A CASE REPORT OF REFRACTORY CONGENITAL CHYLOUS ASCITES IN INFANT – SURGICAL TREATMENT WITH FIBRIN GLUE

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Congenital chylous ascites is a rare disease that results from abnormal development of the intra-abdominal lymphatic system. No gold standard treatment has been described so far, however, a combination of medium–chain triglyceride based diet or total parenteral nutrition along with octreotide and abdominal paracentesis is considered as a conservative management. This treatment is often a challenge to physicians since chylous ascites is often refractory and result in malnutrition and immune deficiency because of the loss of proteins and lymphocytes. We report a four-month old boy with congenital chylous ascites who was refractory to medical treatment with prolonged bowel rest, total parenteral nutrition, octreotide and repeated paracentesis. The baby well responded to surgical treatment with application of fibrin glue on the surface area of the leak site and was discharged after 2 month of hospitalization. When following up the patient had no recurrence of the ascites and he was growing up normally.

Keywords: Congenital chylous ascites, Fibrin glue.

I. INTRODUCTION

The first report of chylous ascites was in a two-year old boy with tuberculosis since the 17th century. The theory that lymph is formed by diffusion from blood through vessel walls was not accepted until 1849.[1] Press et al reported an incidence of 1 per 20,464 admissions at the Massachusetts General Hospital during 20 years.[2] Chylous ascites is milky appearing peritoneal fluid that is rich in triglycerides and lymph. Congenital chylous ascites is defined as the accumulation of chyle into the peritoneal cavity in infants younger than three months.[3,4] The most common cause is malformation of the lymphatic vessels either atresia or stenosis of the major lacteals or mesenteric cysts or lymphangiomatosis.[3] No gold standard treatment has been described so far, however, medium-chain triglyceride based diet or total parenteral nutrition along with octreotide and abdominal paracentesis is considered as a conservative management.[2,5] This treatment is often challenging to the physician since chylous ascites is often refractory and is responsible for serious malnutrition and immune deficiency because of loss of proteins and lymphocytes.[2,6]

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II. CASE PRESENTATION

A four-month old boy was transferred to the National Children's Hospital because of recurrent abdominal ascites. His medical history showed that he had been diagnosed with isolated fetal ascites at 28 week gestation. He was the firstborn, full term, birth weight 3.7 kg. He was exclusively breastfed and put on 3 kg body weight for the first 3 months. He

developed abdominal distention and peripheral edema from 3 months of age.

On examination, the baby had edema and fever with temperature of 38°C. He was hemodynamically stable. His body weight was 7 kg. His abdomen was soft but bloating, normal bowel sounds, no masses or hepatosplenomegaly were palpated. On percussion, shifting dullness was observed, which suggested ascites.

Initial investigations showed raised C reactive protein (26 mg/L, reference range 0 - 6 mg/L) and a white cell count of 14.5 G/L (reference range 4.0 - 10.0 G/L). Lymphocyes and neutrophils were 5.38 and 7.17 G/L, respectively. Hemoglobin was 85g/L (110 - 133 g/L), MCV 67 fL (78.2 - 83.9 fL), MCH 22 pg (25.7 - 29.7 pg) and platelets were 331 G/L (140 - 440G/L). An abdominal ultrasound scan showed a large peritoneal effusion (60 mm) with clear fluid.

The baby was hospitalized and laboratory testing showed persistent hypoalbuminemia (20 - 30 g/L), immunoglobulin deficiency (IgA 0.02 g/l; IgG 0.32 g/l; IgM 0.55 g/l), normal pancreatic enzymes, kidney function, and aminotransferase enzymes. The fluid of 600 ml/24h obtained by abdominal paracentesis was chyle. The biochemical analysis of the ascitic fluid showed the concentration of protein: 19.7 g/L; Triglyceride: 1.74 mmol/L; Cholesterol: 0.63 mmol/L; LDH: 81 U/L; Microscopy showed a large number of lymphocytes. (Cells: > 2000 cells/µl: 95% lymphocyte, 2% neutrocyte, 3% monocyte), PCR for *Mycobacterium tuberculosis* was negative; microbiological cultures were negative. Because he had a high alpha-fetoprotein level (αFP 300 UI/mL), we checked other tests to distinguish between malignant and benign conditions. He had normal βHCG, testicular ultrasound, cranial MRI, abdominal and thoracic MSCT results. An ultrasound of the portal vein and echocardiography were carried out with the normal results. Abdominal MRI showed no lymphatic malformation or cyst.

