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CASE REPORT
Coronary heart disease

A case report of myocardial infarction with non-obstructive coronary artery disease: Graves' disease-induced coronary artery vasospasm

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Background Coronary artery spasm can occur either in response to drugs or toxins. This response may result in hyper-reactivity of vascular smooth muscles or may occur spontaneously as a result of disorders in the coronary vasomotor tone. Hyperthyroidism is associated with coronary artery spasm.

Case summary A 49-year-old female patient with a 2-day history of intermittent chest pain and electrocardiographic evidence of myocardial ischaemia was referred for emergency coronary angiography. This revealed severe right coronary artery (RCA) and left main (LM) coronary artery ostial vasospasm, both subsequently relieved with administration of multiple doses intracoronary nitroglycerine. Intravascular optical coherence tomography showed absence of atherosclerosis and no evidence of thrombus or dissection confirming the diagnosis of coronary artery vasospasm. Laboratory tests of the thyroid function were performed immediately after coronary angiography revealing Graves' disease as the cause of vasospasm.

Discussion Our case represents a rare presentation of Graves' disease-induced RCA and LM coronary artery ostial vasospasm. In patients with coronary artery vasospasm thyroid function study should be mandatory, especially in young female patients.

Keywords Case report • Myocardial infarction • MINOCA • Coronary artery vasospasm • Thyrotoxicosis

Learning points

- Coronary artery spasm can be induced by a hyperactive thyroid.
- When angiography demonstrates spontaneous severe multivessel coronary artery vasospasm, the presence of a systemic condition as underlying cause should be considered.
- In patients with coronary artery spasm thyroid function study should be mandatory, especially for the young female patients.

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Introduction

Myocardial infarction in the absence of obstructive (>50% stenosis) coronary artery disease (MINOCA) is found in approximately 6% of all patients with acute myocardial infarction (MI) who are referred for coronary angiography.[1,2] The term MINOCA should be reserved for patients in whom there is an ischaemic basis for their clinical presentation and should be considered a 'working diagnosis'. There are a variety of causes that can result in MINOCA and it is important that patients are appropriately diagnosed so that specific therapies to treat the underlying cause can be prescribed when possible. Thus, in the evaluation of patients presenting with clinical evidence of MI and a rise or fall in cardiac biomarkers but absence of obstructive coronary artery disease (CAD) at coronary angiography, it is important to exclude (i) overt causes for the elevated troponin (e.g. sepsis, pulmonary embolism), (ii) overlooked obstructive disease (e.g. occlusion of a small coronary artery subsegment resulting from plaque disruption or embolism), and (iii) subtle non-ischaemic mechanisms of myocyte injury that can mimic MI (e.g. myocarditis).[3]Once abovementioned causes are excluded by use of available diagnostic resources, a diagnosis of MINOCA can be made.

There are disparate aetiologies causing MINOCA and they can be grouped into[2]:

(1) Atherosclerotic causes of myocardial necrosis (i.e. secondary to epicardial coronary artery disorders), such as atherosclerotic plaque rupture, ulceration, fissuring, erosion, or coronary dissection with non-obstructive or no CAD [MI Type 1 according to the 'Fourth Universal Definition of Myocardial Infarction' (2018)].[4]
(2) Non-atherosclerotic causes of myocardial necrosis (i.e. imbalance between oxygen supply and demand), such as epicardial coronary artery spasm, coronary microvessel dysfunction, coronary embolism/thrombosis, spontaneous coronary artery dissection, or systemic conditions resulting in supply-demand mismatch (e.g. tachyarrhythmias, anaemia, hypotension, thyrotoxicosis) [MI Type 2 according to the 'Fourth Universal Definition of Myocardial Infarction' (2018)].

We report a case of MINOCA with a rare underlying cause resulting in severe right coronary artery (RCA) and the left main (LM) ostial vasospasm.

