Spontaneous celiac artery aneurysms in 13-year-old and 10-year-old brothers with *PLOD1*-related kyphoscoliotic Ehlers-Danlos syndrome

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ABSTRACT

PLOD1-related kyphoscoliotic Ehlers-Danlos syndrome is a rare, autosomal recessive connective tissue disorder characterized by congenital hypotonia, early-onset, progressive kyphoscoliosis, and generalized joint hypermobility. *PLOD1*-kyphoscoliotic Ehlers-Danlos syndrome is also associated with heightened vascular fragility, resulting in an elevated susceptibility to recurrent vascular complications such as arterial aneurysms, dissection, and spontaneous arterial rupture. We report the cases of two affected brothers: a 13-year-old boy presenting with spontaneous rupture of a celiac artery aneurysm and a 10-year-old boy presenting with a rapidly enlarging celiac artery aneurysm requiring urgent repair. (J Vasc Surg Cases Innov Tech 2024;10:101465.)

Keywords: Arterial rupture; Celiac pseudoaneurysm; Kyphoscoliotic Ehlers-Danlos syndrome; Vascular complications; Vascular fragility

PLOD1-related kyphoscoliotic Ehlers-Danlos syndrome (kEDS) is a rare autosomal recessive disorder, characterized by congenital muscle weakness, early-onset kyphoscoliosis, and joint hypermobility. The incidence of kEDS is estimated at 1 in 100,000 persons.[1] This disorder results from lysyl-hydroxylase-1 deficiency, a post-translational modification enzyme critical in forming collagen cross-links, due to pathogenic alterations in the *PLOD1* gene.[2,3] Individuals with *PLOD1*-kEDS are at increased risk of experiencing life-threatening vascular complications given their heightened susceptibility to both aneurysm formation and spontaneous arterial rupture from severe blood vessel fragility, affecting medium-size arteries.[4,5] These complications can be particularly challenging to manage. We report the cases of two brothers diagnosed with *PLOD1*-kEDS: a 13-year-old boy presenting with spontaneous rupture of a celiac artery aneurysm and a 10-year-old boy presenting with a rapidly enlarging celiac artery aneurysm requiring urgent repair. Both patients provided verbal and written consent for the report of their case details and imaging studies.

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CASE REPORT

Patient 1: Ruptured celiac artery aneurysm. In January 2018, a 13-year-old boy with *PLOD1*-kEDS presented with abdominal pain. At birth, he had congenital hypotonia, undescended testes, and bilateral congenital hip dislocation. In childhood, he experienced severe thoracolumbar scoliosis, generalized joint hypermobility, and poor wound healing. In June 2017, he experienced a spontaneous pneumothorax and underwent bullectomy, pleurectomy, and gastrostomy tube insertion for feeding issues. However, he experienced tube feeding intolerance after discharge and was hospitalized for nutritional support in January 2018.

A computed tomography (CT) scan revealed a celiac axis abnormality (Fig 1, *A*), retrospectively identified as an aneurysm, and evidence of severe spinal curvature. Within 24 hours, the patient developed severe abdominal pain and a precipitous hemoglobin decrease, necessitating the initiation of a massive transfusion protocol. A repeat CT scan confirmed a celiac aneurysm rupture (Fig 1, *B*), and vascular surgery was consulted. The patient underwent emergent laparotomy. A supraceliac clamp was applied to the aorta, the hematoma was entered, and the celiac artery was ligated with two pledgeted 5-0 Prolene sutures and a clip. The splenic and hepatic arteries were ligated as well. The bowel and liver were viable on completion of the procedure. In the event of liver ischemia after ligation, the proposed reconstructive approach involved implementing an aortic–hepatic bypass, using either a prosthetic graft or a conduit constructed of bovine patch material.

The patient's postoperative course was complicated by seizure, renovascular hypertension likely secondary to compression from a perinephric hematoma, and right upper extremity deep vein thrombosis, for which he was appropriately medically managed. Subsequent CT scans showed no recurrent aneurysms at a follow-up of 5 years, and he is currently enrolled in college.

