Lymphomas and Chylous Ascites: Review of the Literature

TONY ALMAKDISI, SAMUEL MASSoud, GEORGE MAKDISI

Temple University/Conemaugh Memorial Medical Center, Department of Medicine, Johnstown, Pennsylvania, USA

Key Words. Chylous ascites • Lymphoma • Cirrhosis

Learning Objectives
After completing this course, the reader will be able to:
1. Describe how common medical diseases can cause chylous ascites.
2. Interpret the chylous ascites fluids analysis.
3. Manage chylous ascites based on etiology.

Introduction
Chylous ascites is a rare and challenging clinical condition that occurs as a result of disruption of the abdominal lymphatics. We include a review of the literature describing the etiology, diagnosis, and therapy of chylous ascites. The Oncologist 2005;10:632-635

Pathophysiology and Etiology
Chylous ascites might occur due to different mechanisms: (a) obstruction of the lymph flow caused by external pressure (mass) causing leakage from dilated subserosal lymphatics into the peritoneal cavity; (b) exudation of lymph through the walls of dilated retroperitoneal vessels lacking valves, which leak fluid through a fistula into the peritoneal cavity as in congenital lymphangiectasia; and (c) traumatic thoracic duct obstruction causing direct leakage of chyle through a lymphoperitoneal fistula [9].

The most common causes in Western countries are abdominal malignancy (especially in adults, in whom lymphoma accounted for at least one third of the cases in one large series of patients identified over 20 years) and cirrhosis (which accounts for over two thirds of all cases) [10]. In contrast, infections, such as tuberculosis and filariasis, account for the majority of cases of chylous ascites in Eastern and developing countries [10, 11]. Infection with Mycobacterium avium intracellulare has been described...
as a cause of chylous ascites in patients with AIDS [11, 12]. Other causes include congenital lymphatic abnormalities like primary lymphatic hypoplasia or hyperplasia, which are more common in the pediatric population. The yellow-nail syndrome is a disorder of unclear etiology seen in childhood. It is a combination of yellow discolored nails, lymphedema, pleural effusions, and/or chylous ascites; patients have hypoplastic lymphatics leading to chylous effusions [13]. In children, the Battered Child Syndrome, which accounts for approximately 10% of chylous ascites cases in the pediatric population, should be excluded [14, 15]. Other causes include inflammatory disorders such as those resulting from radiation therapy to the abdomen/pelvis, which can cause fibrosis and obstruction of the lymphatic vessels in the small bowel and mesentry [16]. Acute or chronic pancreatitis can cause compression of adjacent lymphatic channels resulting in chylous ascites and pleural effusions [17]. Constrictive pericarditis can cause chylous ascites by increasing hepatic venous pressure, thereby increasing lymph production [18]. Other rare inflammatory disorders, such as idiopathic retroperitoneal fibrosis [19], sarcoidosis [20], and Whipple’s disease [21], have been reported as causes of chylous ascites. Disorders like nephrotic syndrome have also been reported to cause chylous ascites and chyllothorax, although the underlying pathogenesis is not well understood [22]. Carcinoid tumors should be excluded in patients with chylous ascites and secretory diarrhea [23]. Chylous ascites secondary to small bowel angiosarcoma [24] and malignant B-cell lymphoma has been reported [25]. Postoperative or traumatic causes are also important causes of chylous ascites [26]. Kaas et al. reported that 12 (7.4%) of 163 patients with complex surgical procedures developed chylous ascites [27]. Postoperative and traumatic chylous ascites can occur early (around 1 week) after abdominal surgery due to disruption of the lymphatic vessels or late (several weeks to months) due to adhesions or extrinsic compression of lymphatic vessels [28]. The surgical procedures resulting in chylous ascites include aortic and abdominal aneurysm repair [29], retroperitoneal lymph node dissection, inferior vena cava resection, catheter implantation for peritoneal dialysis, distal splenorenal shunts, and liver transplantation. In a series of 73 consecutive liver orthotopic transplantations performed in 60 patients from June 1983 through June 1989, there were two cases of chylous ascites [30].

The mechanisms leading to the formation of chylous ascites vary with each condition. For example, chylous ascites is present in 0.5% – 1% of patients with cirrhosis who have ascites, and decompression of the portal vein in patients with portal hypertension may relieve the lymphatic hypertension [31].

**EVALUATION**

Chylous ascites frequently presents as progressive and painless abdominal distention, occurring over the course of weeks to months depending upon the underlying cause. Patients who have undergone abdominal or thoracic surgery may present with an acute onset.

Patients may complain of weight gain, shortness of breath, and dyspnea resulting from increased abdominal pressure. Other features include nonspecific abdominal pain, weight loss, diarrhea and steatorrhea, malnutrition, edema, nausea, enlarged lymph nodes, early satiety, fevers, and night sweats. However, in the majority of cases, the diagnosis is not suspected before performing a diagnostic paracentesis, which is the most important diagnostic tool. A prospective study identified 45 patients with malignancy-related ascites among 448 ascites patients (10% of the total); chylous ascites (6.7%) was characterized by a milky appearance, negative cytology, and an elevated ascitic fluid triglyceride concentration [32]. Chyle typically has a cloudy and turbid appearance, in contrast to the yellow and transparent appearance of ascites due to cirrhosis and portal hypertension. In some patients with cirrhosis, the appearance of ascites may be opalescent due to infection or malignancy without actually containing high levels of triglycerides [33]. The triglyceride levels in ascitic fluid are critical in defining chylous ascites. The values are typically >200 mg/dl. The total protein content varies depending upon the underlying cause, ranging from 2.5–7.0 g/dl. The serum-to-ascites albumin gradient should be calculated by subtracting the ascitic fluid value of albumin from the serum value to determine if the ascites is related to portal hypertension or other causes. In addition to triglyceride levels, ascitic fluid should be sent for cell count, culture, Gram stain, measurements of total protein concentration and albumin, glucose, lactate dehydrogenase, and amylase levels, and cytology. Tuberculosis smear, culture, and adenosine deaminase (ADA) measurement should be performed in selected cases when tuberculosis is suspected. ADA is an enzyme involved in the conversion of adenosine to inosine, which is released by macrophages and lymphocytes during the cellular immune response. ADA values in peritoneal fluid are used as an indirect guide for the diagnosis of tuberculous effusions. Studies outside the U.S. have reported high sensitivity and specificity in the diagnosis of tuberculous peritonitis in areas of high prevalence for tuberculosis. In contrast, the utility of ADA measurement in populations with a high prevalence of cirrhosis, such as the U.S. population, is limited. The diagnosis of tuberculous peritonitis usually requires a peritoneal biopsy [34].

