Complex Multi-Stage Total Aortic and Subclavian Artery Replacement in a 9-year old boy with Loeys-Dietz-Syndrome

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Abstract: BACKGROUND Loeys-Dietz Syndrome is a rare connective tissue disorder that is associated with arterial pathologies such as aortic dissections, tortuosity and aneurysms. We present a child with Loeys-Dietz Syndrome type 2 that received total aortic and bilateral subclavian artery replacement. CASE REPORT A 9-year old boy with Loeys-Dietz Syndrome type 2 and acute type B aortic dissection received an urgent complete thoracic and thoraco-abdominal aortic repair within three days. First, the ascending aorta and aortic root were replaced in a Tirone David and Frozen Elephant Trunk procedure. Then, the descending and supramesenteric aorta was replaced by a Dacron interposition graft with direct implantation of the celiac trunk. During the 15 months follow-up, the patient required three more surgical interventions for rapid expanding aneurysms of both subclavian arteries and the infrarenal aorta. No major adverse event nor secondary interventions occurred. Ultrasonographic and magnetic resonance imaging follow-up is continued at 6-months intervals. CONCLUSION Children with Loeys-Dietz Syndrome may require extensive aortic repair for aortic dissection and show rapidly expanding aneurysms. Referral to a center with pediatric vascular expertise and long-term follow-up examinations are crucial.

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Case Report

Complex Multi-Stage Total Aortic and Subclavian Artery Replacement in a 9-year old boy with Loeys-Dietz-Syndrome

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Background: Loeys-Dietz Syndrome is a rare connective tissue disorder that is associated with arterial pathologies such as aortic dissections, tortuosity and aneurysms. We present a child with Loeys-Dietz Syndrome type 2 that received total aortic and bilateral subclavian artery replacement.

Case Report: A 9-year old boy with Loeys-Dietz Syndrome type 2 and acute type B aortic dissection received an urgent complete thoracic and thoraco-abdominal aortic repair within three days. First, the ascending aorta and aortic root were replaced in a Tirone David and Frozen Elephant Trunk procedure. Then, the descending and supramesenteric aorta was replaced by a Dacron interposition graft with direct implantation of the celiac trunk. During the 15 months follow-up, the patient required three more surgical interventions for rapid expanding aneurysms of both subclavian arteries and the infrarenal aorta. No major adverse event nor secondary interventions occurred. Ultrasonographic and magnetic resonance imaging follow-up is continued at 6-months intervals.

Conclusion: Children with Loeys-Dietz Syndrome may require extensive aortic repair for aortic dissection and show rapidly expanding aneurysms. Referral to a center with pediatric vascular expertise and long-term follow-up examinations are crucial.

INTRODUCTION

Non-traumatic aortic dissection or aneurysm rarely present in pediatric patients. Typical etiologies involve vasculitides such as Takayasu’s arteritis and connective tissue disorders such as tuberous sclerosis, Ehlers-Danlos syndrome or Marfan syndrome.1,2

In 2005, another rare autosomal-dominant connective tissue disorder caused by mutations of the transforming growth factor-β receptors (TGFBR) was introduced as Loeys-Dietz syndrome (LDS).3,4 Similar cardiovascular, craniofacial, cutaneous and skeletal features are described for affected patients including hypertelorism, bifid uvula or cleft palate and aortic/arterial aneurysms and tortuosity as the first described triad.3,5 Arterial involvement is characterized by a generalized high risk of aneurysm and dissections and compared to the more common Marfan syndrome by a more aggressive vascular course with higher rates of surgical re-intervention especially in the aortic arch.5,6

Pediatric vascular surgery is not comparable to adult surgery and requires special techniques.

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allowing the patient’s vessels to grow without later anastomotic stenosis. We present our experience on the staged replacement of the entire aorta and both subclavian arteries in a 9-year-old boy with LDS type 2.

**CASE REPORT**

A 9-year-old boy (130 cm, 25 kg) with LDS due to a heterozygote TGFBR-2 gene mutation (type 2) presented to the Children’s Hospital Zurich, Switzerland with sudden-onset, progressive thoracic back pain. Detailed medical history and comorbidities are summarized in Table 1. His disease-specific timeline is presented in Figure 1.

The immediately performed computed tomography angiography (CTA) detected an acute aortic dissection Stanford type B (TBAD) with extension to the renal arteries and involvement of the subclavian arteries and the celiac trunk (Fig. 2). The true lumen and all aortic branches were well perfused. After transferal to our intensive care unit (ICU), his blood pressure was optimized initially by intravenous and then step-by-step by oral antihypertensive medication. Abdominal organic function and leg perfusion remained normal and his back pain responded well to analgesics. The false lumen initially remained unchanged but CTA after twelve days showed rapid progression of the descending aorta of 1 cm. Maximum aortic diameter was 36 mm in the descending aorta compared to 21 mm in the aortic arch. Because of the relative dilatation of the ascending aorta (maximum diameter of 34 mm) and the difficulties related to a cross-clamping of a fragile and excessively large aorta, it was decided to resect the whole dilated aorta proximal to the dissection and set a landing zone for the subsequent treatment of the descending aorta.