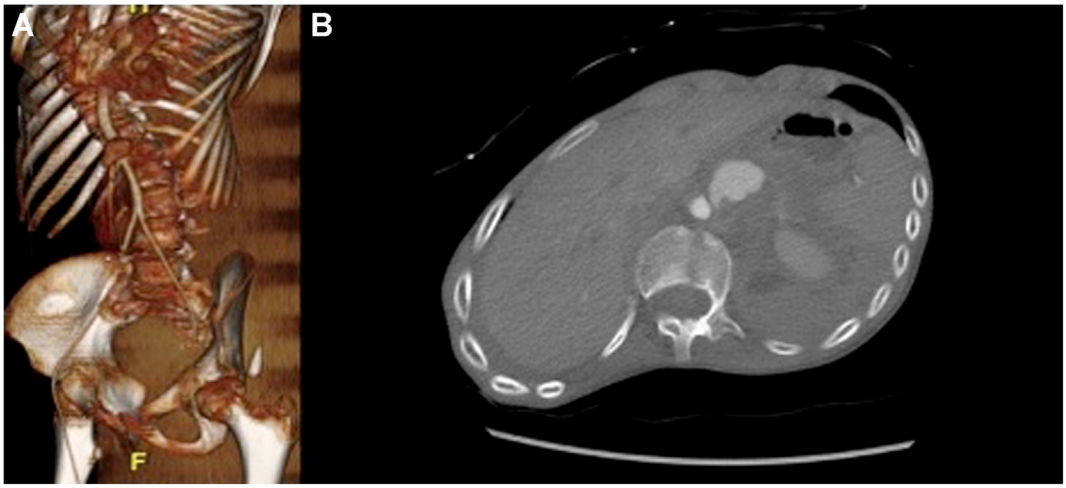

Fig 1. Patient 1. **A,** Computed tomography (CT) scan showing a celiac axis abnormality, retrospectively identified as an aneurysm, and severe spinal curvature. **B,** Repeat CT scan confirming celiac artery pseudoaneurysm rupture.

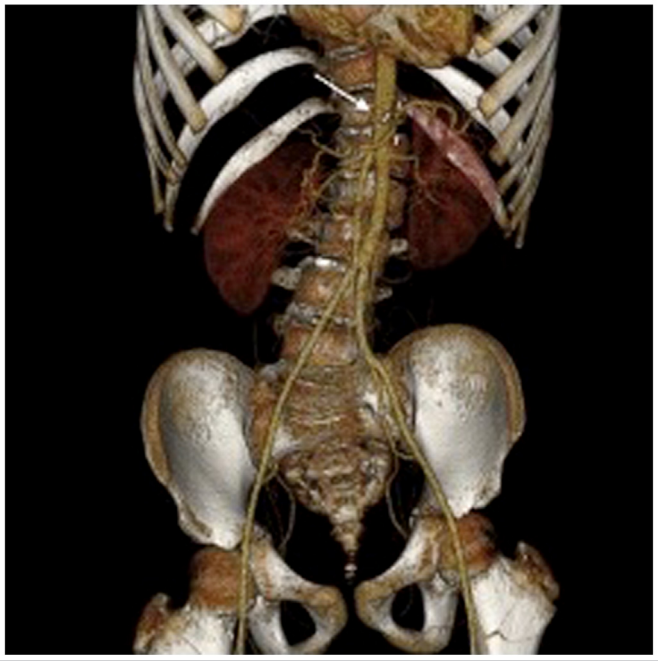

Fig 2. Patient 2. A follow-up computed tomography (CT) scan at 8 months postoperatively revealed a 9.5-mm recurrent pseudoaneurysm at the previous ligation site.

Patient 2: Rapidly enlarging celiac aneurysm with recurrence. In August 2019, patient 1's 10-year-old brother, also diagnosed with *PLOD1*-kEDS, experienced severe postprandial epigastric pain. He had a history of hypotonia, developmental hip dysplasia, progressive thoracolumbar scoliosis, joint hypermobility, poor wound healing, and easy bruising. At age 7, he suffered a rupture of the right eye, necessitating primary repair, which was complicated by retinal detachment.

On admission, the patient was hemodynamically stable, with a benign abdomen on physical examination and resolution of his epigastric pain within 2 hours of onset. There was no clinical evidence of infection and no positive cultures. An initial CT scan revealed proximal celiac artery occlusion with reconstitution of the common hepatic, splenic, and left gastric arteries and patent mesenteric arteries with no evidence of bowel ischemia. Conservative management was initiated with plans for repeat imaging, and the patient resumed a regular diet without postprandial pain.

A subsequent CT scan showed a rapidly growing 1.7-cm celiac artery aneurysm without rupture or bowel ischemia, necessitating urgent laparotomy and celiac artery ligation. Intraoperatively, the base of the celiac artery was clamped and ligated with two pledgeted 4-0 Prolene sutures. The aneurysm capsule was debrided, and the distal celiac artery was ligated similarly. The capsule was not sent for culture. The procedure was successful, and the patient's postoperative recovery was uneventful.

In April 2020, a follow-up CT scan identified a 9.5-mm pseudoaneurysm at the previous ligation site (Fig 2); however, the patient remained asymptomatic. He underwent reexploration for the pseudoaneurysm. He had only a few adhesions, and, due to his small size, it was straightforward to identify the pseudoaneurysm and ligate it primarily. Pledgeted sutures were used, and intraoperative ultrasound confirmed completed pseudoaneurysm repair. Subsequent CT scans showed no recurrence at 3 years, although he has had progression of his kyphoscoliosis. Given his confirmed diagnosis of kEDS, a multidisciplinary team, including a pediatric cardiologist, orthopedic surgeon, pediatrician, and ophthalmologist, continues to oversee his care due to complications associated with kEDS. From a vascular surgery standpoint, our surveillance protocol involves annual monitoring with CT angiography or magnetic resonance angiography.

