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GRAND ROUND
Cardiovascular imaging

A case report of a myocardial ischaemic attack: a novel hyperenhancement pattern on cardiac magnetic resonance in focal ischaemic injury

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Background Delayed enhancement cardiac magnetic resonance (DE-CMR) is the reference standard for the non-invasive assessment of myocardial fibrosis. DE-CMR is able to distinguish ischaemic from non-ischaemic aetiologies based on differences in hyperenhancement distribution patterns. Hyperenhancement caused by ischaemic injury typically involves the endocardium, while hyperenhancement confined to the mid- and epicardial layers of the myocardium suggests a non-ischaemic aetiology.

Case summary This is a case of a 20-year-old male with an unremarkable medical history with an acute ST-elevation myocardial infarction. DE-CMR revealed two distinct patterns of hyperenhancement: (i) a 'normal' wavefront-ischaemic pattern, and (ii) multiple atypical mid-wall and epicardial areas of focal hyperenhancement. Invasive coronary angiography (ICA) and coronary computed tomographic angiography (CCTA) showed multiple intracoronary thrombi and distal emboli in the left anterior descending, ramus circumflexus, and in smaller branches of the LCA. All hyperenhancement patterns observed on DE-CMR perfectly matched the distribution territories of the affected coronary arteries.

Discussion This case with an acute myocardial infarction showed intracoronary thrombi and emboli on ICA and CCTA. Interestingly, DE-CMR showed two different patterns of hyperenhancement in the same territories of the coronary thrombi. This observation may challenge the concept that these non-endocardial areas of hyperenhancement on DE-CMR are always of non-ischaemic aetiology. It is hypothesized that occlusion of smaller distal branches of the coronary arteries may result in mid-wall or epicardial fibrosis as opposed to subendocardial fibrosis commonly found in patients with a large epicardial coronary occlusion. Clinicians should be aware of these atypical patterns to be able to initiate adequate medical therapy.

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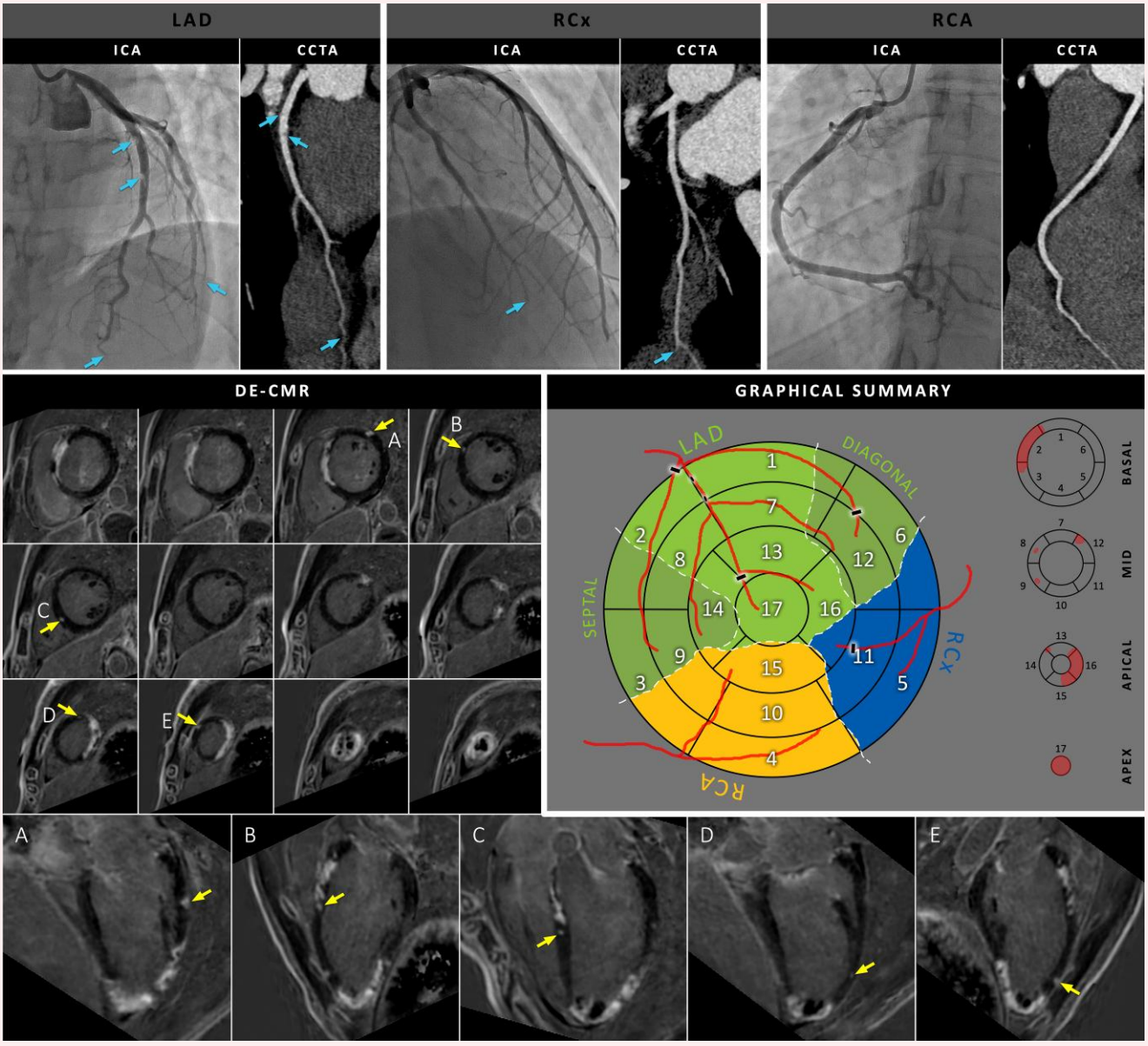
Graphical Abstract



