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Vascular Ehlers-Danlos Syndrome: A Rare Disorder Presenting with Focal Convulsions

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ABSTRACT

Vascular Ehlers-Danlos Syndrome (VEDS), previously called Ehlers-Danlos syndrome type-IV, is a heterogeneous group of heritable connective tissue disorders characterized by thin, translucent skin, easy bruising, arterial, intestinal, and/or uterine fragility. There is large vessel involvement that leads to arterial rupture often preceded by aneurysm, arteriovenous fistulae, or dissection. Noninvasive imaging studies such as CT angiography and MR angiography are preferred as diagnostic studies for this condition. We are reporting a 4 years old girl who was presented with right sided unilateral convulsions and hypertension. CT angiogram showed stenosis with post-stenotic dilatation of coeliac and superior mesenteric arteries. There were extensive calcified plaques with atherosclerotic changes in the segment of right common iliac artery with aneurysmal dilatation of celiac, superior mesenteric and common iliac artery. Radiological findings were consistent with vascular Ehlers-Danlos syndrome. She was successfully managed with anti-hypertensive and anti-convulsants.

Key Words: *Vascular Ehlers-Danlos syndrome. Focal convulsions. Computerized tomography. Angiogram.*

INTRODUCTION

Vascular Ehlers-Danlos Syndrome (VEDS) is a heterogeneous group of heritable connective tissue disorders, characterized by thin, translucent skin, easy bruising, and arterial, intestinal, and/or uterine fragility. Due to the perceived rarity and nature of the disorder,¹ in majority of the cases, the disease has been asymptomatic for a prolonged period and incidentally detected in individuals who have undergone investigations for unexplained vascular symptoms. The disease remains unrecognized in children with negative family history.

The clinical presentation depends on the location of the arterial event. Vascular complications include rupture, aneurysm, and/or dissection of major or minor arteries.² The sites of arterial rupture are the thorax and abdomen (50%), head and neck (25%), and extremities (25%).³ In significant number of cases, VEDS is identified only after severe vascular complications or death. Affected individuals can have classical radiological findings with involvement of large vessels or organ rupture. Molecular genetic testing of COL3A1, the only gene in which mutations are known to cause VEDS, is available on a clinical basis.⁴

Currently, no consensus exists regarding the appropriate extent of evaluation and management. This report describes a young girl toddler with the condition, which was successfully managed with anti-convulsants and anti-hypertensive agents.

CASE REPORT

A 4 years girl toddler presented with 6 months history of fever, generalized body rash and right sided weakness. She also had recurrent abdominal pain and two episodes of right sided focal convulsions during this period. Examination revealed a lean child with generalized wasting and erythematous rash all over the body. Her blood pressures were more than 95th percentile for age and height. Neurological examination revealed generalized weakness more on the right side with diminished tone and power and brisk reflexes. Child was admitted for workup.

Investigation showed normal blood indices except platelets which were $575 \times 10^9/L$. ESR was 58 mm after first hour. Coagulation profile and renal biochemistry was normal. Urinalysis revealed hematuria with proteinuria. Rheumatoid factor was positive but ANA, Anti-DNA and ANCA were negative. CT angiogram showed stenosis with post-stenotic dilatation of coeliac and superior mesenteric arteries (Figure 1A). There were extensive calcified plaques with atherosclerotic changes in the segment of right common iliac artery (Figure 1B). Volume rendered 3-D reconstruction shows aneurysmal dilatation of celiac, superior mesenteric and common iliac arteries (Figure 2). These findings were consistent with the vascular Ehlers-Danlos syndrome.

She was given Amlodipine 2.5 mg twice daily and Enalapril 5 mg once a day for hypertension and also

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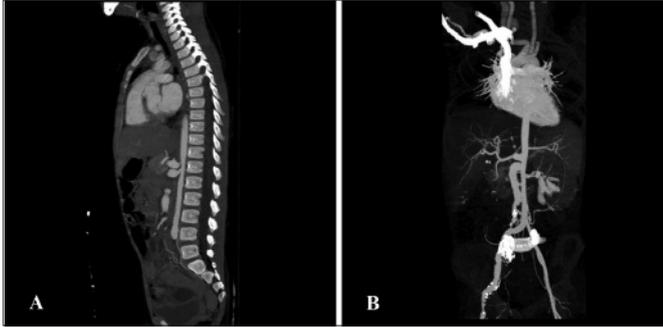


Figure 1(A,B): CT angiogram shows (A) Origin of celiac and superior mesenteric artery is narrow with post-stenotic dilatation (B) Ectatic right common iliac artery with calcification.



