

A Case of Protein losing Enteropathy - Intestinal Lymphangiectasia

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ABSTRACT

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Primary intestinal lymphangiectasia (PIL) is a rare disorder of unknown etiology characterized by diffuse or localized dilation and eventual rupture of the enteric lymphatic vessels in mucosa, submucosal, and/or subserosa. The main symptom is variable degrees of pitting edema of bilateral lower limbs.

Keywords: Lymphangiectasia, Edema, Rupture of lymphatics

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INTRODUCTION

Primary intestinal lymphangiectasia (PIL) is a rare disorder of unknown etiology characterized by diffuse or localized dilation and eventual rupture of the enteric lymphatic vessels in mucosa, submucosal, and/or subserosa. Lymph, rich in all kinds of proteins and lymphocytes, leaks into the gastrointestinal tract via the affected lymphatic vessels causing hypoproteinemia and lymphopenia. The main symptom is variable degrees of pitting edema of bilateral lower limbs. Increased enteric protein loss that may cause severe hypoproteinemia usually get overlooked, and the lymphatic system disorders always put the diagnoses in a dilemma

CASE REPORT

A 20 year old CA student hailing from Thrissur with no known comorbidities was referred to Jubilee Mission hospital. 11 months back he developed mild edema of both lower limbs. It increased progressively and involved abdomen also. In the mean time he also began developing facial puffiness in the morning hours. He also had intermittent episodes of loose stools with presence of blood and mucus in the stools. There was no history of persistent cough, chest pain or palpitation. No orthopnea with minimal distension. No hematuria or malena. No h/o prolonged fever. He was a non-smoker, non-alcoholic and had no significant past medical history. His family history was unremarkable and he had no known allergy.

On admission, he was afebrile and relatively healthy, and vital signs were stable. Physical examination revealed severe pitting edema on both lower extremities. Gross Ascites and bilateral pleural effusion was detected on examination. Cardiovascular system was clinically normal.

Peripheral blood hemoglobin was 15.5gm/dl, white blood cell count $5.4 \times 10^9/L$ with 84% neutrophils and 6.4% lymphocytes, platelet count $297 \times 10^9/L$ and ESR was 25 mm/hour. Serum electrolytes and Renal function test was normal. Marked hypoproteinemia was revealed in the baseline investigations. Urine analysis ruled out proteinuria. He was also found to have hypocalcemia. A Protein losing enteropathy was suspected. Tuberculosis work up was negative. Peripheral Blood smear examination was normal. ANA and RA factor were negative (**table 1**).

Ascitic fluid tapping was done and fluid was sent for investigations (**table 2**). Nature of ascitic fluid was

Table 1. Relevant Baseline Investigations

Test	Result
Differential Count	N 84 , L 6.4
Total Protein/Albumin/Globulin	2.46/1.26/1.2 g/dl
Urine Protein	Absent
Serum calcium	4.4. mg/dl
Serum Triglycerides	90.3 mg/dl
Thyroid Function Test	Normal
Peripheral Blood smear	Normal

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Table 2. Ascitic Fluid study	
Parameter	Result
Albumin	0.08g/dl
Protein	0.19g/dl
Glucose	100.7mg/dl
Cell count	4.4. mg/dl
Serum Triglycerides	No cells seen
Triglycerides	140.3mg/dl
ADA	0.9

milky and showed high SAAG, decreased protein with elevated triglycerides levels

He was investigated for protein losing enteropathy. Upper GI endoscopy was normal till D1. D2 and D3 villi showed whitish powdering precipitates suggestive of intestinal lymphangiectasia. Colonoscopy was normal

The following were the summary of Histopathology as in **table 3** and **figure 1**

Table 3. Histopathology	
Site	Finding
Terminal Ileum	Mild Lymphangiectasia
Colon	No abnormality seen
Duodenum	Mild Lymphangiectasia
Rectum	Focal active Proctitis
Stomach	Mild Chronic Gastritis

Lymphoscintigraphy was suggestive of mild to moderate lymphatic leak into the abdominal cavity probably leak from level of cisterna chyli.

CT Thorax was done to rule out any secondary causes and was normal

Under the diagnosis of primary intestinal lymphangiectasia as no secondary causes were detected, dietician has prescribed a high protein and low fat diet with medium chain fatty acids. He has been asked to avoid mutton, pork, beef, big fishes, bakery foods, coconut,

groundnut, sesame seeds, oil, salt, butter, ghee, pickles, salt dried fish, papad. At the time of discharge, abdominal distension has decreased

DISCUSSION

Intestinal lymphangiectasia is a disease characterized by hypoproteinemia, edema, and lymphocytopenia, resulting from dilatation of intestinal lymphatics and loss of lymph fluid into the gastrointestinal (GI) tract.¹ It can be primary or secondary to other disease processes.

