Tunneled left anterior descending artery in a child with hypertrophic cardiomyopathy

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**SUMMARY**

**Background** A 10-year-old boy presented with a history of severe angina on exertion. A two-dimensional echocardiogram showed mild asymmetric left ventricular (LV) hypertrophy localized to the interventricular septum, consistent with nonobstructive hypertrophic cardiomyopathy. A maximal treadmill exercise test was terminated early owing to marked downsloping of the ST–T segment on all precordial leads, associated with mild chest discomfort. Cardiac MRI and coronary angiography showed that the left anterior descending (LAD) artery was ‘tunneled’ from its origin to the junction of the middle and lower segments, causing systolic obliteration. PET showed diffusely blunted myocardial blood flow after dipyridamole infusion. A beating-heart technique was used to perform surgical mobilization of the superficial and lateral surfaces of the LAD artery. The patient was asymptomatic at 6 months after surgery. A repeat exercise test showed considerable improvement in exercise tolerance, which was associated with a marked decrease in ST–T changes on exertion.

**Investigations** Physical examination, laboratory tests, 12-lead electrocardiography, two-dimensional echocardiography, exercise testing, cardiac MRI, coronary angiography, PET, Holter electrocardiographic monitoring.

**Diagnosis** Angina caused by extensive myocardial tunneling of the LAD artery in nonobstructive hypertrophic cardiomyopathy.

**Management** Bisoprolol therapy and surgical mobilization of the tunneled LAD artery.

**KEYWORDS** angina, hypertrophic cardiomyopathy, myocardial bridging, myocardial ischemia, myocardial tunneling

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**THE CASE**

A 10-year-old boy presented with a 4-year history of severe angina on exertion, which had worsened substantially in the last 2 years. On physical examination, the patient was in good general condition, and his body size was normal for his age (height 133 cm; weight 35 kg). Cardiac auscultation was unremarkable, and no signs of heart failure were observed. A 12-lead resting electrocardiogram showed diffuse signs of left ventricular (LV) hypertrophy and LV strain, and a deep Q wave in lead III (Figure 1A). Two-dimensional echocardiography showed mild asymmetric LV hypertrophy localized to the interventricular septum, with a maximum thickness of 15 mm at the midseptal level. The basal septum was irregularly hyperechogenic, which indicated that areas of intramyocardial fibrosis existed (Figure 2). LV systolic function was preserved with a pseudonormal transmitral pulsed wave Doppler pattern. In resting conditions, no anterior systolic movement of the mitral valve or obstruction of the LV outflow tract (LVOT) was observed. The patient’s family history was unremarkable, and a comprehensive panel of diagnostic tests excluded a metabolic or mitochondrial cause of the cardiomyopathy. The patient was diagnosed as having nonobstructive hypertrophic cardiomyopathy (HCM). He was started on bisoprolol therapy, and titrated to the maximum tolerated dose of 2.5 mg daily. A maximal, symptom-limited, treadmill exercise test that used a modified Bruce protocol was performed while the patient received treatment, but was terminated early owing to marked downsloping of the ST–T segment on all precordial leads, associated with mild chest discomfort (Figure 1B). A second exercise test yielded very similar results, despite the addition of amlodipine 5.0 mg daily. A 24 h Holter electrocardiogram did not show ventricular or supraventricular arrhythmias; however, marked ST–T downsloping was repeatedly evident during moderate physical activity (brisk walking).
Cardiac MRI demonstrated that the proximal two-thirds of the left anterior descending (LAD) artery had an intramural course, and confirmed the presence of mild, LV septal hypertrophy, with normal LV cavity dimensions and systolic function (Figure 3). Coronary angiography showed extensive obliteration of the LAD artery during systole. Notably, arterial lumen reduction persisted during the initial two-thirds of diastole (Figure 4). Quantitative assessment of LV myocardial blood flow by PET after dipyridamole infusion showed an average value of 1.63 ml/min per gram of myocardium, with a blunted vasodilator response at the anteroseptal level, in the region of distribution of the LAD artery (Figure 5).

