

Primary Intestinal Lymphangiectasia

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Primary intestinal lymphangiectasia (PIL) is a rare disease of intestinal lymphatics presenting with hypoproteinemia, bilateral lower limb edema, ascites, and protein losing enteropathy. We report a series of 4 children from Chennai, India presenting with anasarca, recurrent diarrhea, hypoproteinemia and confirmatory features of PIL on endoscopy and histopathology.

Key words: Hypoproteinemia, Intestinal lymphangiectasia, Protein losing enteropathy, Waldmann's disease.

Intestinal lymphangiectasia (IL) is an important cause of protein losing enteropathy (PLE) characterized by diffuse or local ectasia of the enteric lymphatics, often in association with extraintestinal lymphatic abnormalities. Waldmann and Schwabb in 1961 reported this rare entity with intestinal protein loss leading to hypoproteinemia and anasarca(1). IL can be either primary (idiopathic) or secondary. Primary intestinal lymphangiectasia (PIL) usually occurs in children and adolescents, due to the congenital deformity of the small bowel lymphatic system, whereas secondary intestinal lymphangiectasia is more often seen in adults and occurs secondary to an elevated lymphatic pressure as in lymphoma, systemic lupus erythematosus, inflammatory bowel disease, malignancies, constrictive pericarditis, and cardiac surgery(2,3).

CASE REPORT

Case 1: A 8 year old girl presented with history of recurrent small bowel diarrhea and anasarca from the age of 5 years. This illness was not associated with fever, vomiting, abdominal pain, rash, arthralgia or

urinary symptoms. There was no history of contact with tuberculosis. The present hospitalization was for swelling of hands and feet which had increased with worsening of diarrhea. She was first born to non-consanguineous parents, with a birth weight of 3.5 kgs and was apparently well till 5 years of age. On examination, she had generalized anasarca and her vitals and systems examination were normal. She weighed 21.6 kgs as against 26 kg. Biochemical and hematological profile is summarized in **Table I**. USG abdomen showed ascites and bilateral pleural fluid. Barium meal and follow through demonstrated coarse mucosal folds and flocculation in the small intestine. Her lipid profile was normal except for low HDL levels. The characteristic "snow flake appearance" of the duodenum was seen on upper gastrointestinal endoscopy (**Fig. 1**). Dilated lymphatics, the typical histopathological feature of IL was reported in the duodenal biopsy (**Fig. 2**). She was given medium chain triglycerides (MCT) based diet supplemented with albumin transfusions. Diarrhea and anasarca improved over 2 weeks but she succumbed later at the age of 8 years and 6 months due to an intercurrent viral illness.

Case 2: A 9 year old female, presented with anasarca and recurrent loose stools suggestive of small bowel diarrhea for 20 days. She was first born of non consanguineous parents and remained apparently well till 9 years of age except for body asymmetry. The right side of her body including her extremities and face was noted to be more prominent than the left. She had minimal motor delay and poor scholastic performance. On examination her face was dysmorphic with depressed nasal bridge, puffy eyelids and small mouth. She had asymmetrical

generalized edema with lymphedema involving the right side of her body including the genitalia and both feet. Her blood pressure and systems examination were normal. A diagnosis of Hennekman Syndrome was made based on the phenotypic features. Investigations are summarized in **Table I**. She was managed with albumin transfusions, low fat with MCT diet and genetic counseling was offered to the parents.

Case 3: A 36 day old male infant presented with

TABLE I CLINICAL AND LABORATORY DETAILS OF 4 CHILDREN WITH PRIMARY INTESTINAL LYMPHANGIECTASIA

	Case 1	Case 2	Case 3	Case 4
Age at diagnosis	8 Yrs	9Yrs	36 day of life	5yrs
Gender	Female	Female	Male	Male
Age of onset	5 yrs	9 yr	day 5	1 year
Hemoglobin (g/dL)	13.5	11.6	12.2	8
WBC (cells/cmm)	10,000	6500	8500	4100
Differential count	P68,L22,E8,M1	P54,L44,B2	P65,L30,E5	P55,L45
Serum bilirubin (mg/dL)	0.4	0.5	0.3	0.2
SGOT (IU/L)	40	24	40	40
SGPT (IU/L)	35	23	35	40
Serum proteins(g/ dL)	3.6	3.6	2.8	3.8
Serum albumin (g/dL)	2.3	2.3	2	1.7
Serum globulin (g/dL)	1.3	1.3	0.8	2.1
Serum IgA (mg/dL)	90	41	10	165
Serum IgG (mg/dL)	700	561	35	800
Serum IgM (mg/dL)	120	189	14	49
Serum IgE (IU/ML)	160	59	2	70
Cholesterol (mg/dL)	133	75	79	163
HDL (mg/dL)	25	16	45	36
LDL(mg/dL)	81	47	80	80
VLDL(mg/dL)	27	12	22	23
TGL (mg/dL)	100	60	48	50
HIV Elisa	Non reactive	Non reactive	Non reactive	Non reactive
T cell workup	Not done	Not done	Normal	Not done
Barium meal	Malabsorptive pattern	Malabsorptive pattern	Malabsorptive pattern	Malabsorptive pattern
Snow flake appearance in UGIE	Yes	Yes	Yes	Yes
Biopsy proven lymphangiectasia	Yes	Yes	Yes	Yes

P: polymorphs; L: lymphocyte; E: eosinophils, M: monocytes.