FAMILY HISTORY AND GENETIC TEST RESULTS

The parents are first cousins. An older brother to our patients was born with dorsiflexed feet, bilateral cryptorchidism, and congenital hypotonia. Skin fragility was noted during his orchidopexy repair. He had a history of poor wound healing and thoracolumbar kyphoscoliosis.

In 2018, molecular testing of all three affected brothers revealed a homozygous deletion of exon 2 of the *PLOD1* gene, consistent with the diagnosis of kEDS. The parents were confirmed to be carriers of the deletion.

DISCUSSION

EDSs encompass a group of rare genetic disorders comprising 13 subtypes that affect connective tissues and can potentially result in serious complications, especially within the cardiovascular system.[6] Although the vascular subtype of EDS (vEDS), linked to the *COL3A1* gene pathogenic variant, is well-documented for its life-threatening cardiovascular complications, *PLOD1*-kEDS carries a lower, yet still significant, risk of such complications, including aneurysms, arterial dissections, and intracranial hemorrhages.[6,7] Due to the disease's rare occurrence and lack of comprehensive, well-defined patient cohorts, the prevalence of vascular complications in patients with *PLOD1*-kEDS remains unknown. Ocular fragility with scleral rupture after minimal trauma is a serious potential vascular complication, as occurred in patient 2. Severe kyphoscoliosis can result in restrictive lung disease, recurrent pneumonia, and cardiac failure.[1]

The two cases presented in this report add to the limited body of reported cases describing vascular complications in individuals with *PLOD1*-kEDS. Henneton et al[7] previously summarized cases of kEDS patients with detailed vascular incidents, with most of the eight identified patients being children. Notably, the vascular injuries in the pediatric cohort were internal jugular vein ectasia after catheterization,[8] spontaneous superior vena cava rupture after extubation,[3] spontaneous brachial and profunda rupture,[9] intraoperative abdominal aorta, iliac artery, and common iliac vein rupture, and intraoperative superior gluteal rupture during spinal surgery.[10] Given the predisposition of patients with kEDS to severe vascular fragility, any invasive procedures should be carefully evaluated for potential risks and performed by experienced surgeons well-acquainted with the need for heightened caution given the tissue fragility and its associated complications.[11] The proximity to available emergent vascular consultation should also be considered before performing invasive procedures on patients.[12]

A recent report by Foy et al[13] further emphasized the risk of spontaneous vascular injuries, particularly arterial aneurysms and dissections, due to the high vascular fragility in *PLOD1*-kEDS patients across all age groups. This heightened fragility increases the likelihood of recurrent spontaneous arterial dissection or rupture, as illustrated by patient 2 with a recurrent pseudoaneurysm detected during surveillance imaging that required intervention.

Vessel ligation with umbilical tape has been described in the literature to be preferential to direct repair in vEDS.[14,15] However, the anatomy in both our patients was not amenable to this type of repair. In patient 1, the celiac artery was not intact to ligate with umbilical tape. In patient 2, the tissue was highly friable and would not hold ligation with umbilical tape. Therefore, pledgeted sutures were used for repair.

Limited literature exists on screening recommendations for assessing vascular beds in those with *PLOD1*-kEDS. Regular 5-year follow-up with a cardiologist is advised, even if the initial echocardiogram is normal. Maintaining vigilant blood pressure control is crucial to reduce the risk of arterial rupture.[1] In both our patients, blood pressure control was used with a target systolic blood pressure of <110 mm Hg, and no antihypertensive medications were required to achieve this target.

Considering that patients with kEDS face acute, life-threatening arterial events, in addition to other complex medical issues affecting multiple organ systems, it is imperative to implement multidisciplinary management that includes appropriate cardiovascular care and ongoing monitoring of blood pressure and noninvasive arterial screening. This includes methods such as ultrasound, CT, or magnetic resonance imaging, to detect arterial dissections and dilations.[5,11] In addition to symptomatic management and routine follow-up, psychological counseling and family support play a crucial role in helping individuals and their loved ones come to terms with the disorder.[11]

CONCLUSIONS

Our report underscores the importance of recognizing vascular risks in *PLOD1*-kEDS patients and advocating for a cardiovascular management approach similar to that used for vEDS patients. The specific type and location of the vascular complication will determine the most appropriate treatment strategies. Engaging a multidisciplinary team that can explore various treatment options and mitigate the risk of iatrogenic vascular injury is imperative to improve the care of this rare group of patients. Patients should be followed up closely with vascular imaging such as magnetic resonance imaging or CT. Finally, a critical need exists for systematic documentation of vascular complications and their management in patients with kEDS to advance our understanding and improve patient outcomes.

DISCLOSURES

None.

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