Therefore, a two-staged total aortic repair was planned in cooperation with the local pediatric heart surgery team. The 1st step involved a Tirone David procedure (aortic root replacement with preservation of the aortic valve, using a
Table I. Medical history and comorbidities

| vascular                          | tissue and skin                                      |
|-----------------------------------|-----------------------------------------------------|
| • aortic sinus and annulus dilatation (33 and 22 mm) | • hematoma and epistaxis tendency                   |
| • severe elongation and tortuosity of the brachiocephalic trunk + extra- and intracranial carotid and vertebral arteries musculo-skeletal | • prior herniotomy 2011                              |
| • muscular hypotension o retarded walking at 2 years o bilateral upper leg orthosis o hypermobility (Brighton-score 9/9) | • polyvalvulopathy o mitral valve prolapse and medium-grade insufficiency o tricuspid valve prolapse + medium/high grade insufficiency o tricuspid aortic valve + low-grade central insufficiency |
| • prior non-union + subluxation of C2/3 with paresthesia + ataxia o posterior fusion of C2-C4 2012 o reposition and posterior fusion of C2/3 2012 o reposition and anterior fusion of C4/5 2013 o current external orthesis | • narrow upper respiratory tract (multiple prior vertebral surgery) o chronic pneumopathy due to prior dysphagia with silent aspirations and pulmonary hypertension (regressive after surgery) o prior adenotonsillectomy 01/2015 |
| • arthrogryposis o bilateral thumb subluxation o prior finger flexion contractures | • combined central-obstructive sleep apnea with overnight non-invasive CPAP ventilation (since 2011) |
| • pectus excavatum | other |
| • fracture-associated lumbar spondylolisthesis craniofacial | allergic rhinoconjunctivitis drugs |
| • central face hypoplasia with micrognathism | • sartan-therapy for aortic dilation since 05/2017 |
| • hypertelorismus, astigmatism + hyperopia, blue sclera | • beta-blocker |
| • turricephaly | • acetylsalicylic acid |
| • high-arched palate and uvula bifida | |
| • hypoplasia of the corpus callosum | |

Valsalva graft) and replacement of the ascending aorta and aortic arch using a Frozen Elephant Trunk (FET) procedure (E-vita OPEN PLUS, JOTEC GmbH, Hechingen, Germany) with re-implantation of the supra-aortic trunks. Median sternotomy was difficult due to the pectus excavatum. A single dose of crystalloid cardioplegia (Bretschnieder, volume 1232 ml), was given through the ascending aorta to protect the myocardium (care was done not to directly manipulate the fragile coronary ostium). The aortic valve was tricuspid and intact. The suture lines of the coronary arteries and supra-aortic trunks were reinforced using a thin bovine pericardial patch. Total procedure time was 552 min, bypass time was 389 min, selective antegrade cerebral perfusion was 82 min and circulatory arrest was 14 min.

Two days later, a thoracic-abdominal approach according to Crawford with replacement of the thoraco-abdominal aorta using a 20 mm Dacron interposition graft between the distal FET graft end and the supra-mesenteric aorta was performed. One
large intercostal artery was re-inserted into the aortic graft using a 6 mm Dacron graft. The celiac trunk was directly re-inserted into the aortic graft. A liquor drainage was used for neuroprotection. Total procedure time was 445 min.

Postoperative complications on ICU included pneumonia, acute kidney injury, intestinal ulcers and liquor infection, which could all be managed conservatively. No procedure-related adverse event occurred and the patient was transferred to our ward after 16 and discharged home after 25 postoperative days. Acetylsalicylic acid therapy was started. Follow-up was conducted by the Children’s Hospital Zurich using magnetic resonance imaging (MRI) and ultrasound.

After six months, the right subclavian artery showed rapid aneurysmatic progression (25 mm) and was replaced by a 6 mm Dacron subclavian-to-brachiocephalic/trunk interposition graft via a supraclavicular incision (Fig. 3). The boy was discharged home after four days.

Two months later, the left subclavian artery and the pararenal aorta rapidly progressed in size reaching respectively 25 and 38 mm (Fig. 4). A staged approach with primary aortic treatment was planned. First, a 16-8 mm Dacron bifurcation prothesio-biilac interposition graft with direct re-implantation of the superior mesenteric artery and both renal arteries was used for replacement of the abdominal aorta. The graft was implanted with an intentional length excess to allow patient’s growth. Intraoperative legs and (selective) organ perfusion were provided by extracorporeal membrane oxygenation in normothermia via the right femoral vessels using a 6 mm Dacron arterial conduit to avoid iatrogenic dissection. Again, spinal liquid drainage was used for neuroprotection. Operation time was 315 min, ICU and in-hospital stay were five and seven days, respectively.

Three months later, the left subclavian artery aneurysm, which had grown up to 28 mm, was treated with a 12-6 mm Dacron bifurcation graft for brachiocephalic trunk interposition and left subclavian-to-prothesial leg end-to-end anastomosis. The left vertebral artery was re-inserted into the graft. Duration of the procedure was 266 min and postoperative length of stay was six days. No adverse events occurred during both procedures.

