CHYLOUS ASCITES REVISITED - OLD DISEASE, NEW MANAGEMENT

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ABSTRACT

Extravasation of chyle from the intestinal lymphatics into the peritoneal cavity results in chylous ascites, identified by its characteristic milky appearance. Chylous ascites is rare, but it has been suggested that its incidence may be increasing in the adult population. Successful management depends on identifying the underlying cause of the lymphatic disruption. The spectrum of causative pathologies seen in adult and paediatric practices are vastly different: congenital lymphatic problems predominate in the latter, while occult malignancy often causes adult chylous ascites. This review looks at the various aetiologies, diagnosis and the recent advances in the management of this condition.

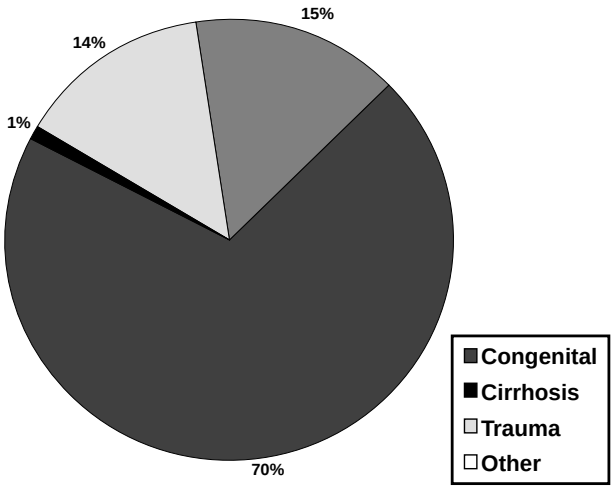

FIGURE 1A
Causes of paediatric chylous ascites.*
*(% taken from 506 patients from literature)[5,6,7,13,14]

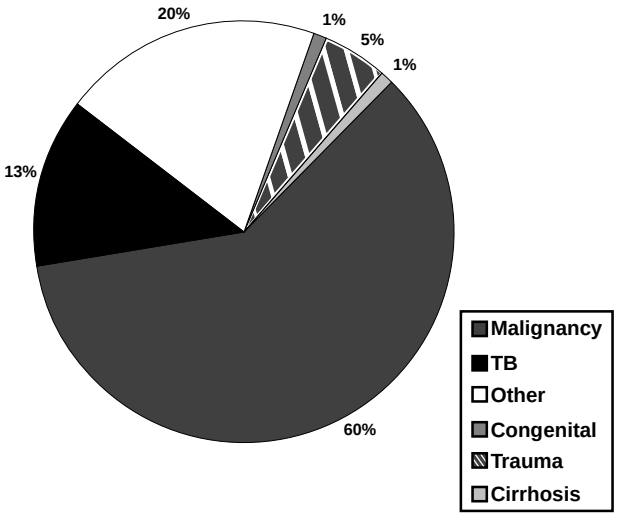

FIGURE 1B
Causes of adult chylous ascites.*
*(% taken from 506 patients from the literature)[5,6,7,13,14]

INTRODUCTION

The word ascites is derived from the Greek *askos* which means bag or sac and refers to the pathological accumulation of fluid into the peritoneal cavity. Chylous ascites was first accurately described in 1691 by Morton, after performing a paracentesis on an 18-month-old baby.[1] It develops whenever there is disturbance in the lymphatic flow at any point from the intestinal lacteals, to the cisterna chyli and thoracic duct, to the left brachiocephalic vein. Subsequent collection of chyle within the peritoneal cavity gives rise to chylous ascites.

The occurrence of chylous ascites is uncommon, probably accounting for between 1:20,000 to 1:200,000 of hospital admissions.[2] It is found in both adult and paediatric practices. In adults there is a female predominance, due to gynaecological malignancies, while in the paediatric population, both sexes are affected equally. It has been suggested that the incidence of chylous ascites may be increasing in line with higher incidence of malignant disease and complications of HIV infection. The reason for this may simply reflect increased reporting of the disorder, or it may be due to increasing diagnostic capability.

The majority of early reports of chylous ascites describe anecdotal cases, and there are very few series describing the causes and management of the condition. This again reflects the rarity of chylous ascites.

