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Case Report

# Atypical Presentation of Forearm Compartment Syndrome in a Case of Vascular Type Ehlers-Danlos Syndrome

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**Abstract**

We describe a 30-year-old Chinese gentleman with vascular type Ehlers-Danlos Syndrome ("vEDS") presents with spontaneous right forearm compartment syndrome due to pseudoaneurysms along the radial artery. There was no history of injury. Urgent CT Angiogram showed multiple pseudoaneurysms along radial and ulnar arteries. Emergency fasciotomy and reconstruction of radial artery with saphenous vein graft was performed. After subsequent skin grafting, his right forearm wound healed well eventually and his right upper limb function was preserved.

Pathological examination of the diseased radial artery showed variable smooth muscle thickness, partial loss of muscle wall, aneurysmal dilatation, fibrinoid necrosis and inflammation. Genetic test showed a heterozygous missense variant c. 1852G>C in COL3A1 gene, which has not been reported and is likely pathogenic of vascular type of Ehlers-Danlos Syndrome.

There was no complication or rupture of reconstructed radial artery up to 4 four years' follow-up. We believe that autologous saphenous vein grafting is a safe, durable option to reconstruct a long segment of arterial defect in this group of patients.

**Keywords:** compartment syndrome; ehlers-danlos syndrome; Hong Kong; Chinese; pseudoaneurysm; saphenous vein graft

## Introduction

Compartment syndrome of limbs is an orthopaedic emergency, which is usually caused by trauma. Spontaneous presentation of compartment syndrome without any injury or pre-existing coagulopathy is extremely rare. Proper management of compartment syndrome includes timely diagnosis and urgent fasciotomy to decompress the muscle compartments to prevent muscle necrosis and the need for amputation [1].

We would like to present a case of spontaneous forearm pseudoaneurysm presented as compartment syndrome in a young Chinese gentleman with vascular type Ehlers-Danlos Syndrome ("vEDS"), which is a rare connective tissue disorder characterised by rupturing of fragile vessels and internal organs. There are published case reports of spontaneous compartment syndromes over different parts of body in patients with vEDS. But to our knowledge, such presentation of vEDS has not been reported in Chinese Population.

## Case Report

A 30-year-old gentleman labelled as Ehlers-Danlos Syndrome ("EDS") due to positive family history, with past history of epilepsy, admitted to our unit in year 2017 with bilateral forearm redness and swelling for 2 days, with right side being more severe. There was no recent history of epileptic convulsion, insect bite or trauma. The patient did not complain of any paraesthesia of both upper limbs.

On admission, he had normal blood pressure and was afebrile. His bilateral forearms were mildly erythematous with bruising, mildly tender and with increase in temperature. His bilateral wrists movement was normal. White blood cell count was 17.2 x $10^9$/L and C-reactive Protein (CRP) was 190.1 mg/L. He was therefore treated as cellulitis initially with antibiotics.

During patient's stay, progressive right forearm swelling was noted. Repeated physical examination found tense forearm compartments, and there was also limited right wrist and fingers movement; the radial pulse was weakened. Left forearm compartments were not tense. There was no numbness over bilateral upper limbs. (**Figure 1**)

**Figure 1: Clinical Photo of patient on admission. There was marked swelling, bruising over bilateral forearms. (Yellow arrows)**

Compartment pressure was measured and found to be up to 62mmHg. An urgent CT angiogram of the right forearm showed multiple pseudoaneurysms along radial and ulnar arteries. (**Figure 2**)

