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DISORDERS OF THE INTESTINAL MESENTERIC LYMPHATIC SYSTEM

U. Fox, G. Lucani

General Surgery Department, Ospedale "Santa Corona" — Garbagnate Milanese, Milan, Italy

ABSTRACT

Disorders of the intestinal lymphatic transport system are rare and typically associated with protein losing enteropathy (PLE). Hypoproteinemia caused by intestinal lymphangiectasia is often associated with lymphedema of the legs and occasionally with chyluria, chylometrorrhea and chylous ascites. This article examines the varied presentations of lymphangiectasia syndromes including its pathophysiology. Diagnosis is based on signs and symptoms, specific laboratory findings, and confirmed by contrast small bowel series, lymphography and best of all laparoscopy. We describe 12 patients with PLE secondary to primary intestinal lymphangiectasia (1980-1991). Treatment was non-operative (dietary) in 8 patients and surgical in 4 including segmental resections of the jejunum in two, lymphatic-mesenteric venous anastomosis in one, and peritoneal-venous (LeVeen) shunt in one with overall satisfactory results.

Disorders of the intestinal lymphatic transport system are one of many syndromes whose salient feature is leakage of large amounts of plasma proteins into the intestinal lumen (so-called protein-losing enteropathy or PLE). This term was coined by Gordon (1) in 1959 and then elaborated upon by Waldmann (2), who emphasized the role of incompetent enteric-mesenteric lymphatics in patients with intestinal lymphangiectasia.

Actually, intestinal lymphangiectasia with PLE is only one manifestation of defective intestinal lymphatic transport. Other signs and symptoms include chyluria, chylometrorrhea, chylous ascites, and chylous reflux with peripheral edema. These disturbances are best understood in light of the anatomy of the intestinal lymphatics and the potential collateral pathways that develop with obstruction including lymphedema of the legs which commonly coexist. Peripheral lymphedema usually derives from lymphatic dysfunction of the legs as part of a generalized lymphatic dysplasia in these patients. Leg edema may also develop secondary to hypoproteinemia from PLE and chylous reflux often in conjunction with chylous ascites secondary to lymph blockage in the pelvis or mesentery.

LYMPHATIC ANATOMY

Abdominal lymphatics are interspersed with lymph nodes of which the following groups can be distinguished:

Right Lateroaortic

- *caval interaortic*
- *precaval* (one superior and one inferior)
- *laterocaval*
- *retrocaval*

Left Lateroaortic

These include the iliac lymph nodes from

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the aortic bifurcation to the aortic hiatus of the diaphragm:

- *primary iliac chain* (from the legs and pelvis)
- *lymphatics of the genitalia*
- *collectors of the retroperitoneum including kidneys and adrenals*
- *collectors of the abdominal viscera* (hepatic on the right side and superior mesenteric on the left side)

Preaortic

- *superior mesenteric*
- *renal*
- *inferior mesenteric* (left and right colon)

Retroaortic

These communicate with the left lateroaortic nodal group and receive lymph collectors from the primary iliac nodes and rectum.

These periaortic lymph nodes extensively interconnect and form a major lymphatic plexus surrounding the large blood vessels. The periaortic lymphatics drain into major lumbar trunks. On the right side they connect into the right lateroaortic system whereas on the left side, which is better developed, they drain to the left lateroaortic and retroaortic nodes and are joined by the intestinal lymph trunk at the region of the superior mesenteric blood vessels.

The confluence of the lumbar with the intestinal lymph trunks varies. When low in the retroperitoneum (35% between L1 and L2), they form an ampullar dilation known as the cisterna chyli or Pecquet's cistern which is ~30mm long and 15mm wide and continues as the thoracic duct. When high in the retroperitoneum (65% between T11-T12) it forms a thoracic duct as an upside-down Y with the lumbar collectors.