Timeline

2 days prior to presentation	Start of intermittent chest pain.
2 h prior to presentation	Acute onset of severe chest pain, shortness of breath, and severe sweating.
At presentation at the referral hospital	Ongoing severe chest pain and electrocardiographic signs of ischaemia for which acute coronary syndrome medication was administered. Transfer of the patient to an interventional centre.
Arrival at our hospital (60 min after first medical contact)	Emergency coronary angiography was performed. This showed severe vasospasm of both ostia of the right coronary artery and left main coronary artery. After administration of intracoronary nitroglycerine, the electrocardiogram normalized and the patient was relieved from her symptoms.
90 min after arrival at our hospital	Thyroid values showed a severe overactive thyroid and strumazole was started.
After 2 days	The patient was transferred back to the referral hospital.

Continued

Case presentation

A 49-year-old previously healthy Caucasian woman presented to the emergency cardiac care department of a local hospital with a 2-day history of intermittent retrosternal chest pain. Since 2 h the pain worsened and she developed shortness of breath, nausea, and severe sweating. She was an active smoker and had a negative familial history for cardiovascular disease. She was not taking any regular medication and had no history of drug abuse. Physical examination documented a blood pressure of 185/92 mmHg, heart rate of 112 b.p.m., respiratory rate 25 per minute, and temperature 37.9°C. Heart sounds were normal on auscultation with no audible murmur. The rest of the clinical examination was unremarkable. The electrocardiogram showed a sinus tachycardia with widespread ST-segment depression in the inferior leads and leads V_4–V_6 with inverted T waves and ST-segment elevation in lead aVR and V_1 (*Figure 1*). Assuming an MI, a loading dose of aspirin 300 mg and ticagrelor 180 mg was administered and intravenous heparin 5000 IE was given. Moreover, metoprolol 2.5 mg intravenously was administered and nitroglycerine continuous infusion was started. Promptly, the patient was transferred to our hospital for emergency diagnostic coronary angiography. On arrival at the catheterization laboratory, the patient had continuous chest pain and her electrocardiogram (ECG) was unchanged. Coronary angiography revealed severe RCA and the LM ostial vasospasm (*Figure 2A* and *B*, Supplementary material online, *Movies S1* and *S2*), with dampening of the blood pressure tracings, both subsequently relieved with administration of multiple doses (200 µg/dose) intracoronary nitroglycerine (*Figure 3A* and *B*, Supplementary material online, *Movies S3* and *S4*). Intravascular optical coherence tomography (OCT) was performed showing both arteries without atherosclerosis, thrombus or dissection (*Figure 3C* and *D*, Supplementary material online, *Movies S5* and *S6*). Finally, left ventricular angiography showed no wall motion abnormalities (Supplementary material online, *Movie S7*). The patient was free of symptoms when she left the catheterization laboratory and the ECG was normalized.

Further investigation revealed a Troponin T maximum of 0.451 µg/L (range 0–0.05 µg/L), N-terminal pro-B-type natriuretic peptide of 293 ng/L (range 0–249 ng/L), elevated serum free thyroxine of 59.9 pmol/L (range 12–22 pmol/L), suppressed thyroid-stimulating