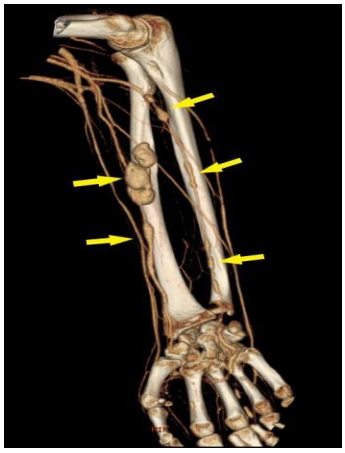

**Figure 2: CT Angiogram showed multiple pseudoaneurysms along radial and ulnar arteries (Yellow arrows)**

Urgent forearm fasciotomy was performed. Intraoperatively, a 15cm segment of the radial artery was found to be thinned-wall and friable, with multiple sites of rupture. (**Figure 3**) The pathological segment was excised and reconstructed with a saphenous vein graft. (**Figure 4 & 5**) Circulation of the right upper limb was restored. The fasciotomy wounds were covered with full thickness skin graft 6 days after the index operation. (**Figure 6**)

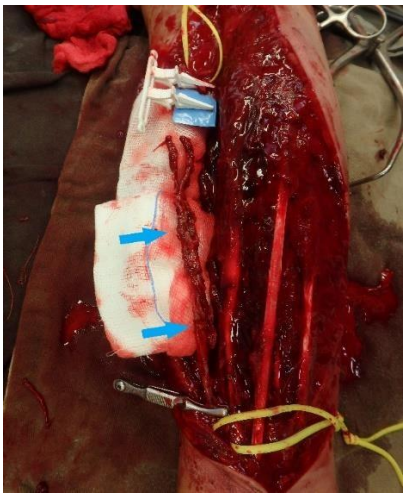

**Figure 3: 15cm segment of the radial artery was found to be thinned-wall and friable, with multiple sites of rupture (Blue arrows)**

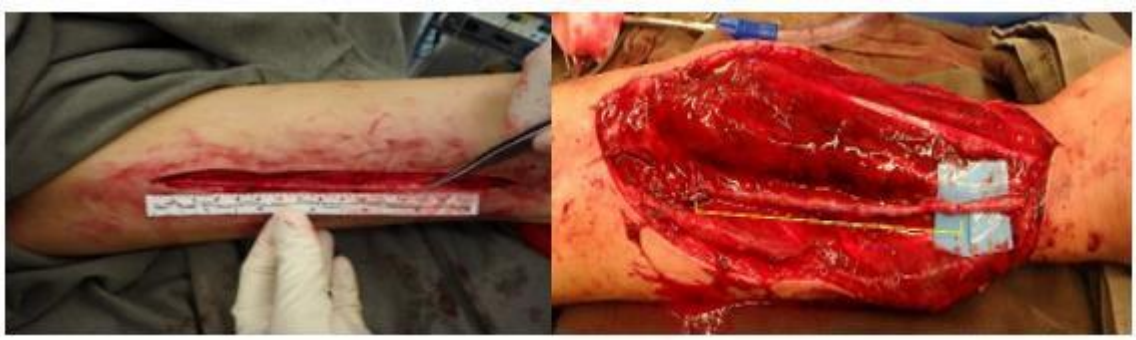

**Figure (4 & 5): Saphenous vein graft was harvest from left medial thigh and was used to reconstruct the vascular defect (Yellow segment).**

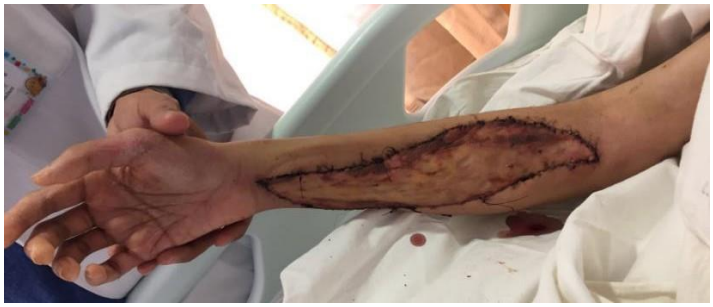

**Figure 6: Clinical Photo of patient's right forearm after skin grafting.**

Microscopic examination by pathologist found that the radial artery was with variable smooth muscle thickness, partial loss of muscle wall, aneurysmal dilatation, fibrinoid necrosis and pseudoaneurysm surrounded by moderately dense mixed inflammatory infiltrate and fibroblastic reaction. There was absence of internal elastic lamina and loss of muscle wall at the aneurysmal sites. There was also variable decrease in elastic fibers and smooth muscle cells in the tunica media. Similarly, the adjacent small to medium sized veins had focal deficient or fragmented elastic fibers noted in the tunica media.