The direction of peripheral lymph flow is normally centrally and towards the cisterna chyli and thoracic duct, but in diseased states

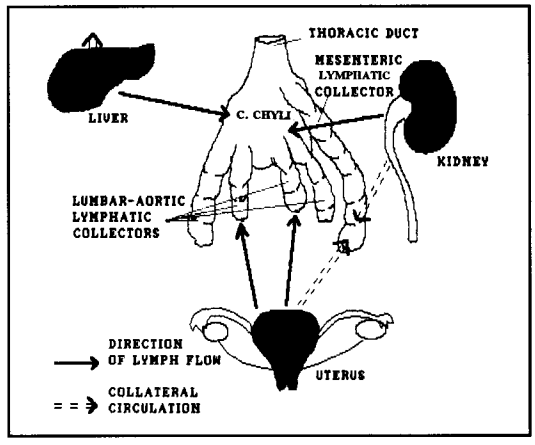

Fig. 1. Schematic outline of major intraabdominal lymphatic collectors and directional flow.

collateral lymphatics develop as shown schematically in *Fig. 1.*

Perihepatic System

Lymphatics drain from the right lateroaortic nodal system to the liver through capsular (Glisson) collectors and from there via the transdiaphragmatic lymphatics to thoracic and mediastinal lymph trunks.

Perirenal and Periureteral System

Lymph from periaortic and mesenteric trunks drain via retroperitoneal collectors to the kidneys and ureters.

Pelvic System

In females, periaortic and mesenteric lymph collectors connect with uterine lymphatics.

PHYSIOLOGY AND PATHOLOGY (ETIOPATHOGENESIS)

Deranged intestinal mesenteric lymph transport with PLE has a multitude of causes *(Table 1).* Primary PLE is distinguished from secondary by coexistent disorders. Idiopathic

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TABLE 1
Causes of PLE*

Primary
Intestinal Lymphangiectasia

Secondary
Cardiac
- constrictive pericarditis
- complication of Fontan-Mustard operation
- congestive cardiomyopathy

Oncologic
- lymphoma
- nodal metastasis
- Kaposi sarcoma in AIDS
- angiotropic lymphoma

Infectious
- filariasis
- giardiasis
- Clostridium perfringens
- Campylobacter pylori

Malformations
- Lymphangioma
- Klippel-Trenaunay syndrome
- congenital retroperitoneal lymphangiectasia

Autoimmune
- lupus erythematosus
- mixed connective tissue disorders

Gastroenterologic
- ulcerative colitis
- regional ileitis

Iatrogenic
- post-radical nodal dissection
- post-irradiation

Traumatic

*protein-losing enteropathy

intestinal lymphangiectasia represents congenital hypoplasia of part or nearly all of the intestinal lymphatic network (3). Common to all of the disorders, however, is retrograde flow of intestinal lymph as a consequence of obstruction to flow with increased intraluminal pressure, dilatation of mesenteric lymphatics, and finally valve incompetence with leakage of lymph into the bowel lumen (3,4). Depending on the specific location of the block and the subcompartment of lymph collectors effected, the outward manifestations differ.

Subcisternal Blockage of the Lumbar-Aortic Trunks (Fig. 2)

This condition causes lymphedema of the legs and of the external genitalia. Uterine lymphatics usually drain via collaterals into mesenteric lymphatics so that it is rare to have chylometrorrhea. The liver and kidney also can drain into Pecquet cistern as the drainage lymphatics are usually superior to the obstructed site.

High Cisternal or Lower Thoracic Duct Blockage (Fig. 3)

This condition produces total intestinal lymph blockage and collateral pathways enlarge although are insufficient with the development of chylometrorrhea, chyluria, chylous ascites and dilatation of subcapsular lymphatics of the liver.

Blockage of Mesenteric Lymphatic Collectors (Fig. 4)

Here, obstruction may occur at different sites but is uniformly accompanied by PLE. The site of the block accounts for the signs and symptoms produced.

a. Total block: associated with severe PLE, often in conjunction with prominent chylous ascites.

b. Partial block: associated with mild PLE and occasionally chylous ascites.