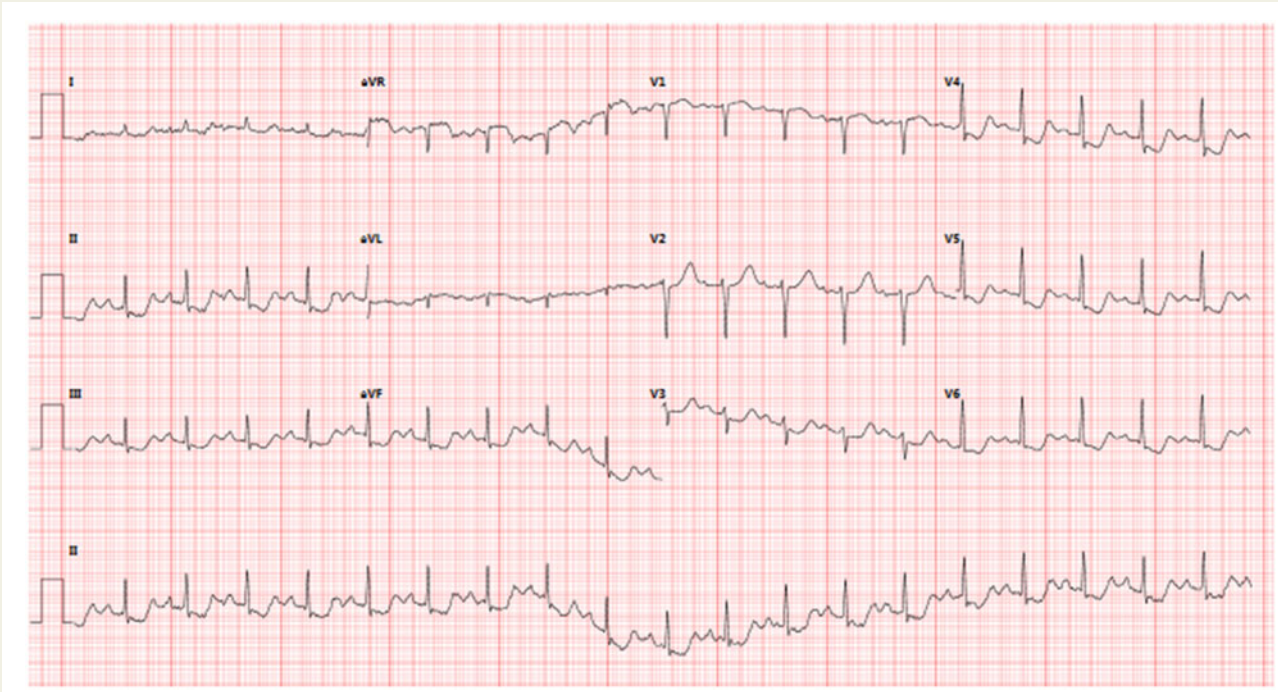

Figure 1 Admission electrocardiogram.

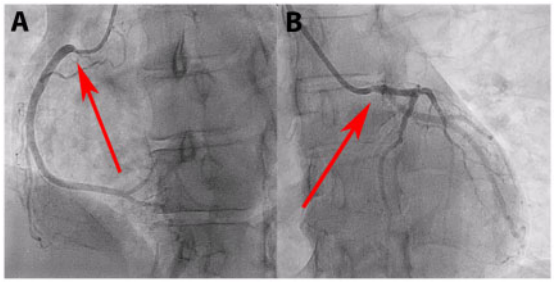

Figure 2 Coronary angiography showing severe right coronary artery (red arrow, *A*) and left main ostial vasospasm (red arrow, *B*).

hormone (TSH) of <0.001 mE/L (range 0.5–5 mE/L), and elevated TSH receptor antibody of 20.2 E/L (range 0–1.8 E/L), confirming the diagnosis of Graves' disease. Physical examination revealed a small nodule in the thyroid gland but no ophthalmological features. An thyroid ultrasound was not performed neither was a toxicology screen. The Burch–Wartofsky Point Scale (BWPS) score can predict the likelihood that biochemical thyrotoxicosis is thyroid storm. The BWPS is an empirically derived scoring system that takes into account the severities of symptoms of multiple organ decompensation, including thermoregulatory dysfunction, tachycardia/atrial fibrillation, disturbances of consciousness, congestive heart failure, and gastro-hepatic dysfunction, as well as the role of precipitating factors. A BWPS score of >45 represents a thyroid storm, between 25–45 an impending storm and <25 storm unlikely. Based on hyperthermia, tachycardia and gastrointestinal-hepatic dysfunction, the patients' score was 25 indicated an impending thyroid storm. She was started on thiamazole 30 mg o.d. and within 1 day of treatment serum free thyroxine lowered from 59.9 pmol/L to 42.6 pmol/L. Therefore, iodine therapy or surgery was not considered necessary. Dual antiplatelet therapy was discontinued and a long-acting nitrate and a dihydropyridine calcium channel blocker was prescribed till euthyroidism was restored. At telephone follow-up 1 week after discharge, she was free of symptoms and she experienced no side effects of the medication. As she was a labour migrant, she returned to her home country shortly thereafter.