The patient was treated with blood transfusion, albumin infusion, intravenous immunoglobulin (IVIg), antibiotics. Partial parenteral nutrition and an medium-chain triglyceride (MCT)-based diet (pregestimil milk-formula milk specially designed for infants who experience fat malabsorption and who may also be sensitive to intact proteins) 300 ml/day along with octreotide infusion at 1 mcg/kg/h in 16 hours was started and continued for one week, but the amount of ascetic fluid was not remitted. He had total parenteral nutrition while escalating octreotide to 3 mcg/kg/hour in 16 hours for one week but ascetic fluid still persisted. Lymphography was performed after 2 weeks of medical treatment. It showed a right pelvic lymphatic system that dilated abnormally (figure 1) and the baby was injected with sclerosing agent (Bleomycin). After being sclerotherapy, his condition did not change, his temperature was between 38.5 - 39°C for 3 days continuously, blood culture was positive with *Candida parapsilosis* so we had to add an antifungal agent (fluconazole). One month after sclerotherapy, we decided to perform surgical exploration to check for malrotation, mesenteric cyst, lymphatic malformation or enlarged lymph nodes. We found a fistula at the base of the mesenteric intestine next to the hepatic hilum nodes, fibrin glue (Tisseel Lyo 1) was applied on the surface area of the leak site to achieve adhesions between the glue and diseased tissue area (figure 2).

Postoperatively, total parenteral nutrition (TPN) along with octreotide at 5 mcg/kg/h in 24 hours was transfused continuously for 2 weeks. The abdominal drain which was kept post operatively decreased gradually from

250 ml/24h on the first day to 70 ml/24h on the second day then had no fluid at 6th day after surgery. Daily, we followed up the fluid balance, abdominal circumference and body weight. Ultrasound and biochemical blood analysis were checked once a week. Levels of albumin, protein and immunoglobulin were in the normal range. Oral diet (Pregestimil) was slowly initiated. He was exclusively formula-fed (Pregestimil) from 3 weeks after surgery and the volume of formula milk gradually increased until full feeds were achieved. Then the dose of octreotide was gradually reduced from 5 mcg/kg /h in 16 hours for 2 days to 2.5 mcg/kg /h in 16 hours for 3 days and completely stopped. Abdominal drainage tube was removed on the 18th day after surgery. *Candida parapsilosis* was treated with Amphotericin B. The patient was discharged after 2 month of hospitalization with a body weight was 7.5 kg. He was followed up every month for the first 3 months, abdominal untrasound and blood test results were nomal. He had no recurrence of the ascites and was growing up normally. After 3 months follow up in outpatient clinic, he was asymptomatic and had normal diet with a body weight of 10.5 kg.

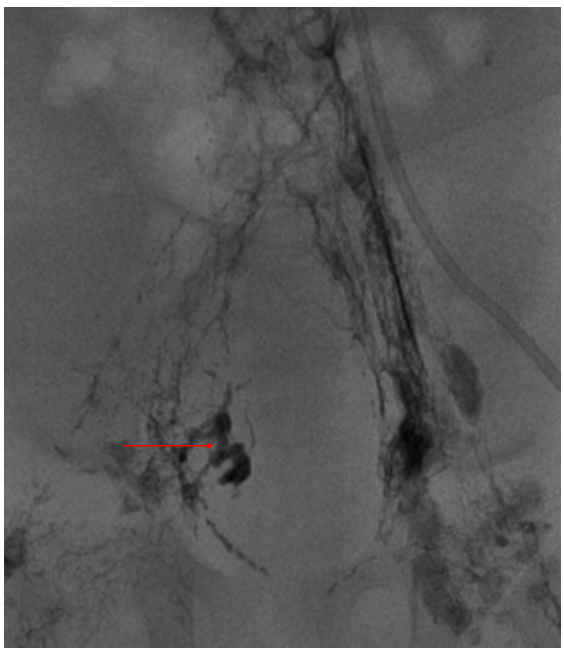

Figure1. Our patient's lymphography: Right pelvic lymphatic system which dilated abnormally (red arrow)