There is a need for a review of this rare cause of ascites to highlight changing aetiology and new therapeutic options.

AETIOLOGY

Between 40-60% of paediatric causes of chylous ascites are of congenital origin (e.g. mesenteric cysts, primary lymphangiectasia, lymphatic stenosis and idiopathic 'leaky' lymphatics).[3] Other causes in children include complications of surgery and post-peritoneal dialysis. Malignancy is an extremely rare cause in this age group (Figure 1a).

In adults, the diagnosis of chylous ascites usually complicates disseminated malignancy, because of lymph blockage within the thorax or abdomen. Reports vary widely, but between 30-87% of affected patients have malignancy,[4,5] with half of these having lymphoma, which in two-thirds of these is a non Hodgkin's lymphoma.[6] Other less common causes include tuberculosis, pancreatitis, sarcoidosis, constrictive pericarditis, small intestinal obstruction and uncomplicated hepatic cirrhosis[7] (Figure 1b). There have also been reports of chylous ascites in HIV patients who have developed chylous ascites secondary to lymphoma, Kaposi's sarcoma and *Mycobacterium intracellularae* infection.[8]

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Chylous ascites complicating acute or chronic pancreatitis is extremely rare, giving rise to <0.5% of cases;[9] this has been described in patients undergoing chronic ambulatory peritoneal dialysis, in whom the incidence of secondary acute pancreatitis is increased.[10] The mechanism by which acute pancreatitis causes chyle leakage is poorly understood, but is thought to be due to activated pancreatic enzymes increasing the permeability of small bowel lymphatics, thoracic duct and the cisterna. In chronic pancreatitis, fibrotic compression of the abdominal lymphatic vessels can cause chyle leakage.

The frequency with which chylous ascites complicates hepatic cirrhosis is variously reported in the literature: between 0.5% up to 90%[11] of cases are reported to be secondary to cirrhosis. It is generally accepted that chylous ascites as a result of uncomplicated cirrhosis is rare (<1%),[12,13] and reports of chylous ascites in cirrhosis are often based on small groups of no more than ten patients. Further discrepancy arises from the way in which chylous ascites is detected: biochemical and clinical definitions can differ significantly, and perhaps biochemical detection may be more common in uncomplicated cirrhosis. In our experience, chylous ascites is unusual in hepatic cirrhosis and its presence usually indicates co-comitant intra-abdominal malignancy.

Chylous ascites as a complication of surgery is rare, usually accounting for less than 1% of cases and it may follow aortic surgery, spinal surgery and retroperitoneal lymph node dissection in patients with urological and gynaecological malignancies[14] (Table 1).

TABLE 1
Causes of chylous ascites.

•Neoplastic	Lymphona, Metastatic deposits from Ca Stomach, Pancreas, Ovary, Lung.
•Infections	Tuberculosis, Filariasis.
•Trauma	Blunt trauma. Post surgery (retroperitoneal dissection, post liver transplantation, aortic surgery).
•Inflammatory	Sarcoidosis, Pancreatitis, Pericarditis.
•Miscellaneous	Hepatic cirrhosis, Peritoneal dialysis, Yellow nail syndrome, idiopathic 'leaky' lymphatics.
•Congenital	Primary lymphangiectasiae, mesenteric cysts, lymphatic stenosis, congenital atresia of thoracic duct.

PATHOPHYSIOLOGY

It is useful to review the physiology of fat absorption and lymphatic circulation to understand the pathogenesis of chylous ascites. Most dietary lipid is absorbed in the upper two-thirds of the jejunum. However before lipids can be absorbed by the jejunal enterocyte, they must be broken down and made soluble by emulsification. Formation of a stable fat emulsion requires dietary and biliary phospholipids, fatty acids from intragastric lipolysis and bile salts.

Lipid breakdown is helped by gastric lipase, pancreatic lipase and co-lipase at a pH>6, which produce a mixture of fatty acids and monoacylglycerols. These too are relatively insoluble in water and are subsequently emulsified with bile salts, forming mixed micelles which are much smaller particles than emulsion droplets that help to transport fatty acids to the enterocyte. At the brush border of the enterocyte, these micelles release lipid-soluble fatty acids which are transported through the membrane predominantly by passive diffusion, but also by facilitated diffusion binding to fatty acid-binding-protein in the brush border.