Discussion

This report illustrates a case of multivessel coronary artery spasm secondary to Graves' disease. In our case, the presence of ST depression ≥1 mm in six or more surface leads, coupled with ST-segment elevation in aVR and/or V1, suggested multivessel ischaemia or LM coronary artery obstruction. Emergent coronary angiography was performed and showed severe ostial vasospasm of the RCA. To exclude the possibility of catheter-induced vasospasm, the initial visualization of the left coronary artery was performed by a non-selective injection which clearly showed severe vasospasm of the ostium of the LM. This severe ostial vasospasm of the RCA and the LM only improved after administration of multiple doses of intracoronary nitroglycerine. Hereafter, we decided to perform an OCT to rule out an atherosclerotic cause of myocardial necrosis. Optical coherence tomography showed a normal vessel wall with a typical three-layer appearance visible in both coronary arteries.[5] Additional laboratory

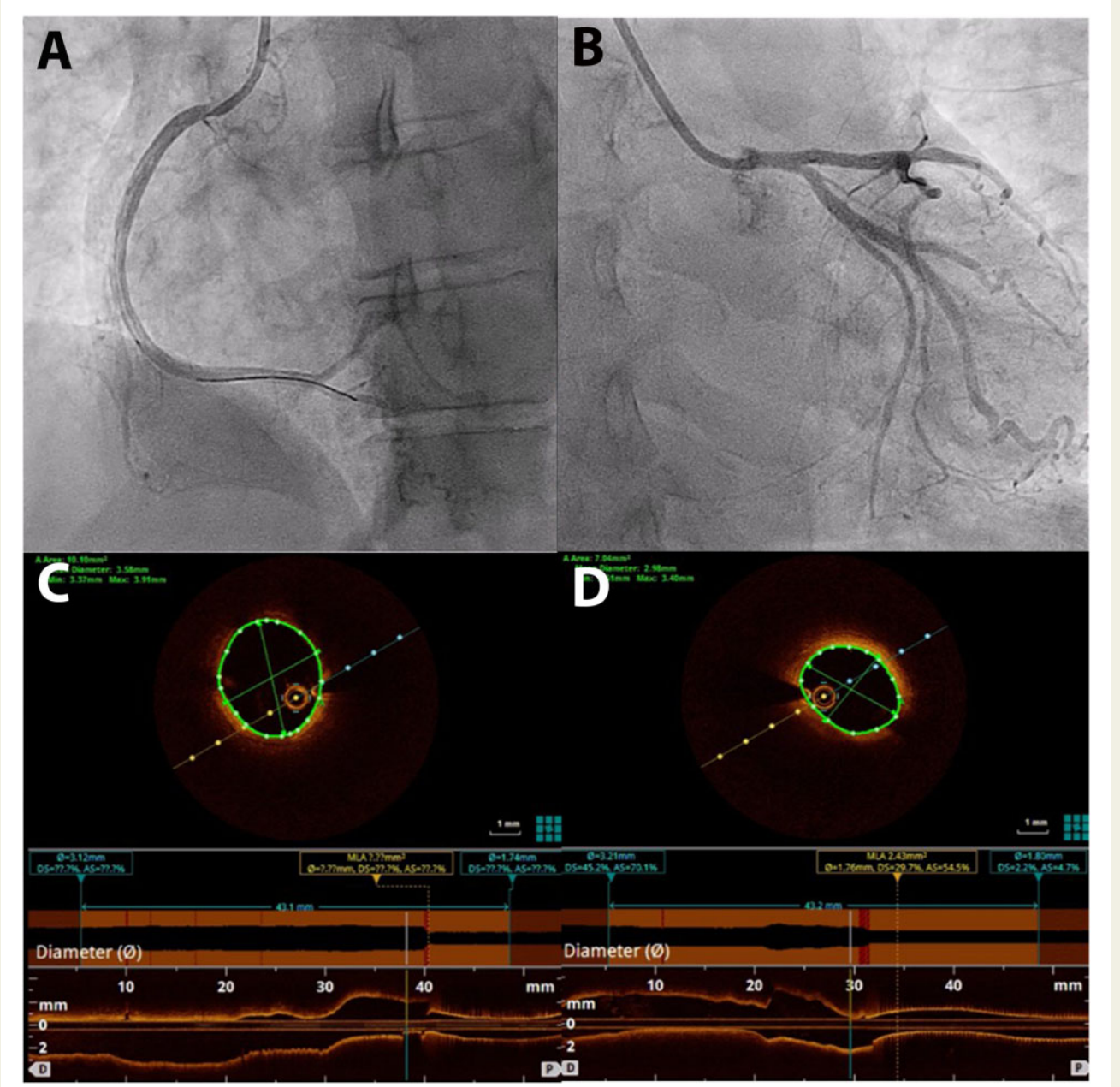

Figure 3 Coronary angiography after administration of nitroglycerine of the right coronary artery (*A*) and left coronary artery (*B*) and intravascular optical coherence tomography of the right coronary artery (*C*) and left coronary artery (*D*) showing absence of atherosclerosis, thrombus, or dissection.

testing revealed hyperthyroidism as a cause of multivessel coronary artery spasm. Although several reports of hyperthyroidism-associated angina pectoris (secondary to coronary spasm) have appeared, to our knowledge, this is one of the few cases with angiographically documented multivessel coronary artery spasm and the first report describing the use of intracoronary imaging with OCT.

Graves thyrotoxicosis is an autoimmune disease and is the most common cause of thyrotoxicosis. It is known that hyperthyroidism can cause coronary artery spasm, in particular in patients with Graves' disease as was the case in our patient. Multiple hypothetical pathophysiological pathways have been suggested for the mechanism of thyroid hormone-induced coronary artery spasm. Hyperthyroidism can lead to a hyperkinetic circulatory system with tachycardia, increased pulse pressure, and decreased peripheral resistance secondary to vasorelaxation.[6] Along with a hypersensitivity to vasoconstrictive agents, this general hypermetabolic state precipitates an imbalance between blood supply and oxygen demand during a thyrotoxic state.[7] The exaggerated vascular reactivity is secondary to an excessive endothelial nitric oxide production and enhanced sensitivity of the endothelial component which can lead to coronary

