A case report of successful complex percutaneous coronary intervention for acute coronary syndrome in a paediatric patient with familial hypercholesterolaemia

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Background
Familial hypercholesterolaemia (FH) is a primary genetic dyslipidaemia characterized by elevation in serum low-density lipoprotein cholesterol and its deposition in systemic arteries, which causes premature atherosclerosis.

Case summary
A 10-year-old girl presented with severe symptomatic coronary artery disease. She demonstrated characteristic morphological features of FH. Despite aggressive medical management and lipid-lowering therapy, her symptoms were not relieved and she had dynamic electrocardiogram changes. Coronary angiography showed a distal left main coronary artery lesion along with significant lesions in ostio-proximal and mid-left circumflex artery which were managed by provisional left main coronary artery to left circumflex artery stenting technique, with good immediate- and short-term results and angina relief.

Discussion
To the best of our knowledge, this is the first reported case of a paediatric patient with FH and acute coronary syndrome treated with percutaneous coronary intervention to left main coronary artery and left circumflex artery using provisional stenting technique. Revascularization strategies for symptomatic coronary artery disease in paediatric patients with FH have multiple unique challenges and remain an unexplored and under-reported subject.

Keywords
Familial hypercholesterolaemia • Coronary artery disease • Provisional stenting technique • Case report

Introduction
Familial hypercholesterolaemia (FH) is an autosomal dominant genetic dyslipidaemia, which in its homozygous form affects 0.2% of the population. It is characterized by an increase in low-density lipoprotein cholesterol (LDL-C) levels because of mutations in the APOB, LDLR, or PCSK9 genes leading to generalized premature atherosclerosis causing coronary artery disease, peripheral vascular diseases, and
supravalvular aortic stenosis. It is usually managed with lipid-lowering drugs (statins, cholesterol absorption inhibitors, PCSK9 inhibitors, etc.) and lipid apheresis. Coronary revascularization may be necessary when ischaemia-producing coronary disease develops.

We report a case of a 10-year-old girl with FH and symptomatic coronary artery stenosis treated with percutaneous coronary intervention (PCI) with favourable immediate- and short-term outcome.

Timeline

| Day | Description |
|-----|-------------|
| Day 1 | Presentation to hospital with severe angina at rest with clinical examination showing tendon xanthomas and electrocardiogram (ECG) showing dynamic ST-T changes with ST-segment elevation in lead aVR |
| Day 2 | Patient underwent diagnostic coronary angiography showing left main coronary artery disease with left circumflex coronary artery (LCx) involvement |
| Day 3 | Patient underwent percutaneous coronary intervention with drug-eluting stent placement of left main coronary artery over LCx using provisional bifurcation technique |
| Day 5 | Patient angina free and discharged |
| Day 30 | First follow-up—patient followed up and given injection evolocumab |
| Day 60 | Lipid profile shows reduction in low-density lipoprotein cholesterol levels of 640 mg/dL from 1010 mg/dL. ECG shows no new ST-T changes, patient asymptomatic |

Case presentation

Initial presentation

A 10-year-old girl, a child of a second degree consanguineous marriage, presented to the cardiology department of our institute with anginal chest pain on exertion (Canadian Classification Society Class 2). She complained chest pain since 1 month which had increased since 1 day to severe angina at rest. She had a history of claudication in both arms and legs since 3 months. There was no familial history of premature coronary artery disease. On examination, the patient’s heart rate was 120/min and her blood pressure was 90/50 mmHg. Multiple painless, firm nodules were present over her elbows, knuckles, knees, and ankles, suggestive of tendon xanthomas; moreover, she presented with corneal arcus (Figure 1). Her peripheral pulses were normal and on cardiovascular examination, she had a soft mid to late systolic murmur with a click.

Diagnostic assessment

The electrocardiogram (ECG) showed sinus tachycardia, normal axis, 3 mm ST segment depression in leads II, III, aVF, V4–V6 with biphasic T waves and 1.5 mm ST-segment elevation in lead aVR, 1 mm ST-segment elevation in V1 (aVR > V1) suggesting left main coronary artery disease (Figure 2). The echocardiogram showed normal left ventricular systolic function, mitral valve prolapse leading to moderate mitral valve regurgitation and mildly dilated left atrium. Stenosis at the origin of left main coronary artery was observed (Figure 3). Her lipid profile showed total cholesterol level of 1010 mg/dL (normal range 130–200 mg/dL), high-density lipoprotein cholesterol of 62 mg/dL (normal range 35–150 mg/dL), LDL-C of 898 mg/dL (normal range 0–129 mg/dL), very-LDL cholesterol of 50 mg/dL (normal <30 mg/dL), and total triglycerides of 250 mg/dL (normal range 30–150 mg/dL). Her troponin I level was elevated. Family screening showed elevated total cholesterol and LDL-C in both parents without skin manifestations. A diagnosis of definite FH was made (total score 23), based on the Dutch Lipid Clinic Network diagnostic criteria for FH. She was managed with intravenous unfractioned heparin infusion, dual antiplatelet agents [Aspirin (5–8 mg/kg) and Clopidogrel (1–2 mg/kg)], Rosuvastatin 40 mg OD, Ezetimibe 10 mg OD, and anti-anginals.

