CASE REPORT

On-pump coronary artery bypass surgery in vascular Ehlers-Danlos syndrome

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SUMMARY

A 58-year-old woman with vascular Ehlers-Danlos syndrome (EDS; type IV) presented to a Canadian tertiary care emergency department with a non-ST elevation myocardial infarction. The patient failed medical therapy and after careful consideration of the options, elected to undergo urgent coronary artery bypass (CABG) surgery. To the best of our knowledge, this is the first reported case of a successful on-pump CABG surgery in a patient with vascular EDS.

BACKGROUND

Ehlers-Danlos syndrome (EDS) represents a group of heritable multisystem disorders resulting from defects in collagen synthesis. The incidence of vascular EDS is estimated in the order of 1 in 250 000 individuals.¹ The four major clinical criteria for diagnosis include the following: easy bruising, transparent skin, characteristic facial features and rupture of arteries, intestine or uterus.²⁻³ These clinical features distinguish vascular EDS from other forms of EDS. Patients with vascular EDS have a mean survival of 50 years.² Nearly 80% of these patients experience a significant vascular or intestinal complication by the age of 40.² Ruptured thoracic and abdominal arteries are the leading cause of death among these patients, who are also at risk of colonic perforations and complications during pregnancy.³

Vascular EDS is considered the most severe subtype and is attributed to mutations in the *COL3A1* gene coding for type III procollagen. Affected individuals have impaired production, retention, secretion and mobility of type III procollagen. While 50% of vascular EDS cases can be attributed to an autosomal dominant pattern of inheritance, the other 50% of affected individuals experience de novo mutations.

Unlike Marfan syndrome, patients with vascular EDS have severe fragility of their arterial tissue. Traditionally, vascular surgery has been avoided in these patients due to very poor results. Despite a lack of evidence, coronary artery bypass (CABG) surgery is generally considered to be contraindicated in vascular EDS. To our knowledge, there have been few reports of successful percutaneous coronary intervention (PCI) and no reported cases of on-pump CABG surgery in patients with vascular EDS.

CASE PRESENTATION

A 58-year-old woman with vascular EDS presented to the emergency department with a non-ST

elevation myocardial infarction (NSTEMI). A suspicion of familial vascular EDS had been raised after her father and her uncle both died in different institutions during CABG surgery. Her father sustained severe tearing of his aorta during cannulation, which could not be successfully repaired, and because of her significant familial history, the patient was referred to our connective tissue disorder clinic. During investigations, she was found to have abnormal fibroblast production of procollagen type III and sequence analysis of her genomic DNA confirmed a *COL3A1* substitution missense mutation (c.1501G>A) at exon 22 on chromosome 2.

The patient had sustained a NSTEMI 10 years previously, at which time she underwent cardiac catheterisation, which showed critical three-vessel disease. She was managed medically in view of the high risk of revascularisation. Since then she had stable Canadian Cardiovascular Society (CCS) class III angina; however, in the months prior to her urgent admission she had deteriorated to CCS class IV, and had frequent nocturnal chest pain. Her other comorbidities included type II diabetes mellitus, hypertension, chronic obstructive pulmonary disease (COPD) due to cigarette smoking, gastro-oesophageal reflux disease, hiatus hernia, arthritis, depression and hypothyroidism. Her medications included: ramipril, esomeprazole, amitriptyline, metoprolol, amlodipone, acetylsalicylic acid, levothyroxine, atorvastatin, paroxetine and a nitroglycerine transdermal patch. She had three pregnancies, one of which was complicated by postpartum haemorrhage. As a child she required a laparotomy for perforated appendicitis; she had no history of vascular aneurysms.

INVESTIGATIONS

The patient's initial ECG showed dynamic changes in the lateral leads associated with elevation of her serum troponin levels. CT of her chest was within normal limits.

After initial resuscitation, she failed to respond to medical therapy for an acute coronary syndrome, and after full discussion of the risks, the patient elected to undergo cardiac catheterisation. Access was gained via the right femoral artery using a 4.0 French sheath. Coronary angiography revealed significant three-vessel disease (figures 1 and 2). Haemostasis was achieved uneventfully with manual compression. There were no femoral vascular complications. After consultation with colleagues at other centres with experience in vascular EDS, the patient was informed of the potential risks and benefits of the available treatment

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Figure 1 Left coronary angiogram in left anterior oblique view. Left coronary angiography revealed severe disease in the circumflex, ramus and the left anterior descending arteries.

modalities; she declined PCI and elected to undergo cardiac surgery.

TREATMENT

Our patient presented with an evolving lateral lead infarct based on her ECG. Nevertheless, her cardiac catheterisation confirmed disease in all three major territories. As such, our preoperative plan was to completely revascularise her with total arterial

Figure 2 Right coronary angiogram in left anterior oblique view. Right coronary angiography revealed severe proximal disease in the dominant right coronary artery, posterior descending branch and the second posterior left ventricular branches.

