Type IV Ehlers-Danlos Syndrome Presenting as Subclavian Thrombosis

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ABSTRACT: Ehlers-Danlos syndrome (EDS) is described as a disorder of connective tissue synthesis and has multiple types that are based on the degrees of clinical severity. The defects in synthesis lead to inherent fragility of different body tissues, including blood vessels and ligaments. The subtypes of this disorder include EDS I to III, which are associated with skin involvement and hypermobility. Type IV, which is described in this case, is associated with vascular issues and is one of the more severe forms of EDS. Type VI is very rare and associated with kyphoscoliosis. Type VII, which is exceedingly rare, has multiple subtypes and is associated with arthrochalasia and dermatospraxis. In this unique case report we describe a young male patient with an initial presentation of subclavian thrombosis who was later diagnosed with type IV EDS.

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A 23-year-old white male with a prior history of left carotid artery dissection presented to the emergency department complaining of a 3-day history of gradual numbness in his left arm. He also described his left arm as being cold and without sensation. A week prior, he had presented with complaints of intermittent left arm pain and was given a presumptive diagnosis of neurogenic thoracic outlet syndrome. He continued to have worsening left arm pain over the next few days. On the day of presentation, the patient stated that he woke up with a feeling of numbness that went from his elbow to his fingers. The loss of sensation was described as intermittent and the patient stated that there was no antecedent history of any physical trauma to his left arm or shoulder. Upon further questioning, it was discovered that the patient had multiple family members that had been diagnosed with aneurysms of both the thoracic and aortic aorta and that two family members had had carotid artery dissections. Vital signs upon admission included a temperature of 36.7°C, a blood pressure of 158/91 mmHg in the right arm, and a pulse rate of 100 bpm. Pertinent findings on physical exam were absence of a radial and ulnar pulse in the left arm and that the left extremity was cool to touch. The patient also had complaints of numbness and tingling as well as mild muscle weakness. Routine laboratory investigation was within normal limits and computed tomography (CT) of the brain revealed no acute intracranial findings. Computed tomography of the upper extremities revealed evidence of occlusion of the left subclavian artery. Due to the patient’s presentation,
we felt that he was presenting with a threatened limb and the patient was emergently taken to the peripheral catheterization laboratory for angiography.

Aortogram revealed a type 1 arch with a patent right innominate artery and left vertebral and carotid artery. Selective angiography of the left subclavian artery revealed a high-grade stenosis of 90% to 95% at the proximal right subclavian artery at the take-off of the thyrocervical trunk (Figure 1A). The flow distal from the stenosis was extremely sluggish, and further angiography revealed severe stenosis with heavy thrombus burden in the proximal axillary and brachial arteries. Due to the significant thrombus burden, the decision was made to utilize a .035” 6 Fr Angiojet (Boston Scientific) in an attempt to perform thrombectomy by making multiple passes through the artery. The lesion was carefully crossed with a stiff angled glidewire and this wire was then subsequently exchanged for a Wholey wire. Repeat angiography after thrombectomy revealed significantly improved flow within the subclavian and axillary arteries but continued heavy burden in the brachial.

Figure 1. Selective angiography of the left subclavian artery revealed a high-grade stenosis of 90% to 95% at the proximal right subclavian artery at the take-off of the thyrocervical trunk (A). Final subclavian angiography showed a widely patent subclavian with continued mild to moderate thrombus burden of the brachial artery (B).
At this point, it was determined that the next course of action would be to perform balloon angioplasty of the brachial artery and 2 inflations were done with a 5 mm x 80 mm balloon. Final subclavian angiography showed a widely patent subclavian with continued mild to moderate thrombus burden of the brachial artery (Figure 1B). Because of this the patient was transferred back to the cardiac care unit with a tPA infusion through a catheter placed in the left brachial artery. At this time, his left arm pain had resolved and there were pulses identifiable by Doppler in the left radial and ulnar arteries. The next day, angiography confirmed a widely patent artery, so the infusion catheter and sheaths were removed. It was initially thought that the patient had presented with an acute vasculitis, but laboratory studies showed that his ESR and CRP were within normal limits. Once the patient was stabilized, he was transferred to a tertiary center where he underwent genetic testing and was diagnosed with type IV Ehlers-Danlos syndrome.

**DISCUSSION**

Ehlers-Danlos syndrome (EDS), comprised of 6 different inherited disorders, is tied together by genetic defects in connective tissue and collagen synthesis and structure. The types of EDS include classical, hypermobility, vascular, kyphoscoliosis, arthrochalasia, and dermatosparaxis types. Ehlers and Danlos first described this disease in the early 1900s with skin hyperelasticity and joint hypermobility. Sack in 1936 and Barabas later in 1967 are credited with correlating EDS with vascular complications. This subtype of EDS, specifically termed vascular EDS or type IV, separates itself from other subtypes because the complications of arterial, intestinal, or uterine rupture have led to premature death. Clinical diagnosis includes identifying 2 of 4 criteria: arterial, intestinal, or uterine rupture; thin or translucent skin; easy bruising; and characteristic facial appearance; however, laboratory tests for confirmation are highly recommended. EDS type IV is typically inherited through an autosomal dominant pattern. The mutation that is usually tested for is COL3A1 gene which leads to type III collagen deficiency.

EDS type IV is very rare, accounting for less than 4% of all EDS cases. Of patients who have this subtype, 80% will have a vascular event before the age of 40. Vascular complications include ectasia, aneurysm, dissection, and occlusion or stenosis in many large- to medium-sized arteries. Case reports have shown pathology in the middle cerebral, vertebral carotid, innominate, ascending/descending/thoracic, and abdominal aorta, superior mesenteric, celiac, hypogastric, hepatic, splenic, inferior mesenteric, inferior epigastic, common/external/internal iliac, femoral, and popliteal arteries. Patients have also been found to have subclavian rupture and pseudoaneurysms. To our knowledge this is the first patient with EDS type IV to present with subclavian thrombosis leading to severe limb ischemia with loss of pulses. Thrombectomy, balloon angioplasty, and eventually tPA infusion was utilized to decrease thrombus burden which extended from the subclavian to the brachial arteries. In our case, the patient tolerated his procedures adequately and by post-op day 2, pulses returned.

According to previous case studies, this is not always
the case and direct repair of ruptures, aneurysms, and stenosis can lead to serious complications. Oderich et al found that of patients who underwent repair of a vascular complication, 46% experienced major morbidity, including excessive bleeding in 37%, re-exploration in 20%, and mortality in 35%. In those who had graft placement, graft complications occurred in 40%. Both the study by Oderich et al and the landmark study by Pepin et al state that survival is shortened in this population mostly due to the risk of vascular rupture, however the risk of intestinal rupture can also lead to morbidity and mortality. They also warn of the complications of intervention or surgery because of the friable nature of the tissue.

When encountering a young patient with vascular rupture, it is important to keep high suspicion for EDS type IV. Additionally, family members should be screened promptly and family history must be completed. Once diagnosed with EDS type IV, these patients do not follow standard operative protocol, and conservative therapy should be utilized unless there is substantial bleeding or rapid progression of aneurysm.

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REFERENCES