Intraoperative Aortic Dissection During Aortic Root Replacement in a Loeys–Dietz Syndrome Type III Patient: A Case Report

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Case Report

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Abstract

Background

Intraoperative aortic dissection during cardiac surgery is a rare but critical complication. At present, no strategies have been developed to prevent it. Here, we report a case of intraoperative aortic dissection during aortic root replacement in a patient with Loeys–Dietz syndrome type III.

Case presentation

A 60-year-old man was admitted to the hospital for Stanford type B acute aortic dissection and given conservative treatment. The patient was found to have aortic root dilatation and severe aortic regurgitation. Therefore, elective Bentall procedure was performed. Postoperative computed tomography revealed new Stanford type A aortic dissection that may have developed during surgery. The patient was given conservative treatment and was successfully discharged to home at postoperative day 34. A genetic test revealed an unreported \textit{SMAD3} frameshift mutation (c.742_749dup, p. Gln252ThrfsTer7), and the patient was diagnosed with Loeys–Dietz syndrome type III.

Conclusion

In patients with connective tissue disorder, aortic manipulations may become the cause of critical complications. Avoiding the use of invasive techniques, such as cannulation and cross-clamping, and implementing treatment strategies such as open distal anastomosis can prevent these complications and may be useful treatment modalities.

Background

Intraoperative aortic dissection (IAD) during cardiac surgery is a rare complication, with a reported incidence rate of 0.04–0.23\% (1–5). However, it is potentially fatal, and its reported operative mortality rate is as high as 35.5–48\% (4–6). Although previous studies suggested strategies to prevent it (6, 7), there are still no established measures to date. Here, we report a case of intraoperative Stanford type A aortic dissection during aortic root replacement in a patient with Loeys–Dietz syndrome (LDS) type III with an unreported pathogenic \textit{SMAD3} mutation.

Case Presentation

A 60-year-old man presented to the hospital with back pain and was subsequently diagnosed with Stanford type B acute aortic dissection. He was hospitalized and given conservative treatment; however, a contrast-enhanced computed tomography (CT) scan at that time revealed aortic root dilatation of 55 mm (Fig. 1). In addition, transthoracic echocardiogram revealed severe aortic regurgitation (AR), and the
patient was diagnosed with annuloaortic ectasia (Fig. 2). Mitral valve insufficiency was not detected. After discharge, elective surgery for the aortic root was scheduled. The patient’s other significant past medical history were hypertension, dyslipidemia, hyperuricemia, sleep apnea, and vasospastic angina, which developed 11 months before. He was 183-cm tall and weighed 83.0 kg and had no specific family history.

During surgery, cardiopulmonary bypass (CPB) was established via cannulation to the ascending aorta and the right atrium using a 24 Fr curved-tip dispersion aortic cannula and 34/46 Fr two-stage venous cannula, respectively. Furthermore, an antegrade cardioplegia (CP) cannula was cannulated to the proximal ascending aorta, and then cardiac arrest was induced with antegrade CP after cross-clamping of the ascending aorta. The initially planned treatment for the patient was the David procedure, but due to the difficulty in controlling AR, valve sparing was abandoned, and the Bentall procedure using a mechanical valve was selected. The antegrade CP cannulation site was resected and replaced with vascular prosthesis. Smooth weaning of CPB was achieved, and the procedure was completed without any problems.

The postoperative course was not complicated. The patient had never complained of chest pain after the operation. However, a routine contrast-enhanced CT scan at postoperative day (POD) 14 revealed new Stanford type A aortic dissection (Fig. 3). The entry was found at the distal ascending aorta. It was thought to be caused by an intraoperative procedure such as aortic cannulation for CPB or aortic cross-clamping because of its entry location. The postoperative dissection was conservatively treated because the aortic root had already been replaced, and neither any symptoms nor malperfusion were observed. There was no enlargement of the ascending aorta, and the patient was discharged without complications at POD 34.

Although he had no family history of cardiovascular diseases, including aortic dissection or aortic aneurysm, connective tissue disease was suspected due to his own history of aortic root dilatation and recurrent aortic dissection; thus, a genetic test was conducted (tested genes: FBN1, FBN2, TGFB1, TGFB2, TGFB3, SMAD2, SMAD3, ACTA2, COL3A1, EFEMP2, FLNA, MYH11, MYLK, SLC2A10). Among the tested genes, heterozygous 8-bases duplication in SMAD3 (c.742_749dup, p. Gln252ThrfsTer7) and heterozygous missense mutation in FBN2 (c.3518C>G, p. Thr1173Ser) were detected, suggesting LDS type III.