Figure 2: CT angiogram with volume rendered 3-D reconstruction shows aneurysmal dilatation of celiac, superior mesenteric and common iliac artery.

started on Sodium Valproate and Levetiracetam for convulsions. She was discharged in a stable condition and later followed in the outpatient after 2 weeks. During that visit she was stable with no active complaints and her blood pressure was also within the normal range. In the future, we are planning to do vascular repair in consultation with vascular surgery.

DISCUSSION

The term vascular Ehlers-Danlos syndrome came into widespread use following the shift from a numerical classification of EDS type-IV to a descriptive one.⁵ Vascular Ehlers-Danlos syndrome (VEDS) is a rare autosomal recessive inherited connective tissue disorders, characterized by thin, translucent skin, easy bruising, and arterial, intestinal, and/or uterine fragility. Vascular phenomena include dissection or rupture, gastrointestinal perforation and organ rupture are the presenting signs in the majority of patients identified to have VEDS. Arterial rupture may be preceded by aneurysm, arteriovenous fistulae, or dissection but also may occur spontaneously.

A minimum estimate of the prevalence is about 1:200,000.⁵ Because many families with VEDS are identified only after a severe complication or death, it is

likely that individuals/families with a mild phenotype do not come to medical attention and, therefore, go undetected. In addition, because of the perceived rarity of the disorder, it is rarely considered and non-vascular complications rarely raise diagnostic suspicion of VEDS.⁶

The manifestation of vascular Ehlers-Danlos syndrome frequently involves multiple vascular segments, with aneurysms and dissections being the most common imaging findings.⁶ Although many individuals diagnosed with VEDS have an affected parent, the family history may appear to be negative because of failure to recognize the disorder in family members or later onset of the disease in the affected parent.⁷ The disease can present at the neonatal age and approximately 12% of neonates with VEDS have clubfoot, and 3% have congenital dislocation of the hips. In childhood, inguinal hernia, pneumothorax, and recurrent joint dislocation or sub-luxation is described. Affected individuals often have a prolonged history of easy bruising.

Vascular complications include rupture, aneurysm, and/or dissection of major or minor arteries. The thorax and abdomen are the commonest sites of arterial rupture (50%), followed by head and neck (25%), and extremities (25%). Rupture of the gastrointestinal (GI) tract occurs in about 25% of affected individuals. The majority of GI perforations occur in the sigmoid colon. Ruptures of the small bowel and stomach have also been reported, though infrequently.⁸ Conventional arterial angiography (with contrast injection) should be discouraged as this may result in arterial tear/dissection at the site of entry of the catheter and injection pressure may lead to arterial aneurysms.⁴ Noninvasive imaging studies such as CT angiography and MR angiography are preferred as diagnostic studies for this population. Patients with vascular Ehlers-Danlos syndrome are frequently unaware of the diagnosis at the time of the first vascular complication. Therefore, radiologists must be familiar with the spectrum of vascular lesions in vascular Ehlers-Danlos syndrome and consider this diagnosis in the appropriate clinical setting.⁶

A recently published clinical trial of the efficacy of a cardio selective β -blocker with β -2 agonist vasodilatory properties (celiprolol) in reducing risk of arterial rupture or dissection concluded that there was a benefit resulting in reduced number of arterial events in the treatment group.⁹ Surgical intervention for bowel rupture is necessary and usually lifesaving. Surgical re-anastomosis can generally be accomplished.¹⁰ Complications during and following surgery are related to tissue and vessel friability, which result in recurrent arterial or bowel tears, fistulae, poor wound healing, and suture dehiscence. Individuals who survive a first complication may experience recurrent rupture. Operative mortality in patients with vascular complications of EDS was not

excessively high, but the incidence of postoperative bleeding complications and late graft-related problems was significant.⁶

Although EDS is a very rare disorder especially in a very young age group, any child with unexplained hypertension or any clinical evidence of vascular involvement should be screened for rare disorders like vasculitis or large vessels disease. Noninvasive imaging such as CT angiography, MRA, and ultrasonography should be considered for routine surveillance.

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