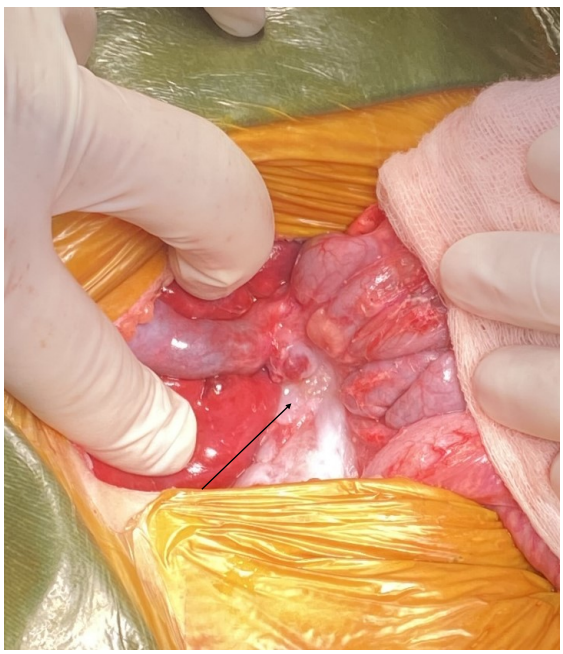

Figure 2. The site of the lymphatic leak was sealed with fibrin glue (black arrow)

III. DISCUSSION

Congenital chylous ascites is rare.[2,3] Three mechanisms in the formation of chyloperitoneum, include ① direct leakage of chyle through a peritoneal lymphatic system fistula associated with abnormal retroperitoneal lymphatic vessel; ② exudation of chyle through the walls of the retroperitoneal lymphatic without a visible fistula; ③ exudation or leakage of chyle after the rupture of dilated lymphatic of the bowel wall and mesentery caused by obstruction of the lymphatic vessel

at the base of the mesentery, cisterna chyli, or thoracic duct.[4,5] There are multiple causes of chylous ascites in infants and children. The most common is the lymphatic abnormalities, as in atresia or stenosis of the major lacteals, mesenteric cysts and lymphangiomatosis.[3,4] Another reason is lymphatic obstruction, as in malrotation, incarcerated hernia, intussusception, inflammatory enlargement of lymph nodes and malignancy. Moreover, the chylous ascites can be caused by trauma during surgery, accidents or child abuse.[5,6] Abdominal paracentesis is the most important tool to diagnose chylous ascites. Chyle typically is a cloudy or milk fluid. Elevated ascitic fluid triglyceride level is diagnosis of chylous ascites. In the past, Staat et al suggest cutoff value of triglyceride is 110 mg/dL (1.24 mmol/L).[7] The current critical diagnosis of chylous ascites uses a cutoff value of > 200 mg/Dl.[8]

Table 1. Characteristics of chylous ascites[8]

Color	**Milky and cloudy**
Triglyceride level	Above 200 mg/dL (2.286 mmol/L)
Cell count	Above 500 cells/μL (predominance of lymphocytes)
Total protein	Between 2.5 - 7.0 g/dL
Cholesterol	Low (ascites/serum rate < 1)
Lactate dehydrogenase	110 - 200 UI/L

Our patient was diagnosed with chylous ascite due to milk fluid, increasing triglyceride level, cell count > 2000 cells/μL, cholesterol ascites/serum rate < 1. Finding the underlying etiologies for congenital chylous ascites is not easy. Ultrasound of the portal vein access presence or absence of underlying portal hypertension which causes chylous ascites.[8] Echocardiography detects structural abnormalities of the heart or pulmonary hypertension. Abdominal MRI is a useful tool to identify lymphatic malformation or cyst and evaluates ascites fluid. In case of refractory to therapy, lymphography is indicated to evaluate the presence of aberrant lymphatic channels.[9,10] Our patient has dilated pelvic lymphatic system on lymphography, that is inadequate to explain chylous ascites. Chyle normally is only present in the mesenteric lymphatics, cisterna chyli, and thoracic duct.[8] Long–chain triglycerides are absorbed into the intestinal lymphatics and transported in the thoracic duct to the venous system. Fatty acid composition of these triglycerides is the same as dietary fat.[4] Conservative management is considered when there is no identifiable surgical cause. It is necessary to relieve symptoms by the abdominal paracentesis and to restore fluid and protein losses. The purpose of the therapeutic approach is to maintain nutrition and decrease the production and flow of chyle. Chronic loss of chyle results in anemia, hypoproteinemia, hypocalcemia, hypolipidemia, serous immunocompromised and malnourishment.[3,5] Medium–chain triglycerides (fatty acids with carbon chain length ≤12) are absorbed as fatty acids directly into the portal venous system, by passing intestinal lymphatics. Therefore, medium–chain triglyceride intake results in less chyle production than a diet rich in long–chained triglycerides.[11] In refractory cases, the administration of somatostatin or its analogue octreotide is needed.[3,5] Kassem et al suggested that a high-protein and low-fat diet with medium-chain triglycerides should be the first recommendation for the treatment of chylous ascites. The second recommendation is total

