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CASE REPORT | PEDIATRICS

Congenital Chylous Ascites and Ehlers-Danlos Syndrome Type VI

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ABSTRACT

We report the first observation of a patient with contgenital chylous ascites (CCA) and Ehlers-Danlos syndrome type VI due to primary lymphatic defect with additional vascular anomaly. CCA is a rare condition, and there is limited understanding of its pathophysiology and treatment options. We also review the patient's treatment course mitigated with octreotide and total parenteral nutritional support, as there are no current established guidelines for CCA. Early recognition of possible association with Ehlers-Danlos syndrome is important for quick intervention and successful management of pediatric patients.

INTRODUCTION

Congenital chylous ascites (CCA) is a rare diagnosis of the exudation of chyle into the abdomen that occurs prenatally or within the first 3 months of life.[1,2] In children, neonatal or infant chyloperitoneum occurs most often as an iatrogenic disruption of the thoracic duct from surgery or mass effect.[3-5] CCA is rarer than iatrogenic causes, estimated at 4% of identifiable cases, and only 50% of CCA cases have identifiable organic causes.[1,2,5] Ehlers-Danlos syndrome type VI (EDS-VI) is an autosomal recessive connective tissue disorder. There are no reported case reports of CCA associated with EDS-VI and vascular disruptions.

CASE REPORT

A 35-day-old male, born at term by repeat cesarean, presented with general hypotonicity, poor perfusion, and respiratory distress secondary to abdominal distension. All prenatal labs and imaging were normal, and there was a history of EDS-VI in his older brother. The patient had notable hypotonia and severe joint and extremity laxity at birth, possibly consistent with EDS-VI. The patient first presented to the primary care physician for abdominal distension, poor feeding, and significant scrotal swelling. A subsequent abdominal radiograph was suggestive of abdominal ascites (Figure 1).

At admission he had respiratory distress due to the abdominal swelling and required oxygen supplementation. Abdominal and pelvic ultrasound confirmed ascites and also revealed a left pelvic aneurysm (Figure 2). A diagnostic and therapeutic paracentesis revealed chylous peritoneal fluid with the following fluid analysis: triglycerides 1,255 mg/dL, albumin 1.5 g/dL, cholesterol 64 mg/dL, pH 7.76, white blood cell count 10,700 per uL with 68% lymphocytes, red blood cell count 217 per uL. Conservative therapy proceeded with medium chain triglyceride (MCT)-based formula by nasogastric tube, and antibiotics were empirically started due to concern for peritonitis.

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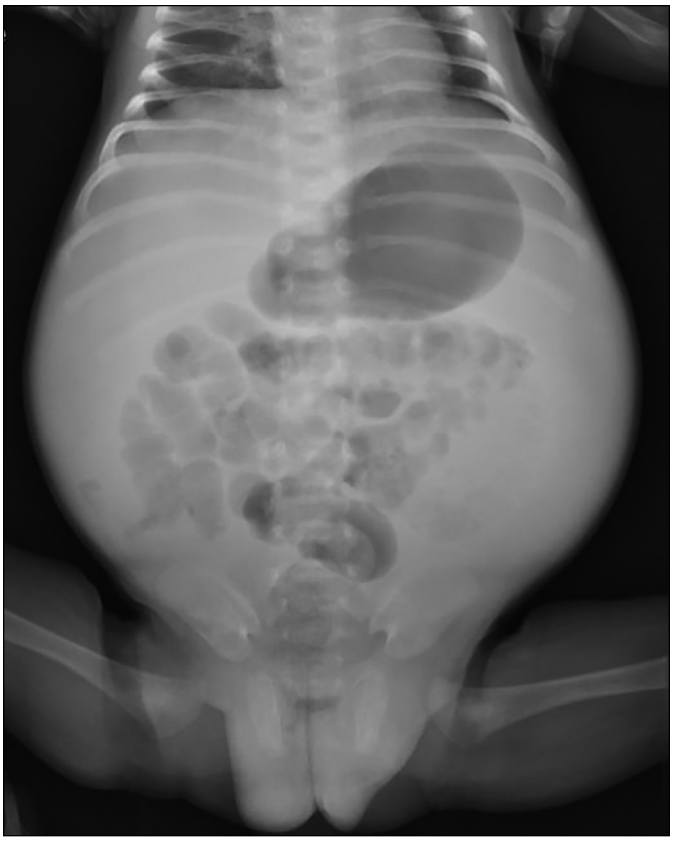

Figure 1. Abdominal radiograph suggestive of ascites.