**Discussion**

Although the occurrence of IAD is rare (1–5), there have been several reports of IAD in connective tissue diseases. Yoneyama et al. reported the case of a patient with LDS type III with MYH11 comutation who developed intraoperative Stanford type A aortic dissection immediately after the initiation of CPB (8). Furthermore, cases of IAD during cardiovascular surgery in patients with Marfan syndrome have been reported (7, 9, 10). Patients with connective tissue disease are at a high risk of developing iatrogenic aortic dissection. Unfortunately, there are currently no established strategies to prevent IAD in such
patients. Kumar et al. stated that using a curved-tip dispersion cannula could minimize the risk of dissection (7). It may prevent lesser curvature intimal tear compared with the use of a straight-tip cannula but may not prevent dissection from cannulation or clamping site similar to this case. CPB with perfusion to other sites, such as common femoral artery (CFA) and axillary artery (AxA), instead of the ascending aorta may be effective for protecting the aorta in such patients. Moreover, perfusion through a prosthetic vascular graft anastomosed to the CFA and/or AxA may be more protective if arterial dissection due to cannulation is a concern. To prevent aortic cross-clamping site dissection, Von Aspern et al. suggested the use of padded aortic cross-clamps or cross-clamps that generate less force (6). However, nonuse of aortic cross-clamping, if possible, seems to be more protective. Open-distal anastomosis under hypothermic circulatory arrest can avoid aortic cross-clamping and may be considered for cases of connective tissue disease. However, this needs further investigation.

The patient had an unreported heterozygous frameshift mutation due to 8-bases duplication in the SMAD3 gene. This is expected to be a loss-of-function mutation by forming a premature termination codon that causes nonsense-mediated mRNA decay. FBN2 mutation is likely benign based on ClinVar (11). On the other hand, SMAD3 mutation is not registered in ClinVar (11), but it seemed to be pathogenic as it has a frameshift occurrence and probably forms a premature termination codon. The patient in this case also had a bifid uvula (Fig. 4). Although he had no history of musculoskeletal disease, such as osteoarthritis, he was diagnosed with LDS type III based on the diagnostic criterion (12).

MacCarrick et al. suggested that a mutation in any of the LDS-associated genes including SMAD3 in combination with documented aneurysm or dissection is sufficient to diagnose LDS (12). Based on this criterion, the patient in this case can be diagnosed with LDS type III. About 75% of LDS type III cases are caused by de novo SMAD3 mutation (13). The mutation of the patient in this case was also thought to be de novo because he did not have a family history of cardiovascular diseases and sudden deaths.

Among his three children, the eldest (30-year-old woman) had the same SMAD3 mutation. She was 178-cm tall and weighed 56.3 kg. She also had bifid uvula but no history of musculoskeletal disease. Contrast-enhanced CT and transthoracic echocardiogram did not show aortic root dilatation, AR, or aortic dissection. We planned to make a follow-up on her and the patient, his father.

**Conclusion**

We experienced IAD in a patient with LDS type III with novel SMAD3 mutation (c.742_749dup, p. Gln252ThrfsTer7). The IAD was suspected to be caused by aortic cannulation or cross-clamping. These can be avoided by using surgical strategies such as AxA and CFA perfusion plus open-distal anastomosis to minimize IAD, especially for patients with connective tissue disease.

**Abbreviations**

IAD
Declarations

Ethics approval and consent to participate

The present study was conducted in accordance with the ethical review board of our hospital (Institutional Review Board #004-4-2).

Consent for publication

Written informed consent for the publication of this case report and any accompanying images was obtained from the patient.

Availability of data and materials

The datasets used during the current report are available from the corresponding author upon reasonable request.

Competing interest

None of the authors have any competing interest to declare.

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None.
Authors’ contributions

Author 1 performed surgery, managed the perioperative course, wrote the manuscript.

Author 2 mainly supervised writing of the manuscript.

Author 3 conducted genetic counseling for the patient's family, supervised the genetic part of the manuscript.

Author 4 performed surgery, managed the perioperative course.

Author 5 performed surgery, managed the perioperative course.

Author 6 mainly performed surgery, managed the perioperative course, conducted genetic test.

Author 7 supervised the patient surgical treatment and the manuscript as a person responsible for the department of cardiovascular surgery.

Author 8 supervised the patient surgical treatment, checked and approved the manuscript as a person responsible for the hospital.

References


Figures

Figure 1
Stanford type B, DeBakey type IIIb acute aortic dissection 14 months before surgery. Aortic root dilatation was also detected.

(a) Stanford type B acute aortic dissection (arrows), aortic root dilatation of 55 mm in (b) axial and (c) sagittal images (arrows), (d) aortic root dilatation (asterisk) in 3D-CT angiography.

Figure 2

Aortic regurgitation due to annuloaortic ectasia on transthoracic echocardiogram.
Figure 3

(a) Postoperative Stanford type A aortic dissection (arrows). Dissection was extended to the left common carotid artery. The aortic root had been replaced (asterisk). (b) The entry was found at the distal ascending aorta nearby the cannulation and cross-clamping sites (arrow).
Figure 4

Bifid uvula (cleft palate was not seen)