Keywords ST-elevation myocardial infarction • Delayed enhancement cardiac magnetic resonance • Wavefront phenomenon • Myocardial ischaemic attack • Case report

ESC Curriculum 2.3 Cardiac magnetic resonance • 2.1 Imaging modalities • 2.4 Cardiac computed tomography • 3.2 Acute coronary syndrome • 3.4 Coronary angiography

Learning points

- To raise awareness that focal mid-wall and epicardial areas of hyperenhancement on DE-CMR may be of ischaemic origin.
- To demonstrate the value of advanced multimodality imaging in a patient presenting with an acute ST-elevation myocardial infarction.

Primary specialities involved other than cardiology

Radiology, clinical physics.

Introduction

Delayed enhancement cardiac magnetic resonance (DE-CMR) is the reference standard for the non-invasive assessment of myocardial fibrosis.[1] DE-CMR is able to distinguish ischaemic from non-ischaemic aetiologies based on differences in hyperenhancement distribution patterns. Ischaemic injury caused by an epicardial coronary occlusion typically starts with myocyte necrosis in the endocardium and progresses as a wavefront towards the epicardium, ultimately resulting in transmural myocardial infarction (MI). Hence, hyperenhancement caused by ischaemic injury typically involves at least the endocardium, while hyperenhancement confined to the mid- and epicardial layers of the myocardium suggest a non-ischaemic origin.[2]

Interestingly, small non-endocardial areas of hyperenhancement are commonly observed in patients presenting with suspected acute non-ST elevation MI (*Figure 1*). These focal lesions are often characterized as non-ischaemic because of their atypical localization, generally not involving the endocardium. However, the observation of these lesions in patients with obstructive coronary artery disease may question this tenet. We hypothesize that both patterns can be of ischaemic aetiology and focal hyperenhancement occurs due to obstruction of the microvasculature following distal embolization. Occlusion of smaller (intramyocardial and microvasculature) coronary arteries may result in mid-wall or epicardial fibrosis as opposed to a typical subendocardial MI observed after occlusion of a large epicardial coronary artery. The origin of these focal non-endocardial lesions may have important implications for medical therapy, especially in patients in whom the diagnosis is unclear when for instance larger epicardial coronary artery disease is absent.