DIAGNOSIS

Primary PLE from intestinal lymphangiectasia is diagnosed from the

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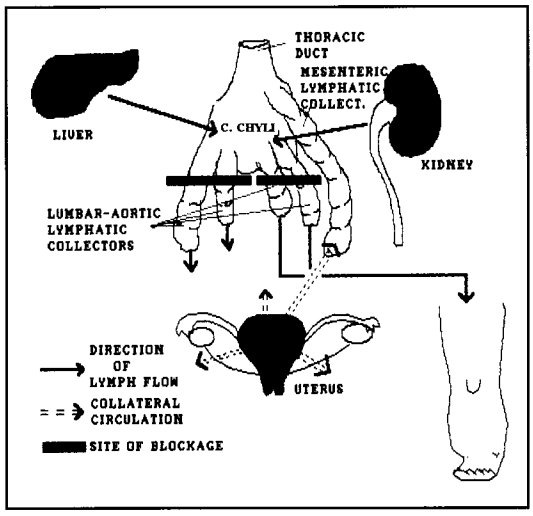

Fig. 2. Schema of intraabdominal lymphatic pathways with subcisternal chyli blockage.

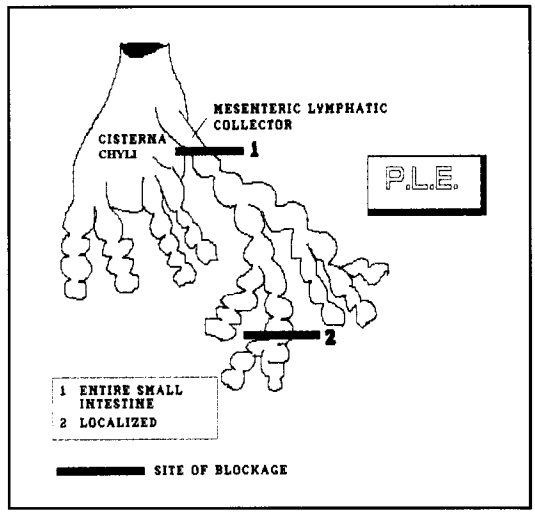

Fig. 4. Schema of lymph dynamics with blockage of mesenteric lymphatic drainage.

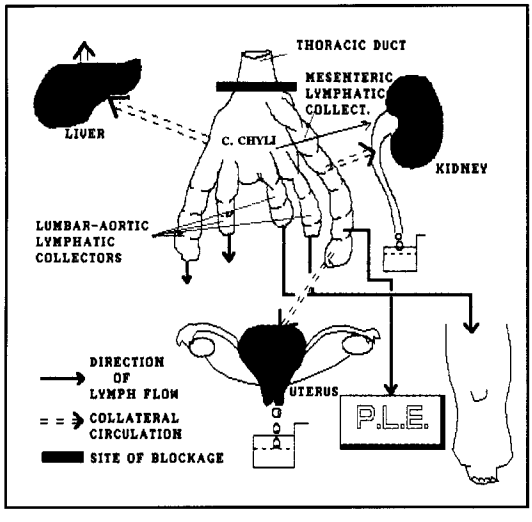

Fig. 3. Schema of lymph dynamics with lymphatic blockage at the cisterna chyli.

clinical history, laboratory findings, a GI survey, direct lymphography, and laparoscopy. The age at appearance of signs and symptoms is relatively young (~11 years). Initial manifestations include edema *(Table 2)* either as lymphedema of the legs (sometimes asymmetrical) or suddenly as generalized

TABLE 2
Signs and Symptoms of Primary Intestinal Lymphangiectasia

- Protein-losing enteropathy
- Chylous ascites
- Chyluria
- Chylometrorrhea
- Lymphedema of the legs
- Chylothorax

TABLE 3
Clinical Experience*

Non-operative (dietary) treatment	8
Small intestinal segmental resections	2
Lympho-venous anastomosis	1
LeVeen (peritoneo-venous) shunt	1

*12 patients with primary intestinal lymphangiectasia

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anasarca. Chylous ascites, chylometrorrhea, and chyluria (5) may also be the sole presentation of this disorder and signify that intraabdominal lymphatic collaterals are well established. Occasionally, diarrhea with steatorrhea, abdominal pain, tetany may coexist. These patients often have a characteristic dentition with abnormal tooth development from calcium deficiency and abnormal dental proteins. The teeth are typically dark, often with thin lamina, fragile, with considerable decay. Hypoproteinemia, especially of albumin and the γ-globulins (IgG, IgA, IgM) is marked. Hypocalcemia, lymphocytopenia with defective cellular immunity, decreased serum transferrin and ceruloplasmin are also common.