Interventions

The patient underwent coronary angiography which showed critical ostial left main coronary artery stenosis and 50% stenosis in the distal left main coronary artery. The left anterior descending coronary artery (LAD) showed a tubular concentric lesion of 50% stenosis in its middle segment with an apparently normal LAD ostium and proximal segment. The left circumflex coronary artery (LCx) was co-dominant, showed concentric tubular stenosis of 70–75% severity at ostium followed by 90–95% severity in proximal part. The mid-LCx showed stenosis of 70–75% (Figure 4 and Videos 1 and 2). Thus she had a Medina 1.0.1 lesion as per the Medina Classification for Coronary Bifurcation Lesions. The right coronary artery showed non-significant plaques. The left internal mammary artery (LIMA) had an 80% stenosis at its ostium (Video 3). The left renal artery also showed an 80% stenosis (Supplementary material online, Video S1). The patient consequently underwent PCI because of a repeat episode of severe symptomatic angina at rest associated with dynamic ST-T segment changes on ECG. The patient underwent the procedure under general anaesthesia with right femoral artery access, using provisional bifurcation stenting strategy. The left main coronary artery was cannulated using 6.0 Fr guide. Both the LAD and LCx were wired using two 0.014 BMV guide wires. The lesion in proximal LCx was pre-dilated with a non-compliant balloon of size 2.5 mm × 13 mm. An everolimus drug-eluting stent (DES) of size 2.5 mm × 33 mm was deployed from the ostium of left main coronary artery to LCx covering the proximal LCx stenosis. The stent was post-dilated with 3 mm × 10 mm non-compliant balloon followed by proximal optimization of the left main coronary artery stent using 3 mm × 8 mm non-compliant balloon. Kissing balloon to open the stent meshes towards LAD was not performed because the proximal LAD was relatively healthy, was not showing any disease and post-LCx stent deployment, there was no ostial LAD compromise. A second stent (DES) of size 2.25 mm × 18 mm was deployed across the mid-LCx lesion. Angiograms obtained showed optimal results with Thrombolysis in Myocardial Infarction 3 flow and no ostial LAD compromise (Figure 5 and Supplementary material online, Video S2).
Outcome and follow-up
The patient was haemodynamically stable post-procedure and was initiated on dual antiplatelets, Rosuvastatin 40 mg OD, Ezetimibe 10 mg OD, and PCSK 9 inhibitor (Injection Evolocumab 420 mg subcutaneous once a month). She was discharged after 48 h and remained asymptomatic for her cardiac condition 4 months post-procedure. Her 60-day follow-up lipid profile showed a reduction in total cholesterol levels to 640 mg/dL from 1010 mg/dL and a reduction in LDL-C to 508 from 898 mg/dL. Her renal artery stenosis and peripheral vascular disease were managed medically. She was advised lipid profile monitoring and a coronary computed tomography after 1 year and family screening.

Discussion
Our case of a 10-year-old child with FH and acute coronary syndrome treated with PCI to left main coronary artery and left circumflex artery is among very few previously reported in the paediatric population, especially ≤10 years of age. Familial hypercholesterolaemia remains widely underdiagnosed, often undertreated, and with regards to its revascularization management especially in paediatric patients, extremely understudied. As a result, the optimal approach for management such as coronary artery bypass grafting (CABG) vs. PCI, DES vs. bioabsorbable scaffolds among others and the optimal timing for these interventions in such patients with stable angina is unknown.
Although rare in children, coronary artery stenosis requiring intervention may occur because of various aetiologies, including congenital anomalies, cardiac surgery, cardiac allograft vasculopathy, and systemic inflammatory and metabolic diseases, such as Kawasaki disease with coronary aneurysms and FH.\(^3\) Though CABG is an established therapeutic option, it has limitations like requirement for open surgery, technical difficulties related to small arterial targets, and potentially decreased graft patency rates among children.\(^3\) Coronary artery bypass graft was not feasible in our patient because of stenosed LIMA.