grafting by off-pump CABG to avoid aortic instrumentation. After isolating her left internal mammary artery (LIMA) and exposing the left anterior descending coronary artery (LAD), it became apparent that the friability of the grafts and her target vessels would require cardiopulmonary arrest for successful anastomoses. The aorta and right atrium were cannulated and the patient was cooled to 31°C. Arrest was achieved with antegrade cardioplegia. Ultimately, the LIMA was grafted to the LAD. The free-right internal mammary artery (RIMA) was end-to-side grafted to the LIMA and to the ramus, and the obtuse marginal 2. There was insufficient length of the RIMA to graft the posterior left ventricular (PLV) branch. As such, we elected to leave the right coronary artery (RCA) territory incompletely revascularised. The rationale for doing so was based on information gathered during the operation. Given that the RCA was not the presenting culprit vessel, we elected to incompletely revascularise this territory when we realised we were unable to gain sufficient length of the RIMA to reach the PLV branch as opposed to risking aortic injury with an isolated vein graft. The aortic cannula was removed under therapeutic hypotension in an attempt to reduce tension on the aorta. A purse-string closure of the cannula site was reinforced with pericardial pledgets. The total cardiopulmonary bypass pump time was 108 min. There was difficulty weaning the patient from cardiopulmonary bypass and an intra-aortic balloon pump (IABP) was inserted via a transfemoral approach. In addition, her sternal closure had to be delayed due to haemodynamic instability. The total estimated blood loss was 0.8 L. The patient remained in the coronary intensive care unit for 36 h with an open sternum and IABP. The patient returned to the operating room on the second postoperative day for sternal closure and for removal of the IABP under direct vision.

OUTCOME AND FOLLOW-UP

After her sternal closure, the patient required ventilatory support in the coronary intensive care unit for 7 days. On postoperative day 12 she developed a sternal wound infection. This was treated with intravenous antibiotics and a vacuum-assisted closure dressing. Postextubation she developed delirium, likely due to selective serotonin reuptake inhibitors withdrawal, which improved after reintroduction of her medications. The patient was discharged on the 39th postoperative day. A follow-up enhanced CT of the chest was performed 4 years post-CABG and the coronary reconstructions revealed patent LIMA and free-RIMA grafts (figure 3). The patient is currently alive and doing well 6 years after her cardiac surgery.

DISCUSSION

Patients with vascular EDS pose a unique challenge. Usually the diagnosis is not made until the patient experiences a severe vascular or intestinal complication that requires emergency surgical intervention. Often these surgeries are further complicated by the extreme fragility of the vascular tissues. Fortunately, in our case, the patient was well known to the cardiology department at our institution and, as far as we are aware, this is the first reported case of successful on-pump CABG in a patient with vascular EDS.

For patients with any of the EDS subtypes, the rate of complications during percutaneous angiography is increased by as much as 65% when compared with patients without vascular EDS.⁴ These complications include: arterial rupture, arterial dissection, false aneurysm formation and arteriovenous fistula formation. In light of these reported outcomes, it is recommended

Figure 3 Thoracic CT angiogram (CTA) with coronary reconstruction. Thoracic CTA with coronary reconstruction 4 years post coronary artery bypass. The CTA revealed a patent left internal mammary artery (LIMA) to the left anterior descending artery (LAD) graft. In addition, there was a patent LIMA to free-right internal mammary artery (RIMA) anastomosis with RIMA to ramus and to OM2 sequential graft.

that non-invasive CT, duplex ultrasound or MRI angiography be utilised for routine vascular imaging.⁴

Surgery should remain a therapy of last resort for patients with vascular EDS. However, should a patient require operative management, special precautions such as the use of padded vascular clamps or the use of umbilical tapes or tourniquets have been advocated.⁴⁻⁵ Elsewhere, it is recommended that sutures be placed interrupted, reinforced and tensionless.⁶ Some centres even suggest cardiopulmonary circulatory arrest during central cardioaortic surgery.⁷ Initially, we planned to perform an off-pump procedure in order to avoid aortic instrumentation. However, we were required to perform a successful aortic cross clamp and cannulation. A standard Fogarty aortic cross clamp was applied with steady compression. Shearing forces on the clamp were carefully avoided. The aortic cannula was removed under therapeutic hypotension and a purse-string closure was reinforced with a single interrupted pledgeted stitch. We were also able to achieve successful graft anastomoses with traditional running sutures, without pledget or sealant reinforcement. Given the friable nature of the grafts and coronaries, our sutures were placed delicately and with less tension than a standard anastomosis.

For patients with vascular EDS, poor wound healing represents an additional concern. With prolonged exposure, sternal wounds are prone to infection, putting patients at risk of sub-optimal survival when compared with uncomplicated patients.⁸⁻⁹

The relationship between different *COL3A1* gene mutations and phenotypic outcomes in patients with vascular EDS is yet to be fully elucidated. However, Leistriz *et al*¹⁰ have recently suggested that haploinsufficiency as a result of null mutations may result in a milder phenotype than the more common missense or splicing mutations of *COL3A1*. Specifically, these patients

may have an extended life span, with their first complication delayed by up to 15 years and major complications limited to vascular events.¹⁰ Further studies are required to better identify patients with vascular EDS with favourable phenotypes who may be better served by early operative management.

Learning points

- ▶ Vascular Ehlers-Danlos syndrome (EDS) is a rare, particularly challenging disorder.
- ▶ Fragile vascular and other tissues make invasive vascular interventions technically challenging.
- ▶ In the setting of severe coronary artery disease failing medical therapy, cardiac surgery can be considered in selected patients with vascular EDS.
- ▶ Cardiac surgery for vascular EDS should ideally be performed in centres with experience in cardiovascular surgery for high-risk patients affected by connective tissue disorders.

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Contributors RPK wrote the case report. JW performed the coronary artery bypass and revised the manuscript. GH performed the coronary angiogram and revised the manuscript. MM revised the manuscript.

Competing interests None.

Patient consent Obtained.

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