parenteral nutrition and pharmacological agents (somatostatin, octreotide…).[12] Our patient did not respond to total parenteral nutrition with octreotide, surgical exploration was performed. Normal lymph flow through the thoracic duct averages 1.0 ml/kg/h and may increase to 200 ml/kg/h following ingestion of a fatty meal.[10] Besides lowering the portal pressure, octreotide also suppresses the pancreatic exocrine function and hence decreases absorption of fat from the intestine so that it decreases thoracic duct flow.[8] Our patient used formula milk (similac HMO 1), blood transfusion and IVIG infusion one day before surgery. Octreotide was ceased 3 days prior to the procedure to increase the production and help us find the lymphatic system's leaking points. Fibrin sealants are considered to be the ideal physiological adhesive. Fibrin sealant consists of fibrinogen and thrombin solution, which generates a crosslinked fibrin clot in a process that mimics the last stage of the physiologic coagulation system, resulting in the formation of a semi-rigid to rigid fibrin clot that consolidates and adheres to the application site. Fibrin sealant also acts as a fluid-tight sealing agent able to stop bleeding and hold tissues and materials in a desired configuration.[10] Fibrin glue has been previously used to treat chyloperitoneum and reported successfully in several researches. Fibrin glue was usually sprayed over the area of lymph leak as an adjunct treatment during operation.[11-13]

CONCLUSION

Congenital chylous ascites is rare and difficult to diagnose underlying etiology. Surgical exploration should be performed in patient with refractory congenital chyloperitoneum. Fibrin glue is the effective physiological adhesive to seal the area of lymph leak.

REFERENCES

1. Aalami OO, Allen DB, Organ CH Jr. Chylous ascites: A collective review. *Surgery.* 2000;128:761-768.

2. Press OW, Press NO, Kaufman SD. Evaluation and management of chylous ascites. *Ann Intern Med.* 1982;96:358-364.

3. Qi H, Bu-jun G, Li-ming L, Zhi-yuan T, et al. Successful management of chylous ascites with total parenteral nutrition, somatostatin and fibrin glue. *Chin Med J.* 2007;120:1847-1849.

4. Mouravas V, Dede O, Hatziioannidis H et al. Diagnosis and management of congenital neonatal chylous ascites. *Hippokratia.* 2012;16(2):175-180.

5. Cochran W.J, Klish W.J, Brown M.R et al. Chylous ascites in infants and children: a case report and literature review. *J Pediatr Gastroenterol Nutr.* 1985;4(4):668-673.

6. Cardenas A and Chopra S. Chylous ascites. *Am J Gastroenterol.* 2002;97(8):1896-1900.

7. Staats B.A, Ellefson R.D, Budahn L.L et al. The lipoprotein profile of chylous and nonchylous pleural effusions. *Mayo Clin Proc.* 1980;55(11):700-704.

8. Bhardwaj R, Vaziri H, Gautam A et al. Chylous Ascites: A Review of Pathogenesis, Diagnosis and Treatment. *J Clin Transl Hepatol.* 2018;6(1):105-113.

9. Fishman S.J, Burrows P.E, Upton J et al. Life-threatening anomalies of the thoracic duct: anatomic delineation dictates management. *J Pediatr Surg.* 2001;36(8):1269-1272.

10. Meinke A.H, 3rd, Estes N.C and Ernst C.B. Chylous ascites following abdominal aortic aneurysmectomy. Management with total parenteral hyperalimentation. *Ann Surg.* 1979;190(5):631-633.

11. Kassem R, Rajab A, Faiz A et al.

Chylous ascites in an infant – Treated surgically with fibrin glue after failed medical treatment - A case report. *Journal of Pediatric Surgery Case Reports.* 2017;19:25-27.

12. Martinowitz U and Saltz R. Fibrin sealant. *Curr Opin Hematol,* 1996;3(5):395-402.

13. Antao B, Croaker D and Squire R. Successful management of congenital chyloperitoneum with fibrin glue. *J Pediatr Surg.* 2003;38(11):E7-8.