Timeline

20 March 2021	Patient admitted to the emergency department with new onset chest pain. The electrocardiogram (ECG) showed significant ST-segment elevation and reciprocal ST-segment depression during an episode of increased chest pain. Invasive coronary angiography (ICA) showed multiple intraluminal thrombi and occlusion of the distal left anterior descending (LAD) coronary artery, ramus circumflexus (RCx), and multiple smaller branches of the left coronary artery. At this moment, the differential diagnosis was a thrombo-embolic MI or spontaneous coronary artery dissection with thrombus formation and distal embolization. Treatment with intravenous tirofiban and dual antiplatelet therapy was initiated. During ICA, the patient became asymptomatic and his ECG showed regression of the ST-segment deviation accordingly.
22 March 2021	Coronary computed tomographic angiography (CCTA) showed multiple soft plaque lesions in the LAD and RCx (distal smaller branches) compatible with intracoronary thrombi.
23 March 2021	Dark-blood DE-CMR imaging showed transmural infarction as well as several focal hyperenhanced areas in the mid-myocardial and epicardial layers. These focal mid- and epicardial lesions perfectly matched the perfusion territory of the coronary arteries affected by thrombi as observed on ICA and CCTA and therefore are considered a result of ischaemic injury. Furthermore, an apical intraventricular thrombus was observed for which additional treatment with therapeutic low-molecular weight heparins was initiated.
29 March 2021	Patient remained asymptomatic during admission and was discharged on triple antithrombotic therapy (aspirin, clopidogrel, and vitamin K antagonist) for 1 month, followed by clopidogrel and a vitamin K antagonist thereafter.
17 May 2021	Extensive examination for an underlying condition was unremarkable, especially with regard to coagulation disorders or fibromuscular dysplasia.
30 August 2021	Follow-up transthoracic echocardiogram (TTE) showed regional wall motion abnormalities consistent with an anteroseptal and apical wall infarction. An apical intraventricular thrombus was no longer observed.
10 December 2021	Repeated DE-CMR recapitulated echocardiography findings and the hyperenhancement patterns remained identical. As no intraventricular thrombus was observed on DE-CMR, vitamin K antagonist was converted to acetylsalicylic acid in addition to clopidogrel. Follow-up was planned at the outpatient clinic cardiology with a TTE in 1 year.

Case presentation

A 20-year-old man with an unremarkable medical history was admitted to the emergency department with acute chest pain. He was an active smoker and had no family history of premature atherosclerosis. At presentation, haemodynamic measurements and physical examination were normal. The ECG showed mild ST-segment elevation in Leads III and V1-2 without reciprocal ST-segment depression (*Figure 2A*). Transthoracic echocardiography showed akinesia of the basal anteroseptal segment and apical inferior and lateral wall segments. Left ventricular ejection fraction was 45–50%. Shortly thereafter, chest pain increased, and the ECG changed significantly with ST-segment elevation in Leads II, III, aVF, and V6, with ST-segment depression in Leads V1–V5 (*Figure 2B*). These findings are suggestive of a diagnosis of ST-elevation MI. Possible aetiologies include plaque rupture or erosion, coronary artery spasm, spontaneous coronary artery dissection, and thrombo-embolism. Differential diagnoses were myocarditis, Takotsubo cardiomyopathy, and pulmonary embolism. Although non-coronary pathology was considered highly unlikely due to the clinical presentation and dynamic ECG changes correlated to patient's complaints, it could not be excluded at this point.

Immediate ICA was performed, showing multiple intraluminal thrombi (mid segment LAD with TIMI III flow) and occlusion of the