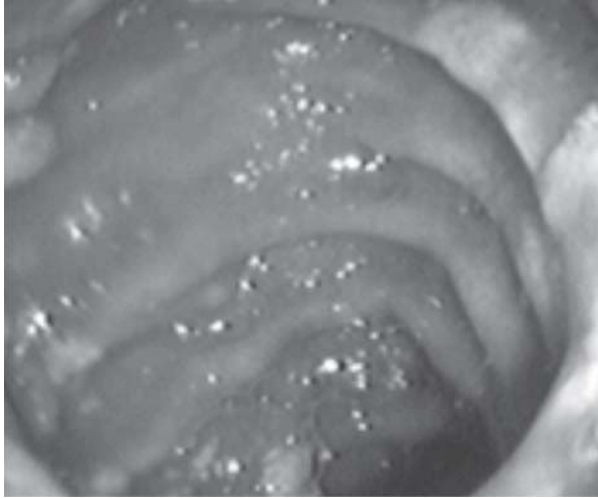


FIG. 1 Upper gastrointestinal endoscopy of duodenum showing the snowflake appearance.



FIG. 2 Histopathology of small intestine showing the grossly dilated lymphatics in lamina propria the hallmark of intestinal lymphangiectasia.

diarrhea and anasarca since 5th day of life. His vitals including blood pressure and other systems examination were normal. Investigations are shown in **Table I**. He was managed with albumin infusions, formula milk containing high MCT and partial parenteral nutrition. The child showed some response to treatment. He is on regular follow up but requires repeated hospitalizations for diarrhea and anasarca.

Case 4: A 5 year old male presented with history of recurrent small bowel diarrhea associated with anasarca since 1 year of age. He was hospitalized thrice for similar complaints. There was no rash, arthralgia, joint pains or contact with tuberculosis. He was alert and had anasarca. Investigations are shown in **Table I**. He was given MCT based diet and albumin infusions following which he responded and is on regular follow up.

DISCUSSION

Primary intestinal lymphangiectasia (PIL) or Waldmann's disease is characterized by malformation of lymphatics leading to obstruction, rupture and leak of lymph fluid into the bowel lumen resulting in hypoalbuminemia, lymphopenia and hypogammaglobulinemia(3). The clinical features of PIL are bilateral lower limb edema, ascites, and chronic diarrhea which was seen in all our 4 cases.

The lung, uterus and conjunctiva may also be involved in IL(4,5). Necrotic migratory erythema, osteomalacia, recurrent gastrointestinal bleeding and recurrent hemolytic uremic syndrome can occur in patients with PIL(3). PIL is generally diagnosed before 3 years of age but may be diagnosed in older children and adults as in our series, where 3 children were diagnosed beyond the age of 5 years(6). The etiology of PIL still remains unknown.

The syndromes linked with intestinal lymphangiectasia include Von Recklinghausen, Turner, Noonan, Klippel Trenaunay, Hennekam and Yellow nail(3). In our case series, one child had features suggestive of Hennekam syndrome (characteristic facial abnormalities, developmental delay, severe limb and facial lymphedema)(7). IL has been associated with celiac disease. Diagnosis of intestinal lymphangiectasia is established by the characteristic histology of grossly dilated lymphatics seen in the lamina propria of the small bowel (duodenum/jejunum/ileum). The villi may be distorted and enlarged but usually without atrophy(6). Endoscopy may be normal if the involvement is patchy and in such cases videocapsule endoscopy helps in localization(8). The immunological abnormalities reported in PIL are reduced immunoglobulin levels (IgG, IgA, IgM), low CD 4+ T cells, lymphocytopenia, skin allergy

and graft rejection(3,9). In our series only 2 children had low immunoglobulin levels.

Life long dietary modification with high protein, restricted fat substituted with medium chain triglycerides (MCT) and vitamin supplements remains the cornerstone in the management of PIL. Exclusion of long chain fatty acids prevents the engorgement and rupture of malformed lymphatics while MCT get directly absorbed into the portal venous circulation(3). In case of poor response to this treatment partial or total parenteral nutrition should be considered. Other treatment modalities described in literature with variable efficacy include antiplasmin therapy, octreotide, corticosteroids, small bowel resection, albumin infusions, peritoneal venous shunt (Levine) and intestinal transplant(3).

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