Within the enterocyte, fatty acid-binding-proteins strongly attract long chain triglycerides (LCT), while medium chain triglycerides (MCT) are not. Subsequently LCTs are transferred into the endoplasmic reticulum where they are re-esterified to form triacylglycerols. These are finally exocytosed into the lacteals of the villus. Conversely, MCTs diffuse across the enterocyte cytoplasm, and simply drain into the blood capillaries and finally back into the portal system (Figure 2). LCTs that have drained into the lacteals form chyle, which drains through a gradually enlarging system of lymphatic vessels, converging at the cisterna chyli, situated under the right crus of the diaphragm (Figure 3). Finally this flow continues along the thoracic duct and back into the venous system (Figure 4).

Chyle is rich in lymphocytes, chylomicrons and proteins. Clearly if lymph flow is obstructed for any reason, the resulting increase in hydrostatic pressure within the channels will cause extravasation of chyle into the peritoneum and development of chylous ascites.

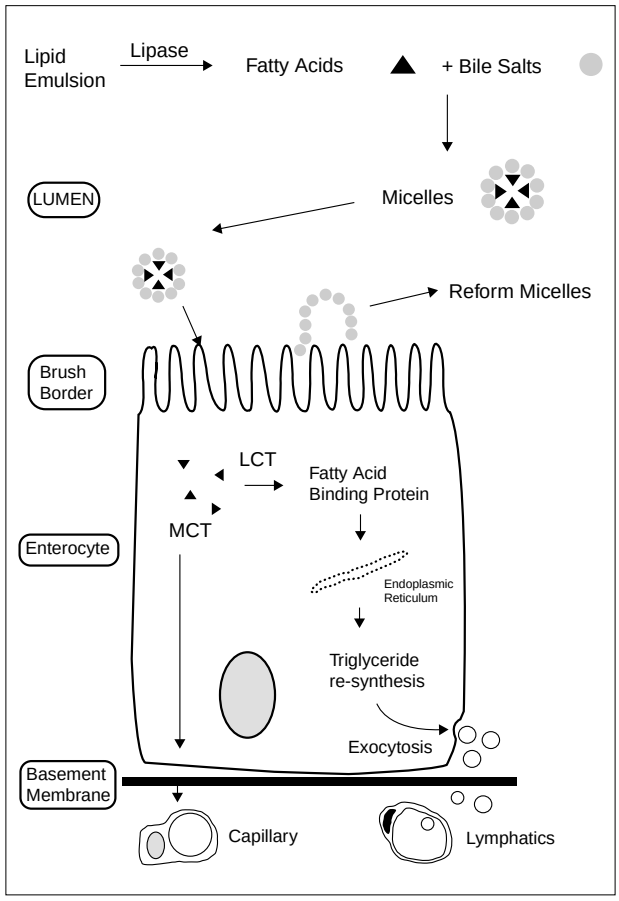

FIGURE 2
Pathophysiology of fat absorption at the level of the enterocyte.