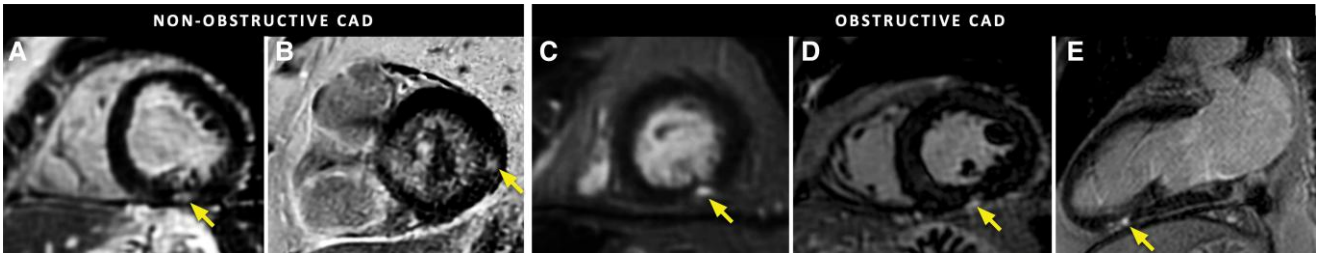


Figure 1 Focal non-endocardial hyperenhancement observed on delayed enhancement cardiac magnetic resonance imaging in patients with acute myocardial infarction. Five delayed enhancement cardiac magnetic resonance imaging examples of atypical focal areas of hyperenhancement in the mid- and epicardial layers of the myocardium (indicated by arrows) in a series of patients with suspected acute non-ST-elevation myocardial infarction based on symptoms, ECG, and cardiac biomarkers. Following invasive coronary angiography, non-obstructed coronary arteries were found in the first two examples (*A* + *B*), hinting towards a non-ischaemic aetiology for the focal hyperenhancement areas. However, similar atypical focal hyperenhancement patterns were found in three cases with obstructed coronary arteries (*C* + *D* + *E*), and likely reflect an ischaemic origin in these cases. Imaging planes: short-axis view (*A* + *B* + *C* + *D*) and two-chamber long-axis view (*E*). CAD, coronary artery disease.

distal segments of the left anterior descending (LAD and diagonal branch) and circumflex (RCx) coronary artery (*Figure 3*, upper panels). The right coronary artery showed no abnormalities. During ICA, patient became asymptomatic and his ECG showed regression of the ST-segment changes (*Figure 2C*). Initially, at the time of the procedure, the differential diagnosis of the observed intracoronary thrombi was a thrombo-embolic MI with distal embolization or a spontaneous coronary artery dissection with thrombus formation. Therefore, no coronary intervention was performed, but as distal embolization was suspected the patient was treated with an intravenous glycoprotein IIb/IIIa inhibitor (tirofiban) and dual antiplatelet therapy afterwards. Laboratory results showed a high-sensitive troponin-T (hs-TnT) peak value of 5146 [<14] ng/L, and creatinine kinase reached a maximum of 2571 [<225] U/L with a creatinine kinase-MB fraction of 204.9 [<4.9] μg/L. Recent drug abuse was excluded with urine toxicology screening. To assess the efficacy of the initiated antithrombotic therapy, CCTA was performed 2 days afterwards. Three soft plaque lesions in the LAD, distal embolization of the first diagonal branch and RCx were observed (*Figure 3*, upper panels). The intraluminal lesions in the mid-LAD on prior ICA were considered to be compatible with intracoronary thrombi. At day 3, CMR was performed to evaluate left ventricular dimensions, function, and infarct size in this young patient. Cine imaging showed akinesia of the mid-basal anterior-anteroseptal, apical inferior-lateral wall segments and true apex with a left ventricular ejection fraction of 47%. Dark-blood DE-CMR showed transmural infarction of the mid-basal septal, apicolateral, and apical segments.[3] In addition, several focal hyperenhanced areas in the mid-myocardial and epicardial layers of the apico-anterior, apico-septal, mid-septal, and basal anterolateral segments were observed in the stack short-axis images, corresponding to LAD and RCx territory (*Figure 3*, middle left panel). The orthogonal long-axis views confirmed that all five observed areas of focal non-endocardial hyperenhancement are clearly isolated and not contiguous with proximal or distal scar (*Figure 3*, lower panels). Furthermore, a mural intraventricular thrombus was observed in the apex. Since this patient was admitted during the COVID-19 pandemic, routine SARS-CoV-2 polymerase chain reaction testing was performed. Although a 'weak' positive test result was obtained (cycle threshold 42), the patient lacked classic respiratory symptoms and fever. No signs of inflammation were observed, as inflammatory markers C-reactive protein < 1 [<10] mg/L and leucocytes 7.6 [3.5–11.0] × 10^9 were not elevated, in addition no characteristic parenchymal abnormalities on CT (i.e. ground-glass opacities, consolidations) were observed.

The patient received triple antithrombotic therapy for 1 month, followed by clopidogrel and a vitamin K antagonist thereafter. The patient had an uneventful recovery and was discharged after 9 days. At 1 year follow-up, no events had occurred. An overview of the follow-up period is given in the timeline.

