A 49-year-old hypertensive male presented to our emergency department with typical chest pain and breathlessness. The electrocardiogram revealed left ventricular (LV) hypertrophy with unusually deep T-wave inversion in the lateral leads (Panel A). The acute ischaemic injury was ruled out with serially negative troponin assays. An urgent outpatient myocardial perfusion scintigraphy scan showed a moderate size, and completely reversible defect at the LV apex with ischaemia involving 20% of the LV myocardium (Panel B). Coronary angiography revealed normal epicardial coronary arteries with a classic spade-shaped LV on contrast ventriculography (Panel C/Video 3). The diagnosis was confirmed with transthoracic echocardiography and gadolinium-enhanced cardiac magnetic resonance, both showing severe LV apical hypertrophy without myocardial scar or apical aneurysm (Panel D/Video 1,2). Genetic testing revealed a heterozygous...
variant in the NRAS gene, autosomal dominant mutations of which have been associated with Noonan syndrome. The patient, himself, did not exhibit the Noonan syndrome phenotype. He was started on bisoprolol 5 mg once daily and a once-daily combination antihypertensive medication containing amlodipine 5 mg, valsartan 180 mg, and hydrochlorothiazide 12.5 mg. The patient remained well with no recurrence of chest discomfort on follow-up.

Ischaemic chest pain is one of the clinical manifestations of apical hypertrophic cardiomyopathy (Ap-HCM) and is likely multifactorial. Demand-supply mismatch from the hypertrophied apical myocardium outgrowing its blood supply and therefore precipitating angina on effort is one proposed mechanism. Elevated wall stress during physical exertion, especially with shortened diastole during tachycardia is likely to induce symptoms due to subendocardial ischaemia. The hypertrophied muscle compressing the intramural coronary vessels may also contribute to the ischaemic symptoms. These mechanisms could explain the reversible ischaemia seen on the perfusion scan. A fixed perfusion defect would be indicative of an infarcted apex with possible aneurysmal transformation.

Noonan syndrome is characterized by mutations affecting the Ras/mitogen-activated-protein-kinase and is associated with a cardiac lesion in 80% of the cases. The most commonly reported lesion is pulmonary valve stenosis. Hypertrophic cardiomyopathy (HCM) is seen in nearly 20% of the subjects. When compared with HCM due to mutations altering sarcomeric proteins, RASopathy-associated-HCM manifests very early in life and more likely to be associated with congestive heart failure and higher LV outflow tract gradients. The association between Noonan syndrome and Ap-HCM is unknown.

In conclusion, Ap-HCM can present with typical ischaemic chest pain and an abnormal perfusion scan despite normal epicardial coronary arteries.

Panel A: Twelve-lead electrocardiogram. Sinus rhythm with one premature atrial contraction. There are clear voltage criteria for LV hypertrophy with deep T-wave inversion seen mainly in the lateral leads I, aVL, V5, and V6.
Panel B: Myocardial perfusion scan. (Panel B-1) Bull’s eye view during stress and rest showing a perfusion defect at the LV apex (star) which reperfuses in the resting state. (Panel B-2) Representative images from the standard vertical long-axis view. During stress, there is a moderate size, moderate intensity, reversible perfusion defect seen mainly at the LV apex (star). (Panel B-3) Representative images from the standard horizontal long-axis view showing an apical perfusion defect during stress that reperfuses during rest. Note dense uptake of radiotracer in the mid-cavity in the region of the papillary muscle (arrows).

Panel C: Contrast left ventriculogram. These still frames were obtained during LV diastole (right) and systole (left). They demonstrate the classic ‘spade-shaped’ configuration of the left ventricle in end-diastole. This pattern of contrast opacification is due to apical cavity obliteration by the hypertrophied apical myocardium.

Panel D: Gadolinium-enhanced cardiac magnetic resonance imaging. These are coronal images from the two-chamber view of the LV. Both the distal anterior and inferior walls as well as the true LV apex are severely thickened. No myocardial scarring or LV apical aneurysm is noted.

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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