The patient's abdominal girth increased over the next 48 hours despite switching to total MCT formula. Enteral feeds were discontinued; a percutaneous intravenous (IV) central catheter was placed and total parenteral nutrition (TPN) was started. Additionally, an octreotide IV drip was initiated at 0.5 μg/kg/hr and increased to 1 μg/kg/hr. Because of continued abdominal distension and tachypnea, a peritoneal drain was placed by interventional radiology (Figure 3). A total of 90 mL/kg of cloudy intraperitoneal fluid was removed over the following 72 hours. The patient returned to his baseline respiratory effort with discontinuation of oxygen. Due to his peritoneal fluid losses, there was significant hypoalbuminemia and hypogammaglobulinemia, and both 25% albumin and immunoglobulin were given intravenously for colloid replacement.

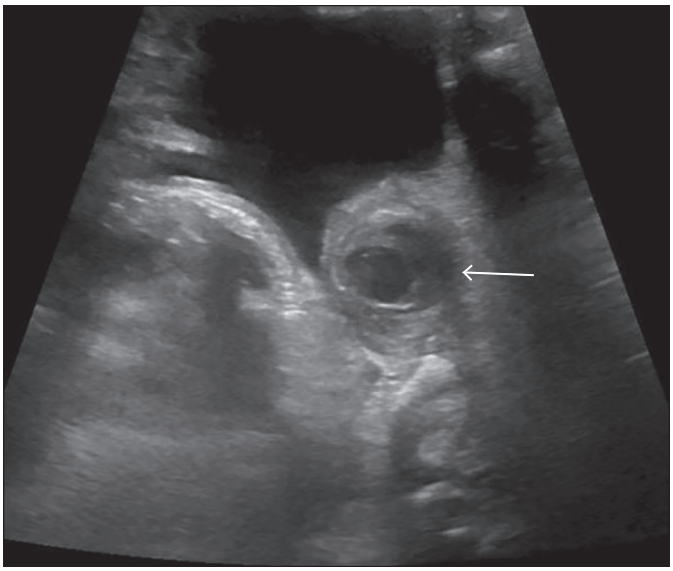

Figure 2. Ultrasound of arterial aneurysm at left lumbosacral junction.

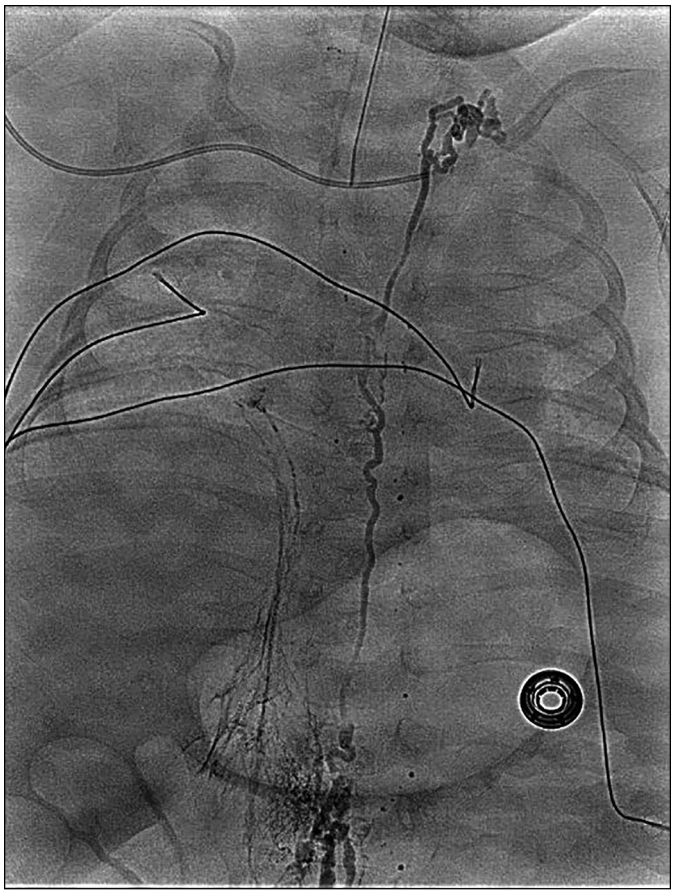

Figure 3. Lymphangiogram revealing extravasation of contrast from the right network of lymphatic channels and the intact left network of lymphatic channels.