Discussion

In this case report, a case of a young man who presented with an acute ST-elevation MI is described, showing intracoronary thrombi and distal embolization on both ICA and CCTA. DE-CMR uniquely showed two distinct hyperenhancement patterns: (i) typical transmural MI, and (ii) multiple mid-wall and epicardial areas of focal hyperenhancement. Although the latter may have been commonly interpreted as of non-ischaemic origin, the focal hyperenhancement lesions observed in the current case; however, perfectly match the perfusion territory of the coronary arteries filled with thrombi and emboli. Despite the lack of histopathological validation, the multimodality imaging in this case supports our hypothesis that focal mid- and epicardial lesions may be the result of ischaemic injury and challenges the concept that these lesions are confined to non-ischaemic origin.

Given the context of COVID-19 infection, it would seem plausible that there is myocardial inflammation. However, since the spatial distribution of the focal areas of scar exactly matches the location of the intracoronary thrombi on CCTA and ICA, myocardial inflammation as underlying cause for focal scar is highly unlikely in this case. In addition, only a 'weak' positive cycle time (42) was observed, patient lacked classical symptoms of a COVID-19 infection and inflammatory markers were normal. Furthermore, the clinical context with sudden worsening of chest pain accompanied by extensive ST-segment deviation is compatible with an acute MI caused by an abrupt occlusion of a coronary artery. Finally, thrombus formation may have been caused by a hypercoagulable state as a result of COVID-19. A pathological study in patients with COVID-19 observed microthrombi as a major cause of cardiac injury and commonly causing focal necrosis.[4]

Although literature on this topic is scarce, prior research has shown that DE-CMR is capable of visualizing small areas (<1 g myocardial tissue) of myocyte necrosis.[5] In a few studies using DE-CMR following percutaneous coronary interventions and transcatheter aortic valve replacement, comparable hyperenhancement patterns have been described.[5–7] Small embolic complications to the microvasculature as a result of these transcatheter procedures, plaque rupture with distal embolization or other causes of intracoronary thrombus (e.g.