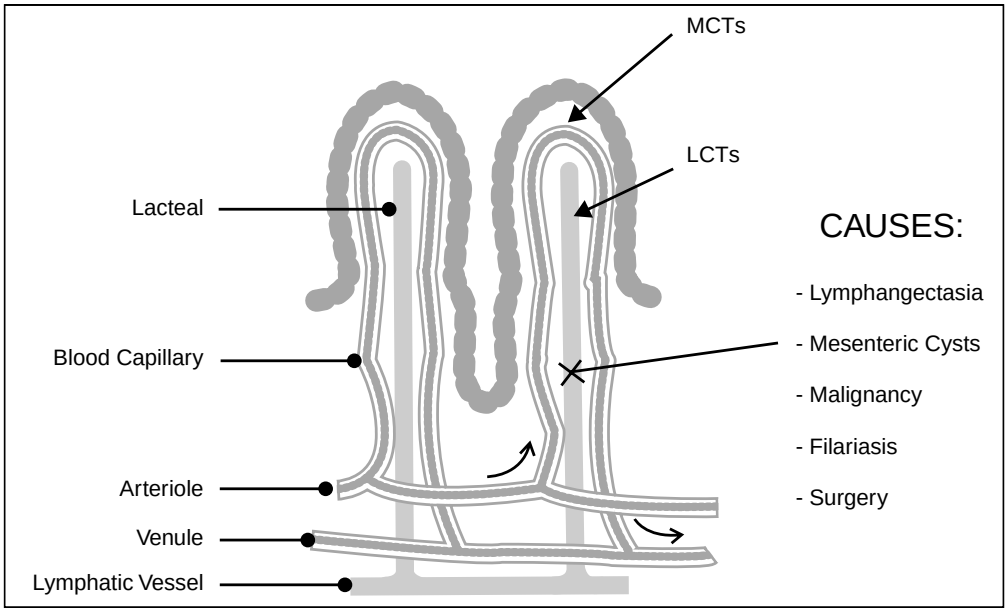

FIGURE 3
Anatomy of the lacteal with causes of lymph flow obstruction.

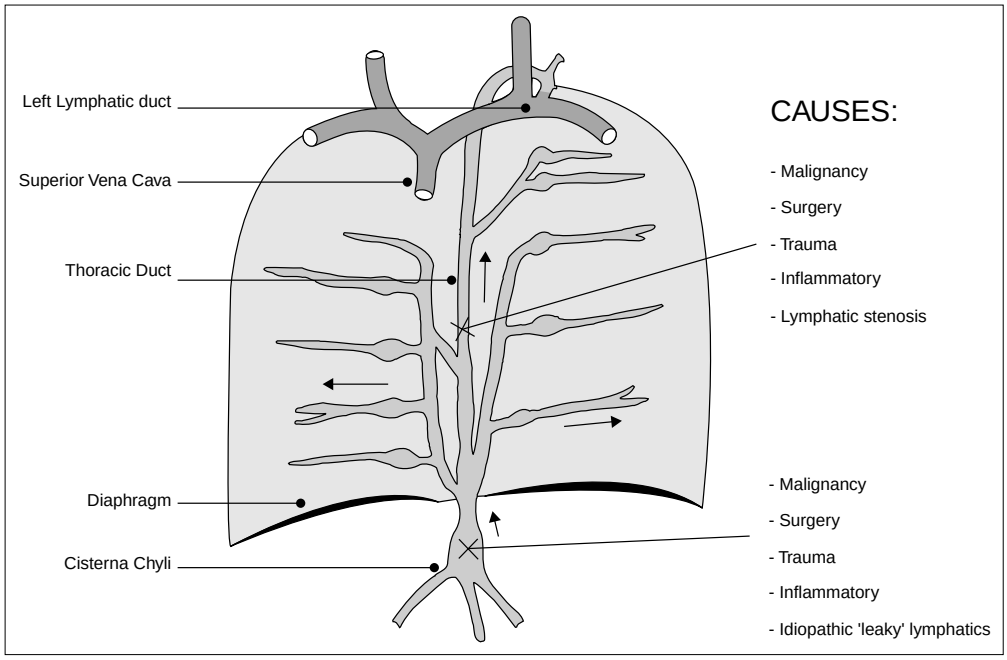

FIGURE 4
Anatomy of the thoracic lymphatic system with causes of lymph flow obstruction.

CLINICAL FEATURES

As with other causes of ascites, symptoms and signs of chylous ascites are nonspecific, and are related to the accumulation of peritoneal fluid with a consequent increase in intra-abdominal pressure. In children, additional features of growth retardation, failure to thrive and peripheral lymphoedema predominate. In adults, constitutional symptoms (anorexia, night sweats and lethargy) occur commonly and strongly indicate the possibility of underlying neoplasia.

In up to 50% of cases, chyle collects in the pleural cavity, giving rise to a chylothorax, often presenting with severe dyspnoea, especially if the abdominal ascites is sufficiently large to cause splinting of the diaphragm.