To date, the etiology is unknown. Intestinal lymphangiectasia is responsible for lymph leakage into the bowel lumen, which leads to hypoalbuminemia and lymphopenia. Edema is the consequence of hypoproteinemia with decreased oncotic pressure. Several genes, such as VEGFR3 (vascular endothelial growth factor receptor 3), prospero-related homeobox-transcriptional factor PROX1, forkhead transcriptional factor FOXC2 and SOX18 are implicated in the development of the lymphatic system. In a recent paper, Hokari et al. reported inconsistently changed expressions of regulatory molecules for lymph angiogenesis in the duodenal mucosa of PIL (primary intestinal lymphangiectasia) patients²

Patients usually presents with features due to hypoproteinemia such as peripheral edema, ascites and pleural effusions. Diarrhoea may also be the presenting complaint

Diagnosis relies on characteristic endoscopic changes (diffused swollen villi with appearance of white dots) and is confirmed by corresponding histology of intestinal biopsy.³ Simultaneously, intestinal lymphangiectasia secondary to constrictive pericarditis, intestinal lymphoma, Whipple’s disease, Crohn’s disease, sarcoidosis, intestinal TB, systemic sclerosis, lymph enteric fistula, radiation and/or chemotherapy, HIV-related enteropathy, or Fontan operation should be excluded.⁴

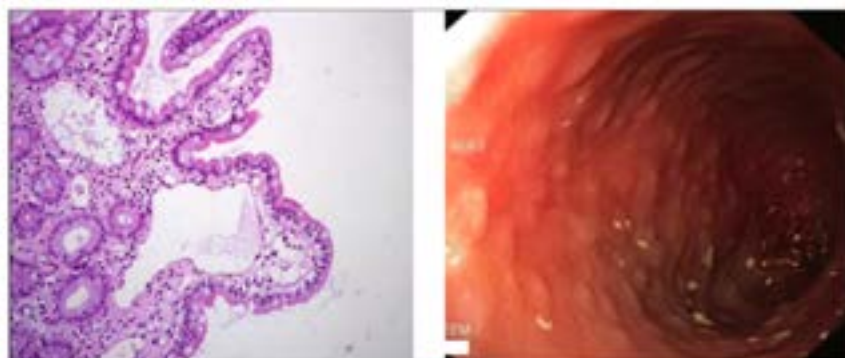


Figure 1. Microscopic section reveals markedly dilated submucosal lymphatics without inflammation H & E stain. Upper G.I endoscopy showing nodularity with white spots in the duodenum

Histological examination of duodenum-jejunum and ileum biopsies confirms the presence of lacteal juice, dilated mucosal (from moderate to severe) and submucosal lymphatic vessels (and also in the serosa) with polyclonal normal plasma cells. Intestinal lymphatics may be dilated in many villi or only a few. Indirect biological abnormalities are suggesting of PIL, such as hypoprotein-

emia, hypoalbuminemia, hypogammaglobulinemia with low IgG, IgA and IgM levels or lymphocytopenia. Exudative enteropathy is confirmed by the high 24-hr stool α 1-antitrypsin clearance due to enteric protein loss. Functional absorption tests, e.g., such as D-xylose test results are normal in PIL

Technetium-99m antimony sulphide colloid lymphoscintigraphy conveniently demonstrates intestinal leakage of lymph in patients with intestinal lymphangiectasia⁵

Low-fat diet associated with supplementary medium-chain triglycerides (MCT) is the cornerstone of PIL medical management.⁶ It is likely that the absence of fat in the diet prevents engorgement of the intestinal lymphatics with chyle, thereby preventing their rupture with its ensuing protein and T-cell loss. MCT are directly absorbed into the portal venous circulation and thus provide nutrient fat but avoid lacteal engorgement. After a few weeks, this treatment may lead to reversal of clinical and biochemical signs (albuminemia, immunoglobulin levels and lymphocyte counts).⁷ In patients not responding to a low-fat diet, enteral nutritional therapy (elemental, semi-elemental and polymeric diets) may be required. In a few very severe cases, total parenteral nutrition is warranted.

Multiple causes of secondary intestinal lymphangiectasia can be addressed surgically. Antiplasmin, octrotide, albumin infusion are the other tried treatment options.

END NOTE

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Editor's Remarks: This case report deals with a rare manifestation presenting as bilateral pitting lower limb edema. Useful information.

Conflict of Interest: None declared

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