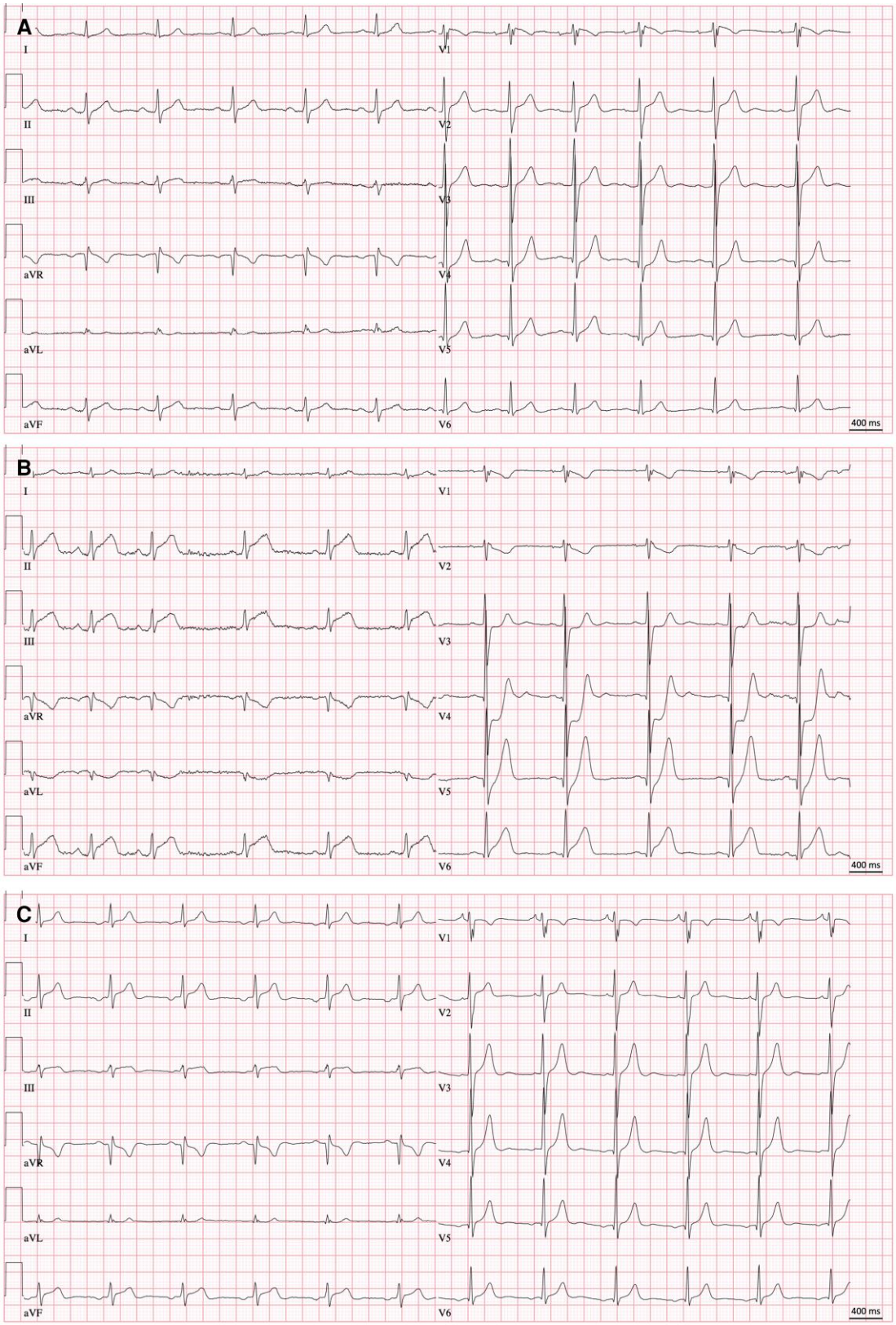


Figure 2 Electrocardiograms. (*A*) Electrocardiogram at presentation, showing mild ST-segment elevation in Leads III and V1-2 without reciprocal ST-segment depression. (*B*) Electrocardiogram with worsening chest pain, showing significant ST-segment elevation in Leads II, III, aVF, and V6, and ST-segment depression in Leads V1–V5. (*C*) Electrocardiogram post invasive coronary angiography and without chest pain, showing regression of the ST-segment changes.