Contrast X-rays of the digestive tract, sometimes show symmetrical and diffuse thickening of the small bowel mucosal folds with hypersecretion (6). Direct oil-contrast lymphography may demonstrate an absence of contrast in some lymphatic segments, blockage of collectors, or delayed opacification of pelvic and lumboaortic lymph nodes (7). Occasionally, leakage of contrast into the intestinal lumen is depicted. Isotope techniques usually do not give adequate images but the extent of PLE can be discerned with α-1 antitrypsin disappearance (8).

Laparoscopy is perhaps the best and most definitive method to diagnose intestinal lymphangiectasia. Using this minimally invasive technique, one detects otherwise subclinical chylous ascites, dilatation of lymphatics on the surface of the small bowel and mesentery. Occasionally, newly formed lymphatic collaterals are apparent especially on Glisson's capsule, which acquires a milky appearance with transport of chylous intestinal lymph. Although laparoscopy may rarely be misleading, when these findings are seen the correct diagnosis is assured.

As a practical matter, when a patient presents with leg edema (even unilateral) and persistent hypoalbuminemia, one should suspect intestinal lymphangiectasia and consider laparoscopy.

TREATMENT

PLE from intestinal lymphangiectasis is usually treated non-operatively with only highly selected patients requiring operation. Non-operative treatment includes a high protein, low fat diet of medium chain triglycerides, which in contrast to long chain triglycerides are absorbed into the portal vein rather than into lymph (9). Sometimes, frequent intravenous infusions of albumin with generalized anasarca is useful.

When lymphatic blockage involves a limited segment of the intestine, operative resection of the involved loops may be curative. If the mesenteric lymphatic collectors are markedly dilated, a lymphatic-venous anastomosis to an adjacent vein is feasible (10). With refractory chylous ascites, insertion of a peritoneo-venous (LeVeen) shunt may alleviate both ascites and hypoalbuminemia (11).

With gravitational reflux into dilated and tortuous lymphatic collectors, placement of ligatures in the mesenteric and crural areas has been suggested (12). Servelle (13) proposed disconnection of the mesenteric lymphatics to interrupt the collaterals for leakage including chyluria and chylo-metrorrhea.

CLINICAL EXPERIENCE

PLE secondary to intestinal lymphangiectasia is a rare disorder. Since 1980, we have managed 12 patients confirmed by laparoscopy. Most (8 patients) were treated non-operatively primarily with dietary substitution. Two patients benefited from resection of a jejunal loop and one patient improved after a lymphatic-mesenteric venous anastomosis. The mesenteric vein was chosen because of its proximity to a mesenteric lacteal. In one patient with intractable chylous ascites insertion of a LeVeen shunt led to restoration of serum protein levels *(Table 3)*.

CONCLUSIONS

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PLE associated with intestinal lymphangiectasia is very rare and is usually discovered in clinics treating lymphedema, because usually lymphangiectasia occurs in conjunction with this disorder. Patients with primary lymphedema and significant hypoproteinemia should be investigated for PLE and possibly laparoscopy as this minimally invasive technique is most likely to diagnose and determine the severity of primary intestinal lymphangiectasia. Treatment is usually non-operative with dietary substitution and is usually satisfactory. Operation is reserved for specific problems of external chylous loss and the procedure chosen depends on the feasibility of bowel resection, lymphatic ligation, or lymphatic-venous anastomosis. Prognosis is reasonably good if the dietary measures are followed. For more severe patients, operations have improved the quality of life and one patient in our series was even able to carry a pregnancy to term.

ACKNOWLEDGMENT

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Professor Umberto Fox, M.D.
Divisione di Chirurgia Generale
Ospedale "Santa Corona"
Viale Forlanini, 121
20020 Garbagnate Milanese
Milan, ITALY

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