A healthy 38-year-old man with premature coronary artery disease

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A fit, nonsmoker who eats well and exercises regularly presents with chest discomfort. Can a healthy individual with no risk factors have severe coronary artery disease?

Key points

- **When a patient has premature coronary artery disease that is not fully explained by the presence of standard risk factors, it is important to examine him further to ensure no other factors have been missed.**
- **New forms of cardiac imaging can be helpful to assess the viability of myocardium to guide decision-making about revascularisation.**

Case scenario

A 38-year-old businessman, and father of two young children, presents to his GP after experiencing chest discomfort during training for a corporate half-marathon. He is a fit nonsmoker with no family history of premature coronary artery disease, who eats healthily and exercises regularly. Of late he has noticed that he is less able to keep up with his running partners despite regular training. You refer him for an exercise stress echocardiogram to investigate for inducible ischaemia.

Commentary

Baseline echocardiography images are obtained and show abnormal left ventricular systolic function with an ejection fraction of 40% and a large anterior wall motion defect (Figure a). The planned treadmill stress test is not performed and the patient attends a consultation with the cardiologist on duty.

A resting ECG shows that the patient has a ventricular rate of 56 bpm and a partial left axis deviation but no pathological Q-waves or ST depression.

The patient's lipid profile is mildly abnormal with the following results:

- total cholesterol 5.9 mmol/L
- HDL cholesterol 0.9 mmol/L (low)
- triglycerides 2.9 mmol/L (raised)
- LDL cholesterol 3.3 mmol/L.

The result of his fasting glucose is 5.0 mmol/L and a glucose tolerance test is normal. He has no family history of diabetes.

The patient is admitted directly to the

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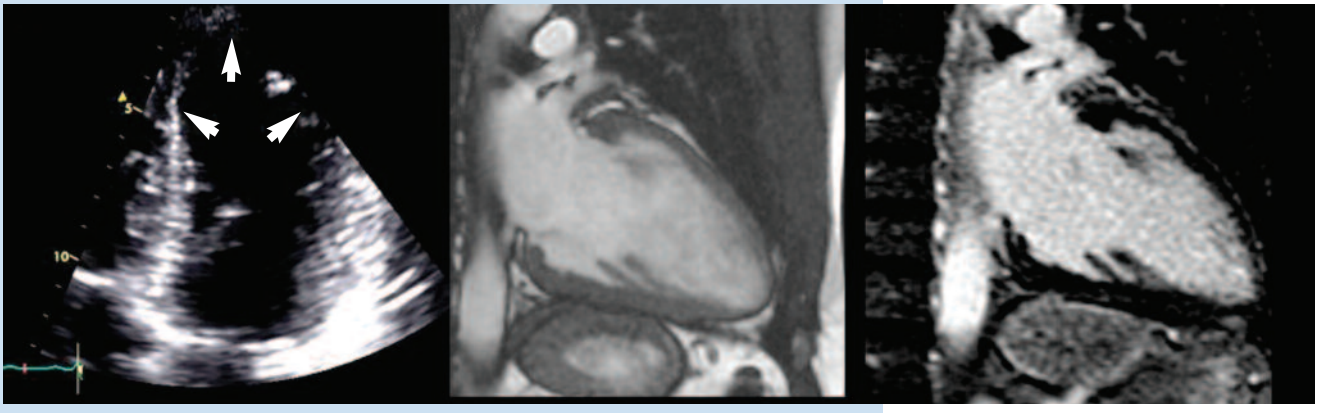

Figures a to c. Imaging from this patient. (a, left). Echocardiography at baseline shows a large anterior-apical wall motion defect (arrows). Cardiac MRI shows anterior wall hypokinesis (b, middle) with no scar (c, right), indicating hibernation of the left anterior descending coronary artery territory.

coronary care unit of the private hospital, but he is told that his private corporate health policy has a 'cardiac exclusion' of which he was unaware. Fortunately, his cardiologist has a part-time staff position at the nearby public hospital, and the patient is transferred by ambulance to the coronary care unit of the public hospital.

On admission, the patient is anticoagulated with a low-molecular weight heparin, a high-dose statin (80 mg atorvastatin), an ACE inhibitor (2.5 mg perindopril) and loaded with 600 mg clopidogrel and 300 mg aspirin. The first measurement of his serum troponin I level on arrival in the critical care unit that afternoon is borderline positive at 0.05 µg/L, and a second troponin measurement taken later in the evening is raised at 1.0 µg/L.