A surgical approach to management was favored because of persistent symptoms and documented regional ischemia, despite optimum medical therapy. An off-pump beating-heart technique was used for surgical unroofing and mobilization of the LAD artery (Figure 6). On inspection, the anterior LV wall appeared fibrosed. Only the distal third of the LAD artery was observed to have an extramural course and the remaining segments of the artery were deeply embedded in the ventricular septum—12 mm proximally and 5 mm distally below the epicardium. Potts scissors were used to incise the myocardium overlying the vessel. Mobilization of the superficial and lateral surfaces of the LAD artery followed, starting from the superficial segment to the bifurcation of the left main coronary artery. Interestingly, a tough, transverse, fibrous band (4 mm in width) covered the LAD artery just distal to the left main coronary artery. This fibrous band was also excised. At the end of surgery, the whole course of the LAD artery had been sufficiently mobilized (Figure 6). No perioperative complications occurred, and the patient made an event-free recovery.
At follow-up, 6 months after surgery, the patient was free from angina, although he still complained of fatigue, which was partly a result of muscular deconditioning. A 24 h Holter electrocardiogram did not show significant changes of the ST–T segment during daily activities. A repeat exercise test showed substantial improvement in exercise tolerance, and marked reduction in ST–T segment changes during exertion (Figure 1C).

**DISCUSSION OF DIAGNOSIS**

Symptoms and signs of myocardial ischemia are often evident in patients with HCM, even if the coronary arteries are angiographically normal. 3–5 Myocardial ischemia is a major determinant of outcome, and has a complex and multifactorial origin in patients with HCM, which reflects the interplay of structural small-vessel abnormalities, reduced arteriolar density, myocardial disarray, and elevated LV end diastolic pressures. 5 In children or adolescents with HCM, however, angina on exertion is often associated with an intramural course of the LAD artery, a condition also referred to as myocardial 'bridging'. 6–13 Systolic compression of an epicardial coronary branch as a result of bridging is seen on angiography in about 15% of patients with HCM, 12 compared with a 1–3% prevalence in the general population. 13 In the majority of cases of myocardial bridging, the middle segment of the LAD artery is affected. 10–13 Although most cases of myocardial bridging in adults are clinically silent and have little bearing on overall outcome, 12 a distinct association seems to exist between myocardial bridging and severe symptoms, ventricular arrhythmias, and sudden death in children with HCM. 7 Importantly, the severity of systolic compression is not directly correlated with the degree of hypertrophy or the presence of LVOT obstruction.

Traditional angiography remains the gold standard diagnostic modality for patients with HCM in whom myocardial bridging is suspected as the cause of angina, dyspnea on exertion, or syncope. 13 Angiography allows the physician to visualize the location, depth, and length of the bridge, and provides an assessment of the
severity of compression throughout the cardiac cycle (Figure 4). CT angiography is a useful and reliable alternative to traditional angiography that avoids the risks of invasive coronary imaging. High radiation exposure is, however, an important concern when CT angiography is performed in children.

Because of technical limitations, the accuracy of cardiac MRI is considerably inferior to traditional angiography or CT angiography for the assessment of coronary circulation. However, cardiac MRI serves as a good adjunct to other imaging techniques, and can be used to characterize the depth and extension of the muscle tunnel precisely, to obtain a very detailed three-dimensional image of the heart, and to identify areas of fibrosis. In selected patients, intravascular ultrasonography can be useful in assessing the functional severity of the bridge or tunnel after inotropic stimulation, but this technique is not necessary in severe cases, such as the one presented here. Finally, assessment of myocardial flow by PET can help to confirm the functional consequences of coronary compression on regional perfusion during near-maximal vasodilation. In this patient, PET confirmed the causal association between arterial tunneling and the child’s symptoms (Figure 5).