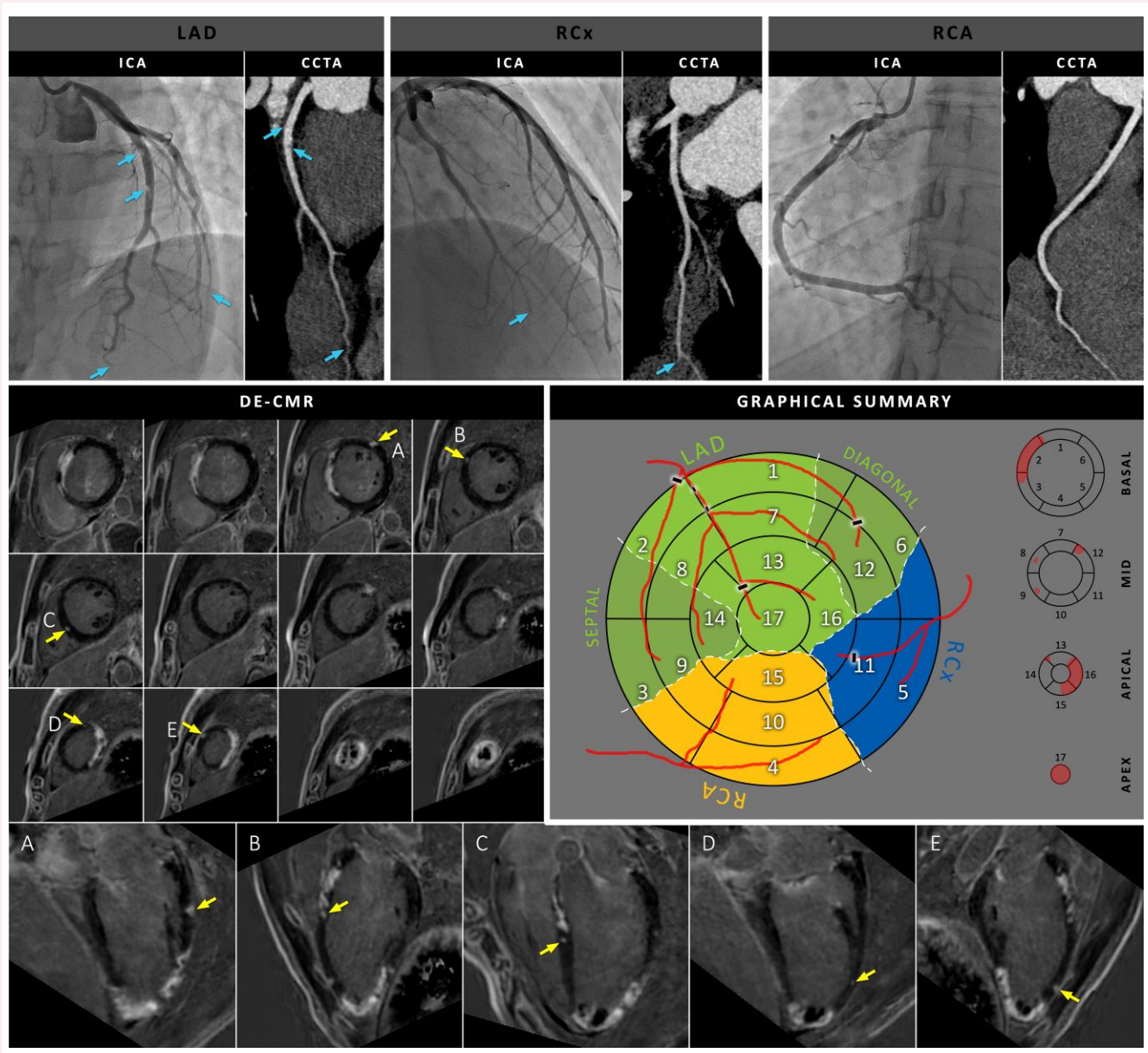


Figure 3 Multimodality imaging using invasive coronary angiography, coronary computed tomographic angiography, and delayed enhancement cardiac magnetic resonance. Upper panels: representative invasive coronary angiography stills and corresponding multiplanar coronary computed tomographic angiography images showing the left anterior descending, ramus circumflexus, and right coronary arteries. The arrows indicate the intracoronary thrombi and distal embolization. Middle left panel: short-axis delayed enhancement cardiac magnetic resonance images showing both transmural (not indicated) and focal mid-epicardial hyperenhancement (arrows *A*–*E*). Also the earlier described intracardiac apical thrombus can be observed in the two most apical views. Lower panels: corresponding orthogonal long-axis delayed enhancement cardiac magnetic resonance images of the five isolated areas with focal mid-epicardial hyperenhancement observed on short-axis views (*A*–*E*). Middle right panel: graphical summary of the coronary anatomy and their perfusion territories, as derived from the invasive coronary angiography and coronary computed tomographic angiography images, superimposed on the 17-segment AHA model. Coronary artery occlusions and thrombi (in the left anterior descending) are marked using black bars and dots, respectively. Four schematic slices on the right illustrate the hyperenhancement patterns as observed on delayed enhancement cardiac magnetic resonance. Note that the perfusion territory of the coronary arteries with thrombi perfectly matches the hyperenhancement patterns observed on delayed enhancement cardiac magnetic resonance.

hypercoagulability) may cause a 'myocardial ischaemic attack (MIA)'. This defines a novel hyperenhancement pattern on DE-CMR of focal ischaemic myocardial injury that is not strictly confined to the endocardium. Clinicians should be aware of these atypical ischaemic manifestations, as is also shown in this case report. Arguably, patients with MIA may benefit from pharmacological and non-pharmacological secondary prevention of coronary artery disease by for instance statins and antiplatelet therapy as well as cardiac rehabilitation.

Conclusion

Atypical focal mid-wall and epicardial areas of hyperenhancement on DE-CMR are regularly observed in patients with acute chest pain. These focal lesions are commonly considered to be of non-ischaemic origin. In this case, we demonstrate, supported by multimodality imaging, that focal mid-wall or epicardial areas of fibrosis may be caused by occlusions/emboli of distal coronary branches or microvasculature, and an ischaemic origin should be considered in such patients.

Lead author biography

Dr Hedwig Nies completed her medical training at the Maastricht University Medical Centre, Maastricht, The Netherlands. Dr Nies has a special interest in cardiovascular pathology and surgical approaches. She spent time at Texas Heart Institute (THI) Houston, at the Cardiovascular Surgery Service under the tutelage of Dr. Denton A. Cooley. Currently, she is working on her PhD regarding cardiac magnetic resonance imaging in patients with (supra)ventricular arrhythmias.

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.

Conflict of interest: None declared.

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