Computed tomography of the abdomen is useful in identifying pathologic intra-abdominal lymph nodes and
masses, and it also helps in determining the extent and localization of fluid, particularly if there is a suspicion of thoracic duct injury. Other studies, such as lymphangiography and lymphoscintigraphy, can assist in detecting abnormal retroperitoneal nodes, leakage from dilated lymphatics, fistulization, and patency of the thoracic duct. Lymphangiography is the gold standard in defining cases of obstruction, but has several complications, such as tissue necrosis, fat embolism, and hypersensitivity, related to the volume and type of contrast used.

Management
The underlying cause should be addressed whenever feasible. In most cases, correction of the underlying pathology will result in resolution of the symptoms and the ascites, especially in patients who have an infectious, inflammatory, or hemodynamic cause. Only few studies have addressed specific treatments aimed at reducing ascites formation [28]. Based on recent recommendations, the initial approach for patients in whom the cause cannot be found or for those who do not respond to underlying therapy is to recommend a high-protein and low-fat diet with medium-chain triglycerides (MCTs). Dietary restriction of long-chain triglycerides (LCTs) avoids their conversion into monoglycerides and free fatty acids (FFAs), which are transported as chylomicrons to the intestinal lymph ducts. In contrast, MCTs are absorbed directly into intestinal cells and transported as FFAs and glycerol directly to the liver via the portal vein. Thus, a low-fat diet with MCT supplementation reduces the production and flow of chyle. Of note, MCT supplementation should not be used in cirrhotic patients with advanced disease because narcosis and coma may occur. Such patients should be managed with a low-sodium diet and diuretics. Patients who do not respond to the above measures can be managed by total parenteral nutrition (TPN) and fasting, since fasting reduces intestinal lymph flow [35, 36]. Somatostatin along with TPN can close the lymphatic leakage or relieve the symptoms effectively and rapidly, in comparison with conventional regimens. Surgery may benefit patients with postoperative, neoplastic, and congenital causes [36]. Prior to surgery, lymphangiography or lymphoscintigraphy is helpful in identifying the anatomical location of the leakage or the presence of a fistula that is refractory to conservative treatment [36]. Surgery is recommended only when conservative treatment fails [37]. In a review of 156 patients with chylous ascites resolved after intervention, 51 patients were successfully treated surgically; 105 patients were treated conservatively. It takes several weeks to 2 months to close the lymphatic fistula adequately with routine conservative regimens [38]. Replacement of intravascular volume with albumin to prevent postparacentesis circulatory dysfunction is not necessary unless the patient has cirrhosis. Repeated large-volume paracentesis is a reasonable option for patients who have end-stage disease not amenable to medical or surgical treatment. Some recommend that continuous peritoneal drainage may be a much better and accepted choice than repeated paracentesis [35]. In one study, 28 cases of chylous ascites occurring throughout a period of 20 years were analyzed for clinical presentation, cause, yield of diagnostic procedure used, and response to therapy [2]. Malignancies were responsible for 21 of 24 adult cases of chyloperitoneum, with lymphomas predominating (13 cases). The dismal prognosis in adult cases (12 patients died within 3 months) shows the need for appropriate diagnostic assessment, including early lymph node biopsy or laparotomy, or both, when indicated. Surgery, chemotherapy, or radiation therapy should be instituted promptly, except in cases resulting from surgical trauma to lymphatics, which frequently resolve with conservative management. The mortality of chylous ascites, especially those caused by surgery, has decreased a great deal, but mortality caused by malignancy remains high [35]. Peritoneovenous shunting may be an option for patients who are poor surgical candidates and are refractory to nonoperative treatment; however, peritoneovenous shunt becomes a less common technique in refractory chylous effusion because of its high rate of complications and morbidity [28]. Lymphatic microsurgery will play more and more important roles in the treatment of chylous diseases [39].

Conclusion
Chylous ascites is a rare form of ascites, in which intra-abdominal malignancy and liver cirrhosis cause the majority of cases. Paracentesis and triglyceride level are the most important diagnostic factors. Various management modalities may be used successfully to treat chylous ascites. One of the first measures to be implemented is a low-fat diet with MCT supplementation. TPN should be reserved for cases when an oral diet fails. Paracentesis is indicated to improve patient comfort, reduce intra-abdominal pressure, and improve renal function. Therefore, treatment should be individualized and adjusted to the severity of lymphatic leakage and its consequences. The outcome mostly depends on the underlying pathological condition. Thus, in the absence of a malignant or congenital underlying pathology, the prognosis in cases of postoperative chylous ascites is good, with the majority of cases responding to conservative measures.

Disclosure of Potential Conflicts of Interest
The authors indicate no potential conflicts of interest.
REFERENCES