From a pathophysiological standpoint, myocardial bridging results in mechanical compression of the artery from both the epicardial and lateral aspects. In addition, repeated systolic compression of the coronary vessel leads to increased wall shear stress and impairment in endothelium-dependent vasorelaxation. These functional alterations are thought to add to the severity of structural lumen compression, and contribute to clinical manifestations of myocardial bridging. Indeed, angiographic and intravascular ultrasonographic studies have shown that vessel compression during systole is followed by a delay in luminal diameter increase during diastole, which affects the predominant phase of coronary perfusion, as seen in this patient. In its most severe form, such as in the individual described here, extensive myocardial bridging is more appropriately referred to as a ‘tunneled’ LAD artery. The extension and depth of the intramyocardial course of the artery are important determinants of ischemia and associated symptoms, and help distinguish forms that are clinically relevant from those that are not.

An assessment of the links between myocardial tunneling, ischemia and symptoms can be a challenge in patients with HCM. Myocardial ischemia is often clinically silent, whereas chest pain is a frequent complaint but is often atypical and not a reliable marker of ischemia. However, in this patient, the clinical presentation included typical exertion-related angina and striking electrocardiographic changes during exercise, which left little doubt about the presence of ischemia. The severity of coronary compression during most of the cardiac cycle, the regional impairment of blood flow seen on PET and the absence of LVOT obstruction or severe hypertrophy all strongly supported a direct causal link between the tunneled LAD artery and the patient’s symptoms.

TREATMENT AND MANAGEMENT
Management strategies for patients with HCM and symptomatic myocardial tunneling have not been adequately investigated, nor has the optimal therapy been defined. Asymptomatic patients, in whom myocardial bridging is an unexpected finding, should undergo exercise testing and a
series of ambulatory Holter electrocardiograms to assess the presence of inducible ischemia and ventricular arrhythmias. In the absence of either finding, adult patients can be managed conservatively. In the presence of symptoms or exercise-induced ischemia, an initial approach with β-blockers can be effective for controlling angina, although the long-term efficacy of this strategy has not been assessed. β-blockers control tachycardia, thereby increasing diastolic perfusion time, and reduce the contractility of the myocardial tunnel. Conversely, nitrates can worsen symptoms and the degree of systolic coronary compression, and should be avoided.

When symptoms attributable to myocardial tunneling persist despite optimum medical therapy, surgery is generally agreed to be the best option. Ultimately, the decision to operate should be on the basis of surgical risk, the experience of the surgical team, and whether LAD artery tunneling exists in association with LVOT obstruction. In a limited number of reports, including small patient series and isolated case studies, relief of symptoms and ischemia after surgery have been consistently described, although the ultimate effects on long-term outcome remain to be established. Downar et al. reported that, in five children from the Toronto HCM cohort, myocardial bridges that caused compression of the LAD artery (associated with severe clinical manifestations and evidence of myocardial ischemia) were successfully treated with supra-arterial myotomy. The authors reported substantial improvement or resolution of cardiac symptoms, without major perioperative complications. Notably, these operations were performed on cardiopulmonary bypass. However, we believe that the optimum surgical approach should involve a beating-heart technique, which significantly reduces operative times and risks, and mobilizes the superficial and—importantly—the lateral aspects of the artery. Such an approach was successfully adopted in the current patient.

Notably, coronary stenting has been attempted as an alternative to surgery in patients with myocardial bridging who do not have HCM. However, this approach is associated with a high rate of major peri procedural complications or short-term restenosis, and should be avoided, particularly in children.

This young patient experienced rapid and marked postoperative improvement in symptomatic status, which was associated with an objective reduction in electrocardiographic abnormalities during exercise. Persistence of mild symptoms related to exercise could be a result of diffuse microvascular dysfunction causing residual hypoperfusion of the myocardium, as well as to muscular deconditioning. In addition, endothelial dysfunction of the LAD artery might have persisted, caused by extended vessel exposure to mechanical stress during systole. Further investigation is needed to test this hypothesis.

CONCLUSIONS
Tunneling of the LAD artery can be the cause of severely limiting symptoms in children with HCM, and should always be suspected in the presence of angina or other manifestations of myocardial ischemia. Surgical correction can be performed successfully with the use of a beating-heart approach. We hope that the detailed discussions of the pathophysiology of the condition, and the surgical technique, presented in this Case Study will help optimize the management of children with HCM who are affected by this potentially serious condition.
References