Genetic evaluation of the patient included an increased ratio of urine de-oxy-pyridinoline to pyridinoline, and sequencing of the procollagen-lysine, 2-oxoglutarate 5-dioxygenase 1 (*PLOD1*) gene showed two intron-splicing pathogenic mutations. These tests confirmed the EDS-VI diagnosis and supported the patient's pathophysiology of lymphatic disruptions in the abdomen.

Magnetic resonance imaging (MRI) revealed a left-sided iliac aneurysm, soon after bifurcation before leaving the abdomen (Figure 2). Bilateral intranodal lymphangiogram confirmed extravasation of contrast from the right network of lymphatic channels in the region

of the porta hepatis, anterior and to the right of the cisterna chyli (Figure 3).

After 9 days of TPN and octreotide therapy, stable abdominal girth, and successful return to full oral feeds, the patient was discharged home. Follow-up at 8 weeks post-hospitalization showed no rebound ascites and adequate growth and development on a MCT-based formula. At 10 months of age, the patient's diet was liberalized to normal infant formula and solids. The aneurysm was followed by sonography and shown to be stable in size at 6 months of age. No further interventions were necessary for the arterial defect.

DISCUSSION

Our patient's CCA most likely resulted from poor chyle resorption due to disrupted abdominal lymphatic channels, while the left iliac aneurysm was an incidental vascular defect but could have contributed to mass effect on distal venous flow and added to the proximal peritoneal chyle accumulation. No inciting incident or medical event could explain these defects, and, given his young age, they were likely present at birth. While the aneurysm and abdominal lymphatic defects appeared to be unrelated processes, they were presumed to be secondary to EDS-VI. Lymphatic disruptions are often reported in EDS-VI, while a review of the literature revealed that no previous cases of EDS-VI had both lymphatic and vascular malformations or any resultant CCA; rather, vascular insults are most commonly found in EDS Type IV.[8-10] Interestingly, our patient had physical findings of both these EDS subtypes.

EDS-VI is a Mendelian inherited autosomal recessive connective tissue disorder (OMIM 225400) with clinical features of kyphoscoliosis at birth or within the first year of life. Other features include severe neonatal hypotonia, thin hyperextensible and bruisable skin, joint hypermobility, and scleral fragility leading to increased risk for globe rupture.[6,7] EDS-VI incidence is rare, with approximately 1 case in 100,000 live births. The pathophysiology of EDS-VI results from a lysyl hydroxylase deficiency from pathogenic *PLOD1* gene mutations.[6-8] Our patient had the constellation of neonatal hypotonia after birth, hypermobility of joints, and hyperextensible skin.

There is no current standard treatment for CCA. For mild to moderate chylous ascites without secondary systemic symptoms, dietary management is the first-line modality. Using an MCT-based formula should slow chyle production. A notable decrease in ascites, however, can take 3–8 weeks on dietary changes alone.[11-13] If the ascites cause respiratory distress, abdominal compartment syndrome, vascular or perfusion deficits, or peritonitis, then a combination of paracentesis, discontinuation of oral feeds, and initiation of octreotide should be considered.[13,14] Our patient experienced hypoxia and worsening respiratory distress due to chylous abdominal accumulation despite MCT formula. We felt this clinical scenario justified immediate TPN and an attempt to slow chyle production with octreotide.

Octreotide is a somatostatin analogue, and its mechanism of action is thought to affect vascular smooth-muscle contractility with resultant decreased flow through lymphatics.[15] Use of parenteral octreotide has been shown to successfully decrease lymph output and chyle leak in both pediatric and adult patients.[11-13,16] No treatment guideline currently exists for octreotide use.[17] Our experience showed resolution of CCA after 5 days of octreotide at 1 μg/kg/hr with a slow dosage wean and discontinuation over 72 hours. Replacement of drained peritoneal fluid with IV albumin and IV immunoglobulin should be given after paracentesis to support intravascular circulation and especially considered in neonatal chylous ascites, due to their immature humoral immunologic system. Finally, laparoscopy should be used for intervention if ascites prove refractory after 4 to 8 weeks of medical and nutritional therapy. Surgical techniques can include drainage, shunting, pleurodesis, embolization, or direct surgery on the thoracic duct.[18-20]

DISCLOSURES

Author contributions: AK Ermarth drafted, reviewed, and revised the manuscript, and is the article guarantor. J. Pohl, B. Esty, JK Sempler, and MA O'Gorman critically reviewed the manuscript. JC Carey reviewed and revised the manuscript.

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