The patient has ongoing chest discomfort, and is immediately taken for urgent coronary angiography. It is discovered that he has a completely occluded left anterior descending artery (LAD), a high-grade lesion in the circumflex artery and moderate right coronary artery disease. The left circumflex artery stenosis is treated percutaneously with a stent.

Subsequently, a cardiac MRI is arranged to evaluate the viability of the territory of his LAD to assess the need for surgical or percutaneous revascularisation. This reveals an ejection fraction of 39% with preserved viability of all myocardial segments but with reduced contractility of the anterior wall, consistent with hibernation of the LAD territory (Figures b and c).

The patient's lipid profile appears discordant with the severe degree of coronary artery disease, and his cardiologist arranges to check his level of serum lipoprotein(a), also known as Lp(a). This comes back raised at 1340 mg/L (normal value, <300 mg/L).

Lp(a) is a plasma lipoprotein that's levels are genetically determined and are not measured on standard cholesterol testing. It significantly elevates cardiovascular risk and causes accelerated atherosclerosis through complex mechanisms (prothrombotic/antifibrinolytic effects and intimal deposition of Lp(a) cholesterol).[1] Niacin therapy reduces Lp(a) levels by between 30%

and 40% in a dose-dependent manner. In a meta-analysis of 11 randomised controlled trials, 1 to 3 g/day niacin reduced:

- major coronary events by 25% (95% confidence interval [CI], 13 to 35%)
- stroke by 26% (95% CI, 8 to 41%)
- any cardiovascular event by 27% (95% CI, 15 to 37%).[2]

However, the Atherothrombosis Intervention in Metabolic syndrome with low HDL/high triglycerides: Impact on Global Health outcomes (AIM-HIGH) study showed no cardiovascular outcome benefit in patients with well-controlled LDL cholesterol using extended-release niacin and simvastatin compared with simvastatin alone.[3] Niacin therapy is not well tolerated due to the major side effect of flushing and extended-release formulations have been developed.

The patient is enrolled in a current ongoing clinical trial of extended-release niacin, and also treated with high-dose purified fish oil (proven in the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico (GISSI) trial to reduce mortality after a myocardial infarction).[4] His health fund agrees to pay for the fish oil supplements.

Given the preserved viability of his LAD territory myocardium and left ventricular dysfunction (ejection fraction, 39%), revascularisation is planned. Single-vessel surgery is discussed, and the patient chooses to undergo angioplasty and stenting of the chronic total occlusion. He undergoes successful percutaneous revascularisation of the LAD artery using a drug-eluting stent.

At six weeks follow up a repeat cardiac MRI study shows recovery of function with no scar, and an ejection fraction improved to 50%. The patient's lipid profile has the following results:

- total cholesterol 3.1 mmol/L
- HDL cholesterol 0.9 mmol/L (unchanged)
- triglycerides 0.8 mmol/L (improved)
- LDL cholesterol 1.9 mmol/L (improved)
- Lp(a) 860 mg/L (improved).

His statin is switched to 40 mg rosuvastatin, to further reduce his LDL cholesterol level and hopefully preserve his HDL cholesterol level, and is given in combination with the high-dose purified fish oil and niacin. He is also taking 10 mg perindopril, to assist in the recovery of his left ventricular function, and long-term prasugrel and aspirin, for antiplatelet activity after

stenting. He is back at work and starts a graded exercise program under the supervision of a cardiac rehabilitation team.

Conclusion

This case illustrates the importance of looking further when a patient has premature coronary artery disease that is not fully explained by the presence of standard risk factors. It also demonstrates the utility of new forms of cardiac imaging to assess the viability of myocardium to guide decision-making about revascularisation.

The patient's prognosis is still guarded because he is likely to have progressive coronary artery disease, and his target LDL cholesterol level should be as low as achievable, while ideally maintaining an HDL cholesterol level above 1.0 mmol/L. Current guidelines recommend LDL cholesterol levels should be less than 2.5 mmol/L; however, in the ASTEROID (A Study to Evaluate the Effect of Rosuvastatin on Intravascular Ultrasound-Derived Coronary Atheroma Burden) trial, coronary plaque regression was seen with LDL cholesterol levels of less than 1.5 mmol/L and this is the target chosen in discussion with this relatively young and motivated patient in the present case who is at high future risk of further events.[5]

The patient is highly-motivated, adhering strictly to diet and lifestyle measures and tolerating his multiple medications, although he and his family are distressed as to how this could happen to such an otherwise healthy individual. You refer him for genetic counselling, to discuss the Lp(a) disorder and if and when his children should be tested. He is followed very closely with stress-echocardiography to monitor for recurrence of ischaemia. **CT**

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