artery spasm in some patients.[6] Controlling thyroid activity will alleviate symptoms and correct the vascular abnormalities without the need of invasive interventions. In our case, laboratory tests of the thyroid function were only performed immediately after coronary angiography. Invasive coronary vascular imaging (intravascular ultrasound or OCT) can help to discriminate between an atherosclerotic vs. non-atherosclerotic cause of myocardial necrosis. Moreover, in MINOCA patients left ventricular angiography, echocardiography, or cardiac magnetic resonance imaging can rule out takotsubo cardiomyopathy or other underlying causes when there is no evident vasospasm at coronary angiography.

In a review by Al Jaber *et al.*[8] evaluating hyperthyroidism-associated angina pectoris, it was shown that the age range of reported patients was 44–75 years, with female predominance, more commonly in Asian patients, and the time from symptom onset to diagnosis varied between days to 8 months. Moreover, hyperthyroid manifestations may be mild or absent. The pattern of cardiac presentation included angina pectoris, MI, cardiogenic shock, ventricular tachyarrythmias, cardiac arrest, and/or pulmonary oedema. Importantly, a review of coronary angiograms in patients with an overactive thyroid showed that the LM coronary artery was significantly more involved than the RCA.[9] Delay in diagnosis of hyperthyroidism-induced myocardial necrosis in these patients may result in complications and unnecessary interventions. With appropriate antithyroid therapy, the prognosis of patients with hyperthyroidism-associated angina pectoris is excellent.[9,10]

Lead author biography

Margo Klomp, MD, PhD, MBA, is a General Cardiologist at the Dijklander Hospital in Noord-Holland, the Netherlands with specific interests in management.

Supplementary material

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

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

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) andassociated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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