Coronary artery stenting poses unique challenges in paediatric patients such as an increased risk of in-stent restenosis. This may occur because of the small diameter of the stents required or because of undefined differences in vascular healing responses in this population. A metallic stent may become undersized because of a child’s growth (a four-fold increase in the diameter of the left main
Successful complex PCI in paediatric FH

coronary artery occurs between infancy and 17 years of age\(^\text{10}\) and the presence of a metallic stent may alter the coronary physiology.

Our patient had coronary artery bifurcation disease classification Medina 1.0,1.5 Several randomized trials comparing one or two stents in the treatment of coronary bifurcations have demonstrated the implantation of a single stent as a preferred strategy. The 15th European Bifurcation Club consensus document provides an overview of the considerations regarding left main bifurcation stenting.\(^\text{11}\)

There was no significant ostial compromise in the LAD with a good distal flow after provisional stenting; therefore a two-stent strategy was avoided. The procedure resulted in technical success with resolution of the acute coronary syndrome and a favourable short-term clinical outcome. Long-term follow-up and further research on coronary revascularization in FH is needed to guide interventional management in these patients.

**Figure 5** Cine images of PTCA showing a drug-eluting stent deployed from left main over left circumflex coronary artery and second drug-eluting stent is positioned in the lesion across mid-left circumflex coronary artery; post-PTCA angiogram showed optimal results with Thrombolysis in Myocardial Infarction 3 flow, no dissection and no ostial left anterior descending coronary artery compromise. DES, drug-eluting stent; LAD, left anterior descending coronary artery; LCx, left circumflex coronary artery; PCI, percutaneous coronary intervention; PTCA, Percutaneous Transluminal Coronary Angioplasty; RAO, Right Anterior Oblique.

**Video 1** Diagnostic coronary angiography video showing ostial left main coronary artery stenosis and 50% stenosis in distal LM. Left anterior descending coronary artery showed tubular concentric lesion of 50% stenosis in mid-part with apparently normal left anterior descending coronary artery ostium and proximal segment in LAO cranial view.

**Video 2** Diagnostic coronary angiography right anterior oblique caudal view showing co-dominant left circumflex coronary artery with concentric tubular stenosis of 70–75% severity at ostium followed by 90–95% severity in proximal part. Mid-left circumflex coronary artery showed stenosis of 70–75%. The distal left circumflex coronary artery was seen filling retrogradely via collaterals arising from co-dominant right coronary artery.
Lovastatin, simvastatin, atorvastatin, and rosuvastatin are approved for use in children more than 10 years of age. The long-term safety of statins in paediatric patients is still unknown, but the current benefits of treatment outweigh the risks for these patients.

Children and adolescents on statin therapy should have regular follow-up, with close monitoring of biochemical parameters such as aspartate amino transferase, alanine amino transferase levels, and creatinine kinase.12

Low-density lipoprotein apheresis is an important treatment option for homozygous FH patients, and it is an Food and Drug Administration (FDA) approved mode of management. However, there is limited data for its safety in paediatric patients.12 For antiplatelet therapy, very little data on its efficacy and safety is available for paediatric patients. Most of the practices are based on extrapolating data from adult studies.13

A study on the efficacy, safety, and tolerability of evolocumab in paediatric patients with heterozygous FH (HAUSER-RCT study) demonstrated that evolocumab is a safe drug (long-term safety studies are awaited) with a significant reduction in LDL-C in study subjects.14

There were a few limitations in our case. Intracoronary imaging would have been an ideal technique in stent sizing and optimization. However, this particular procedure was performed in an emergency setting, in a resource poor setting hence direct stenting technique was performed without the use of intracoronary imaging. Genetic testing was not performed due to financial constraints and lipoprotein apheresis was not offered due to its non-availability.

**Conclusion**

Familial hypercholesterolaemia is a rare disorder with limited data available on the safety and efficacy of various treatment modalities in paediatric FH patients. The optimal approach and timing for intervention in these patients are unknown. Percutaneous coronary intervention by provisional stenting technique in our patient resulted in technical success and good short-term clinical outcome. Long-term follow-up and further research on coronary revascularization in paediatric FH are needed to guide the interventional management in this subset of patients.

**Lead author biography**

Dr Mrunmayee Deshpande is a senior resident in cardiology at Lokmanya Tilak Municipal Medical College and Sion Hospital, Mumbai, India. Her areas of special interest are interventional cardiology and echocardiography.

**Supplementary material**

Supplementary material is available at European Heart Journal - Case Reports online.

**Slide sets:** A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

**Consent:** The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

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