateral papilledema	1	1	1	1	IgG↓			Cryptococcal meningitis in CSF; CD4↓ IgM↓			1				MCT diet Amphoterecin + Flucytosine + Fluconazole orally – good		
[20]	2012	M			Generalized		PL, PE, A		↑			1	1	1	IgG↓	Ca↓			Lymphangiography, 99mTc-HSA		1			1	MCT diet + diuretics – unsuccessful/moderate	After 1a parenteral nutrition + thoracoscopic pericardial window procedure → octreotide - improvement	
[21]	2012	M		37						Severe GI bleeding	1								CT – cystic lesions in the peritoneal cavity		0			1	MCT diet – cessation of bleeding		
[22]	2011	M		58			A			chylaskos	1		1	1		Ca↓			US – thickened small bowel wall					1	Surgery	Postoperative peritonitis with appendicitis	
[23]	2011	F	2m/10y	47	L					Malaise, general weakness		1		1		Ca↓ Mg↓ Ph↑		Hypoglycemia, Parathormone↓	99mTc-HSA		1				MCT diet - good		
[24]	2011	F		49	L		PL, PE			Constipation, shortness of breath		1	1	1				Triglycerides ↓	Lymphoscintigraphy		0 (only on biopsy)	0		1			
[25]	2010	M	12y	57	U+L			1		Frequent influenza in childhood, weight loss, Fatigue,	0	0	1	1	1 + IgG↓	Ca↓		MGUS IgM, Ferritin ↓ Parathormone↑			0	0	1 (After 6 months of MCT diet)		MCT diet – moderate; enteral nutritional therapy		

									tuberculosis											on BX)										
[40]	2003	F		25	-	-	-	-	-												-									
[41]	2001	M	Infancy	21	Generalized			1				1	1	1	IgG↓		Clearance ↑	IgM↓ IgA↓	Lymphangiogram 99mTc-HAS		1									
[42]	2000	M		21	L		PL			Clubbing, acrocyanosis, Noonan syndrome		1	1	1	1				CT – pleural effusion; Bipedal lymphangiography		1									
[43]	2000	F	1m	24	L							1	1	1	IgG↓				Lymphoscintigraphy		1									
[44]	2000	F	40y	58	L	1	PL + A			warts on hands and feet; hepatosplenomegaly		1		1				CD4/C D8 ratio↓	CT scan – thickened small intestine wall		1	1							Centroblastic B cell lymphoma	
[45]	1998	F		34	L					Tetany, extensive warts on fingers and toes				1		Ca↓ Mg↓	Iron↓				1								MCT diet – good	After 18y: intestinal large cell lymphoma
[46]	1993	M	16y	26	U+L	1	A – only on imaging	0				0	1	1		1+ IgG↓		Iron↓ Ferritin↓	Lymphangiography - normal		0								MCT diet - good Surgery - good	After 1m: obstructive ileus → surgery

Abbreviations: M - male; F - female; y - years; m - months; U - upper limb edema; L - lower limb edema; PL - pleural effusion; PE - pericardial effusion; A - abdominal effusion; CT – computerized tomography; CECT – contrast enhanced computerized tomography; MRI – magnetic resonance imaging; US – ultrasound; MCT – medium chain triglycerides

Supplementary Table 2. All case reports reporting on patients with Primary Intestinal Lymphangiectasia (PIL) and lymphoma during follow-up. This table was designed in analogy to Laharie et al. (2005) [33].

Reference	Year	Age at diagnosis	Time after diagnosis (years)	Site of lymphoma	Type of lymphoma	Treatment	Response
[47]	1967	NR	22	Small bowel	NR	NR	NR
[48]*	1972	*	NR	Intestinal	NR	NR	NR
[48]*	1972	*	NR	Gastric	Reticulum cell seroma	NR	NR
[49]	1977	29	10	Jejunum	Poorly differentiated lymphocytic lymphoma	Abdominal radiotherapy	Failure
[50]*	1981	*	6	-	B cell lymphoblastic leukemia	VCR+P	Failure
[51]	1981	26	13	Breast	Diffuse undifferentiated B cell	CVP	Remission of LY and LP
Massachusetts hospital	1984	57	13	Gut	B cell immunoblastic lymphoma	VCP	NR
[52]*	1985	*	15	Retro-peritoneal	Large cell	CHOP	Remission of LY, LP not known
[53]	1993	6	13	Thigh	Diffuse large B cell lymphoma	CHOP + local RT	Remission of LY and LP
[45]	1998	34	18	Jejunum	Diffuse large B-cell lymphoma	Surgery + CHOP	Remission of LY, but not LP
[44]	2000	11	39	Ileum	Centroblastic high-grade B cell lymphoma	Surgery + AVmCP	Remission of LY, LP not known
[44]	2000	58	0	Ileum	Centroblastic B cell lymphoma	PACOB	Remission of LY, but not LP
[33]	2005	20	19	Cervical	Diffuse large B-cell lymphoma	CHOP + local RT	Remission of LY, LP improved
[54]	2013	6	21	Ileum	Diffuse large B-cell lymphoma	Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone	Failure

* These articles were reported by Laharie et al. (2005) [33] – However, full text was not available online anymore.

The following case reports were not considered in this literature review since the full text of the article was not available or written in other languages than English/German: [55-61]

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