Chronic lymphatic obstruction can cause dilatation and rupture of the intestinal lymphatics and secondary intestinal lymphangiectasia. This impedes absorption of chylomicrons and lipoproteins resulting in malabsorption of fat. It can give rise to a protein-losing enteropathy with subsequent lymphopenia, hypoalbuminaemia and peripheral oedema. Lymphopenia may predispose to secondary opportunistic infection.

Rarer clinical signs that may raise suspicion of chylous ascites clinically are dystrophic and discoloured finger nails and 'yellow nail' syndrome. The condition may also be associated with Filariasis and AIDS, and complicated by Kaposi's sarcoma.

FIGURE 5
Characteristic appearance of chylous ascites.

DIAGNOSIS

The diagnosis of chylous ascites is made by the examination of ascitic fluid obtained by standard diagnostic paracentesis techniques. Visual inspection of the ascites reveals an overtly milky fluid and is usually diagnostic (Figure 5). The opacity of the fluid is due to its lipid content and it is this that differentiates it from 'pseudochyle', the latter deriving its opalescence from inflammatory cellular debris. With chyle, biochemical analysis will often reveal triglyceride levels in excess of 23mmol/l (normal <2.3mmol/l). Even when levels are low, the ascitic triglyceride level should be higher than that of serum to be defined as chylous.

DIAGNOSTIC CRITERIA

- Milky opaque ascitic fluid
- Ascitic triglyceride concentration > Serum triglyceride concentration
- Raised lymphocyte count in ascitic fluid
- Low serum-ascites albumen gradient (<1.1g/dl)
- Low ascitic protein concentration (<20g/dl)

Other ascitic characteristics include a raised leukocyte count (lymphocyte predominant), a low serum-ascites albumen gradient (usually <1.1g/dl) but often with a low ascitic protein concentration (<20g/dl).

Gram and other stains and cultures will often reveal no organisms, even when the underlying cause is tuberculosis.

Once the diagnosis of chylous ascites has been made, further evaluation is required to elucidate its cause (Figure 6).

SPECIFIC INVESTIGATIONS

1. Abdominal Ultrasound

Abdominal ultrasound is a useful preliminary examination to confirm the presence of ascites and to exclude focal liver lesions and identify any intra-abdominal lymphadenopathy. A characteristic appearance of chylous ascites has been described by a fat-fluid level that develops in patients in the recumbent position.[15]

2. Barium Follow Through

In patients with symptoms consistent with protein-losing enteropathy, barium follow through is the radiological investigation of choice to exclude primary intestinal lymphangiectasia. Radiological enlargement and thickening of *valvulae conniventes* with slight dilatation of the small bowel are prominent features. Jejunal biopsy may be indicated thereafter which would show dilated mucosal and submuscosal lymphatic channels.

3. CT Scanning

CT scanning remains the initial investigation of choice for chylous ascites. An unusual, but pathognomic, appearance of chylous ascites has been described for both ultrasound and CT scanning.[15] Since both water and chylous fluid have similar attenuation coefficients, radiographic appearance of chylous fluid is typically similar to water with ultrasound and CT. However a fat fluid demarcation level can develop if the patient is maintained in a recumbent position, and this can be subsequently identified by CT and ultrasound.

In addition, CT is valuable in evaluating underlying lymphatic structural obstruction and identifying malignant disease. Some series advocate that the highest diagnostic yield come from a combination of CT scanning and lymph node biopsy where appropriate.[5]