The latest clinical, ultrasonographic and MRI follow-up 15 months after the first surgical procedure confirmed maintained postoperative success with good perfusion of abdominal organs and extremities. No further surgical interventions were required. In relation to his underlying disease, the boy was in a very good clinical condition and well-integrated into daily life. Only a mild ptosis had remained of the postoperative Horner-Syndrome resulting from the right subclavian artery repair and a small abdominal suture hernia was completely asymptomatic. Acetylsalicylic acid therapy was continued. Further MRI follow-up was planned in six months.

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DISCUSSION

Pathologies of the aorta and its branches are a typical characteristic of LDS. In one of the few larger studies on LDS patients requiring vascular surgery (n = 27), the age ranged from 0.5-39 years with 2 of 3 being children. In the majority of cases, the indication for primary procedures in most case reports were aortic root aneurysms instead of TBAD-related descending aorta aneurysm, as it was in our patient. However, TBAD is a common pathology and can occur on minimally dilated or non-dilated aortic dimensions. As demonstrated in our case and reported in the literature, rapid expansion of the aorta and its branches can occur after TBAD, which underlines the importance of frequent sonographic (abdominal pathologies) and/or MRI or CTA follow-up. Even after complete aortic replacement, rapid development of paraanastomotic aneurysms or at other sites may occur due to the systemic character of the disease. Typical post-dissection imaging should be performed at 1, 3, 6 and 12 months and yearly after.

Our patient required multiple vascular surgical interventions, which has been reported in up to 1/3 of LDS patients in the literature. Inoue et al. also reported on a 9-year-old boy with LDS-related TBAD. In contrast to our strategy, their treatment included prior thoracic-abdominal repair using a reversed FET technique before staged aortic arch and valve-saving root repair. This valve-sparing aortic root replacement - which was also chosen by us and other authors - has shown good results in children and is recommended to avoid any prosthesis-related issues, like the need for anticoagulation. Supra-aortic trunk reconstruction included both subclavian arteries in our patient. Sobh et al. also reported on a right subclavian artery aneurysm in a 11-year old girl, that was located proximal to the brachiocephalic trunk and was replaced using a PTFE graft and heart lung machine via a median sternotomy. Besides surgical therapy, our patient received a β-blocker to reduce hemodynamic stress on the vasculature and delay aneurysmal progression which is also recommended in the literature.

Our decision for surgical intervention was based on the rapid aneurysm expansion. This rapid expansion has been described by Iba et al. for adult LDS patients but appears to occur also in pediatric patients. Standardized guidelines for pediatric LDS patients based on larger studies do not exist due to the rare incidence of the disease. Thresholds for vascular reconstructions have been proposed, but they are based only on other author’s suggestions and focus on adult patients except for cerebrovascular arteries (personalized decision making) and the aortic root (depends on absolute diameter, rate of progression, grade of craniofacial disorders). Even though the aortic dissection started at the aortic isthmus and extended only distally, it was decided to resect the whole proximal aorta and aortic arch as well. The reason for this decision was less to remove the already dilated proximal aorta than to avoid the application of a clamp on a thin and fragile aortic wall. Even the softest clamp can lead to wall lesions that can result in troublesome bleeding. Furthermore, the suture line can also degenerate over a short time in dangerous pseudo-aneurysms. The whole proximal aortic resection could be seen as a preparation - creating a landing zone for a safe anastomosis - for the treatment of the dissected descending aorta.

In general, recommendations and surgical techniques for adult patients cannot be adopted completely to pediatric patients due to the smaller vessel’s caliber and length, the immaturity of the vasculature and the longitudinal growth over time. Intentional oversizing of vascular grafts is highly recommended in these patients and was also performed in the presented patient. For anastomoses, authors recommend the use of single sutures and the beveling technique. Alternatives to the reported Dacron graft are polytetrafluorethylene (PTFE), cadaveric vein and homologous or autologous vein grafts. The caliber of autologous vein grafts however is not always sufficient for aortic replacement and may develop aneurysms due to their immaturity and higher pressure in the arterial system. Open conventional surgery is usually preferred over endovascular therapy in LDS and other genetical disorders because the continuous dilation of fixation zones can lead to fixation site failure. In our patient, the descending aorta stent graft as part of the FET procedure served as distal anastomosis for the already planned thoraco-abdominal graft replacement, so native aortic wall fixation was not required. Stent grafting may also be an option as a bridging therapy in acute dissections or rupture or when the landing zones are within formerly implanted Dacron grafts. In that case, oversizing should be maximum 10% to avoid retrograde aortic dissection. Strong tortuosity can limit endovascular approaches in LDS patients.

CONCLUSIONS

Referral to a center with expertise in pediatric vascular surgery is highly recommended for young
LDS patients due to the extensive aortic and arterial involvement and necessity of complex, multi-stage and personalized vascular reconstructions. Frequent surveillance is mandatory due to the rapid progression of aneurysms.

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none

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