Genomic investigation has been carried out and it confirmed that the patient has a heterozygous variant in the COL3A1 gene which is a missense variant c. 1852G>C in exon 26.

It has been 4 years after the operation. Upon follow-up, the wound healed well and patient has good right-hand function and he can write nicely with his right hand. To our knowledge, there was no complications or rupture of the reconstructed radial artery. (**Figure 7**)

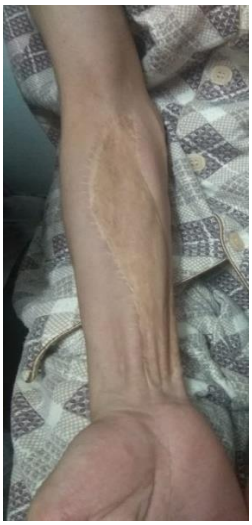

**Figure 7: Four years after operation – The skin graft incorporated and the wound healed well.**

The patient has consented to the publication of this manuscript.

## Discussion

Ehlers-Danlos syndrome ("EDS") is a group of hereditary connective tissue disorders, caused by various defects in the synthesis of collagen. Its overall prevalence lies between 1 in 10,000 to 25,000 in general population [2]. EDS has different subtypes. Type IV or the vascular type Ehlers-Danlos Syndrome ("vEDS"), described by Andras Barbaras in 1967 [3], consists of 5 to 10% of EDS [2]. It is due to pathogenic variants in COL3A1 gene and it is inherited in an autosomal dominant manner [2]. Due to defects in type III collagen, body tissues and organs of patients with vEDS are fragile. Signsof vEDS include: Characteristic facial appearance (thin vermilion of lips, small chin, thin nose, large eyes), acrogeria (skin on the hands and feet

appears prematurely aged) and thin translucent skin [4]. In majority of patient, the diagnosis was only made when there is at least one major complication happened, which is defined as arterial rupture, dissection or organ rupture, like sigmoid colon perforation and perforated gravid uterus The risk of having complication at age of 20 is 25% and rises to more than 80% by age of 40. The average age at the time of the first major complication was 23.5 years old. Median life expectancy of patient with vEDS is 48 years [5].

Prior to this case report, compartment syndrome as a complication of vEDS has also been reported in literatures from different countries. The first case was reported in 1992 with spontaneous bleeding from a gluteal artery resulting in a gluteal compartment syndrome and sciatic neuropathy [6]. There were also cases of abdominal compartment syndrome, compartment syndromes over legs, upper arm and forearm, due to rupture of peroneal artery, posterior tibial artery and ulnar artery. Cases of compartment syndrome in vEDS patients reported in literature are listed in (**Table 1**)