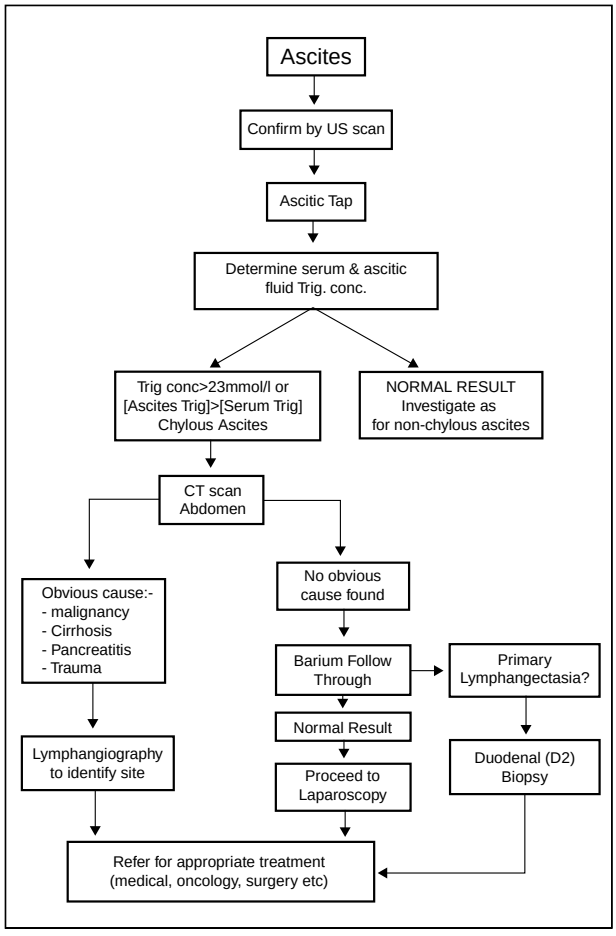

FIGURE 6
Diagnostic algorithm for chylous ascites.

4. Laparoscopy

Laparoscopy is also an important tool in evaluating chylous ascites, especially when CT scanning cannot identify any obvious cause. It allows direct visualisation of the liver and peritoneum, as well as allowing access for biopsy at the same time. Thus conditions such as *carcinomatosis peritonei* which may be missed on CT can be diagnosed with relative ease in this way. In some series, the diagnostic yield of laparoscopy in 'normal' ascites approaches 90%.[16]

5. Lymphangiography

This may be carried out pre-operatively using lipiodol, an oily contrast medium, or intraoperatively using Evan's blue or other dyes to identify the site of leaks prior to surgical repair. It should be noted that lipiodol can be an irritant and should be used with caution when identifying such leaks.[17]

Lymphangiography is particularly useful for identifying retroperitoneal leaks within the lymphatic and thoracic drainage system, and should be considered if CT scanning proves negative.

6. Lymphoscintigraphy

This investigation can also be used peri-operatively. It utilises Technetium 99m dextran (Tc99 DTPA) which is of particular use in identifying lymphatic rupture in patients who have impaired renal function, and hence where lympangiography would be contraindicated.[18]

MANAGEMENT

While the main aim of management of chylous ascites is to treat its underlying aetiology, treatment options for the adult and paediatric populations remain very different because of their vastly differing underlying pathologies.

In adults, efforts to reduce lymph flow from the small bowel are often palliative measures, while any effective treatment is directed toward the underlying disease process. In children, reducing lymph flow and giving the bowel time to 'rest' are often successful in their own right, since this gives immature lymphatics time to mature and develop their normal function.

Therefore as well as palliative short-term measures, antimicrobial chemotherapy for tuberculosis, chemotherapy for lymphomas and surgical intervention to remove tumour bulk or repair lymphatics are all appropriate, if the underlying diagnosis can be established.

Treatment options should therefore include the following:-

i) Salt restriction and diuretics: This involves sodium restriction to 60 mtq daily with the addition of aldosterone antagonists such as spironolactone and (if required) loop diuretics. These measures should help to decrease intercapillary pressure, and hence lymph flow and formation should decrease. Unfortunately this yields disappointing results, in some series less than 10% of patients respond to this method alone.[5]

ii) Paracentesis: This should be carried out to relieve dyspnoea and abdominal discomfort. This should be done with simultaneous albumen level monitoring and administration, and clearly carries a significant sepsis risk. Re-accumulation of chylous ascites usually occurs more often than non-chylous ascites, with repeat paracenteses being required every two to three weeks.

iii) Dietary Measures: Decreasing the absorption of fats by lowering the dietary fat content into the lacteals should decrease flow of lymph and thus aid resolution of the ascites. A low-fat diet supplemented with MCTs has been reported to increase the rate of resolution of chylous ascites, and this treatment alone may be helpful in paediatric patients over a period of months to years. There is, however, an associated high incidence of mental retardation in neonates,[19] presumably due to a lack of availability of essential fatty acids critical for brain growth and development within the first six months of life. Clearly, dietary measures for young adults are much less hazardous and are of particular use in patients with primary lymphangiectasia.