| Author | Year of Publication | Sex | Age | Site/ Artery of involvement | Treatment | Outcome |
|---|---|---|---|---|---|---|
| Schmalzried [6] | 1992 | M | 35 | Left inferior gluteal artery | Embolisation + decompression | Mild lower limb weakness and hyperesthesia. Limited hip flexion |
| Oderich[i] | 2005 | M | 47 | Bilateral renal artery dissection with visceral ischaemia; abdominal compartment syndrome | Abdominal decompression | Alive at age 52 when the paper was published |
| Mandeville[ii] | 2008 | F | 28 | Right peroneal artery | Embolisation | Full recovery |
| Matsushima[iii] | 2009 | F | 27 | Right posterior tibial artery | Embolisation with coils + fasciotomy | No functional loss |
| Barboi [iv] | 2009 | F | 25 | Right calf* | Evacuation | Transient plantar numbness Died at age 39 due to aortic dissection |
| Ikeda [v] | 2012 | M | 33 | artery in left lower leg* & bilateral ulnar artery | Fasciotomy + ligation | No functional loss |
| Domenick[vi] | 2011 | F | 33 | A branch of left brachial artery | Ligation and compartment release | (Not mentioned) |
| Arici [vii] | 2012 | F | 28 | Right posterior tibial artery | Haematoma drainage + Ligation (failed reconstruction) | Peroneal palsy progressively recovered |
| Howard [viii] | 2020 | F | 40 | Left ulnar artery | Fasciotomy + ligation of artery + oversewing of aneurysm | No functional loss |
| Choinski [ix] | 2021 | M | 32 | Left common iliac and external iliac artery aneurysm, left distal anterior tibial occlusion, left tibioperoneal trunk dissection with pseudoaneurysm | Fasciotomy + endovascular stenting to tibioperoneal trunk pseudoaneurysm | No pain. Mild foot drop |
| OUR CASE | 2022 | M | 30 | Right radial artery | Fasciotomy + reconstruction with saphenous vein graft | No functional loss |

* Cases reported as past medical history, not the index condition presented

**Table 1: Reported cases of compartment syndrome in patients with Ehlers-Danlos Syndrome.**

The challenge in these cases of compartment syndrome in vEDS patient is that surgeons also need to tackle the pseudoaneurysms and maintaining adequate blood flow to the limbs apart from performing facsiotomy. Moreover, care has to be taken to avoid profuse bleeding from the fragile or ruptured major vessels. Surgical options of treating pseudoaneurysm were described in those case reports, such as endovascular coil embolization [6,8,9], oversewing of the ends of ruptured pseudoaneurysm with pledgeted suture [14], stenting [15], or ligation of the artery [11-14] if another patent artery suppling the involved limb is present. Yet, endovascular intervention is not free of risk. Rupture and pseudoaneurysm formation at access site [16] and arterial complication secondary to placement of the embolization coils [17] have been reported. Gentle, meticulous technique and careful soft tissue handling are utmost important to minimize intra-operative complications.

In case of a long segment of artery is involved, we recommend reconstruction with vein autograft, like what we have done in our case, as synthetic conduit might not be a feasible alternative option as those of small caliber (d <6mm) is rare in market [18]. However, since the defect in collagen synthesis in vEDS would also cause abnormalities in veins, as evidenced by the histological finding of the veins specimens in our case, the long-term result is uncertain due to limited cases reported in literature. While there was no complication seen after 4 years since the operation in our case, there was another case of saphenous vein graft disruption leading to haematoma formation and reoperation reported by Shalhub [19].

We aware that the major limitation of our case report is that a single case lacks generalizability to confirm the safety and durability of auto-vein-grafting in patients with vEDS. We would therefore recommend further study on the use of autologous vein graft with longer duration of follow-up. Last but not least, the missense variant c. 1852G>C in the COL3A1 gene detected in this patient changed the 618$^{th}$ codon from Glycine to Arginine. It is classified as likely pathogenic by American College of Medical Genetics (ACMG) guideline. This variant has not been reported in literatures or Human Gene Mutation Database. A different missense change c. 1853G>T in the same codon has been reported as disease causing for vEDS phenotypes in previous study [20,21].

## Conclusion

Although rare, acute limb compartment syndrome could happen spontaneously in patient with vEDS. High index of suspicion of compartment syndrome, timely urgent fasciotomy and vascular intervention with meticulous technique and gentle soft tissue handling during operation are the keys to prevent complications. We believe that autologous saphenous vein grafting is a safe, durable option to reconstruct a long segment of arterial defect in this group of patients. However, in view of underlying fragility of patient's own veins, further study is recommended to confirm the long-term outcome of using autologous vein graft in treating patients with vEDS.

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