iv) Octreotide: The known mechanism of action of this drug is that of reducing gut protein loss but it may act in other unidentified ways. There have been reports of successful treatment of chylous ascites in paediatric patients,[20] post-liver transplant patients,[21] and adult patients with intestinal lymphangectasia.[22] The doses of octreotide vary from 100mcg tds up to 200mcg bd administered subcutaneously. When combined with a low-fat diet, resolution of symptoms usually occurred within ten days and subsequently did not reaccumulate.

The use of a long-acting somatostatin analogue such as lanreotide (administered once every ten days) may be more convenient for the patient. However, currently there is no published literature describing its use with chylous ascites.

v) Total Parenteral Nutrition: Bowel rest is a favoured treatment in paediatric patients, but the risk of mental retardation in neonates with the use of low-fat diets limits the usefulness of this treatment in this age group. TPN should theoretically deliver the benefit of giving bowel rest and allowing congenitally leaky or traumatised lymphatics to mature and heal. In addition, TPN can give essential fatty acids that would normally be missing using a low-fat diet alone. There have been documented reports of chylous ascites refractory to dietary manipulation successfully treated with total parenteral nutrition (TPN) with no observed mental retardation.[23] The duration of feeding via TPN was for a minimum of four weeks, using a combination of 10% dextrose, 1.25% synthetic amino acid solution and 4g/kg/day of 10% fat emulsion, averaging about 90kcal/kg/day. In adults around 2000 kcal/day (30-35 kcal/kg/day) may be required, but it is unusual to use TPN alone in the treatment of chylous ascites in adults.

vi) Surgical Shunts: Surgical shunting aims at re-infusing ascitic fluid from the abdomen back into the superior *vena cava* via an unidirectional valve, thereby reducing protein loss and hence further development of ascites. While initial response to the use of such appliances as LeVeen & Denver shunts and the Tenvckoff catheter is good (usually around 75% response rate), medium- and long-term success is unusual as shunt blockage usually occurs within three months of insertion.[24] Other reported problems include shunt infection, sepsis and disseminated intravascular coagulation. Due to these problems, such shunts are rarely used in the treatment of chylous ascites. Their use should be reserved for refractory cases, and perhaps as a palliative measure after other treatment options have failed.

vii) Surgical repairs: Surgical repair of lymphoperitoneal fistulas due to trauma and surgery are almost always indicated. However, surgery alone for these cases is often faced with high recurrence rates. Anecdotal success has been reported when surgery has been combined with TPN and octreotide.[20]

Surgical management of patients with protein-losing enteropathy is also disappointing, since it is often difficult to predict extent of small bowel involvement and such cases are usually better treated conservatively. In contrast, surgical removal of mesenteric cysts are often met with complete success in resolving chylous ascites.

MANAGEMENT OF CHYLOUS ASCITES

- Low-fat diet
- MCT supplementation
- Somatostatin
- Paracentesis
- Treatment of underlying cause (medical or surgical)

SUMMARY

The prognosis of these patients is variable and generally reflects that of the underlying condition. In adults some series report a survival rate of less than 20% at one year after diagnosis.[5] In children the prognosis appears to be much better, with survival rates of up to 80% at ten years after initial diagnosis.[19]

It is the opinion of the authors that all adult patients initially presenting with chylous ascites should be kept on a low-fat diet combined with subcutaneous octreotide for a minimum of ten days. In addition, paracentesis with albumen monitoring should be carried out for symptomatic relief when required.

In the paediatric population a conservative approach has been advocated, since the majority of cases in this age group will resolve spontaneously once the lymphatics have been given enough time to rest. However, surgery should be carefully considered if this treatment does not work, or if there is a clearly identified abnormality that would be amenable to surgery.

In post-operative or traumatic cases of chylous ascites, surgery is generally indicated, perhaps with the addition of an initial treatment combination of TPN and subcutaneous octreotide.

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