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**GRAND ROUND**
*Cardiac imaging*

# A case report of myocardial infarction with non-obstructive coronary arteries as the initial presentation of eosinophilic granulomatosis with polyangiitis

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**Background** Eosinophilic granulomatosis with polyangiitis (EGPA) is a multisystem disorder commonly affecting the lung and skin, with cardiovascular involvement found in up to 60% of patients. We present a case of myocardial infarction with non-obstructive coronary arteries (MINOCA) as the initial presentation of EGPA.

**Case summary** A 52-year-old female with past medical history of asthma, recurrent sinusitis, and peripheral neuropathy presented to our hospital with chest pain, rash, acute vision loss, elevated troponin, and peripheral eosinophilia. Electrocardiogram showed no ischaemic changes and coronary angiography displayed normal coronary anatomy. On a subsequent visit, cardiac magnetic resonance (CMR) showed predominant focal anteroseptal and inferoseptal akinesis with focal sub-endocardial delayed enhancement, indicative of a myocardial infarction involving the septal branches of the left anterior descending artery. Due to the focal findings on CMR, peripheral eosinophilia, and rash, the patient was evaluated for EGPA. Rheumatologic workup and skin biopsy were suggestive of small vessel vasculitis. The patient was diagnosed with multi-organ EGPA, involving the coronaries, which was ultimately thought to be the aetiology of her MINOCA. Following steroid and monoclonal antibody therapy, the patient experienced notable improvement in her cardiac function at follow-up appointments.

**Discussion** This is a unique case MINOCA as the initial presentation of EGPA. Considering the heterogeneous disease presentation of those diagnosed with MINOCA, utilization of CMR is essential to guide diagnosis and management of such patients.

**Keywords** MINOCA • EGPA • Vasculitis • CMR • Late gadolinium enhancement (LGE) • Case report

**ESC Curriculum** 2.1 Imaging modalities • 2.3 Cardiac magnetic resonance • 6.2 Heart failure with reduced ejection fraction

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## Learning points

- Myocardial infarction with non-obstructive coronary arteries (MINOCA) can have a heterogeneous disease presentation and utilization of cardiac magnetic resonance (CMR) is essential to guide the diagnosis and management of such patients.
- In cases of MINOCA, CMR provides a diagnosis, in most of the patients, if done within a short follow-up of index hospitalization.

## Specialties other than cardiology involved

Dermatology, Rheumatology

## Introduction

Eosinophilic granulomatosis with polyangiitis (EGPA), previously known as Churg-Strauss Syndrome, is a rare, small to medium vessel vasculitis, recognized as one form of antineutrophil cytoplasm antibody-associated vasculitis. Hallmarks of EGPA include asthma, chronic rhinosinusitis, and peripheral neuropathy.[1] The average age of diagnosis is 50 and the disease typically manifests in several phases: the prodromal, eosinophilic, and vasculitis phase. The prodromal phase occurs in the second and third decades of life and is characterized by atopic dermatitis, allergic rhinitis, and asthma. The eosinophilic phase is notable for peripheral blood eosinophilia and eosinophilic infiltration of multiple organs, particularly involving the lung and gastrointestinal system. The vasculitis phase is characterized by a life-threatening systemic vasculitis of the medium and small vessels.[1–3] While there are no laboratory tests specific for EGPA, a combination of clinical findings can aid in the diagnosis. Characteristic findings include peripheral eosinophilia, elevated serum immunoglobulin E (IgE), positive rheumatoid factor, and chest radiograph abnormalities including patchy opacities.[4]

In this case, we report EGPA manifesting as the vasculitis of the small intra-myocardial vasculature leading to a diagnosis of myocardial infarction with non-obstructive coronary arteries (MINOCA). Numerous cases have reported myocardial infarction as a sequela of EGPA.[5,6] Notably, up to 60% of patients with EGPA have documented cardiac involvement.[7] Myocardial infarctions are typically caused by coronary artery disease, with coronary thrombosis being a major contributing factor. Less commonly, myocardial infarctions have occurred without significant coronary artery stenosis, as found on coronary angiography or on computed tomography coronary angiography.[5] This clinical constellation has more recently been recognized as MINOCA. MINOCA represents a heterogeneous group of cardiovascular diseases that clinically present as myocardial infarction but have normal to near-normal coronary angiograms.[8] The most common causes of MINOCA include variants of coronary artery disease—spasm, dissection, plaque rupture, and erosion with spontaneous coronary thrombolysis—as well as Takotsubo cardiomyopathy, myocarditis, and microvascular coronary embolism.[8] Coronary vasospasm, though rare, has been documented in EGPA.[5,6,9] While the exact mechanism of coronary vasospasm in EGPA is unclear, it is hypothesized that eosinophilic infiltration of the arterial walls leads to a cascade of chemokines and other inflammatory markers that cause segmental vasoconstriction of the coronary arteries.[9]

## Timeline

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| Day 1 | A 52-year-old female with past medical history significant for asthma, seasonal allergies, and recurrent sinusitis presented with right-sided vision loss and 3 days of chest pain with elevated troponin. |
| Day 2 | Transthoracic echocardiogram showed a left ventricular ejection fraction of 25%, global hypokinesis with predominant septal involvement. |
| Day 4 | Coronary angiography showed normal coronary arteries. |
| Day 5 | Discharged on guideline-directed medical therapy for newly diagnosed Heart failure with reduced ejection fraction (HFrEF). |
| Day 16 | Re-admitted with shortness of breath, bilateral upper extremity weakness, and rash. A biopsy was obtained of the skin rash. Cardiac magnetic resonance showed an ejection fraction of 45% and focal delayed enhancement of the interventricular septum. |
| Day 17 | Histopathology of skin biopsy resulted as small vessel vasculitis, likely EGPA. |
| Day 18 | Treated with methylprednisolone for underlying EGPA involving the coronaries. |
| Day 19 | Patient was discharged on a steroid taper with close follow-up given her diagnosis of multi-organ EGPA with involvement of the coronary arteries. |
| Follow-up at 2 years | Cardiac magnetic resonance demonstrated a focal aneurysm in the distal inferoseptum and mid anteroseptum, precisely at the location of the previously noted delayed enhancement and an ejection fraction of 48%. |

## Case presentation

A 52-year-old female of African American origin, with past medical history significant for asthma, seasonal allergies, recurrent sinusitis, and recently diagnosed peripheral neuropathy presented to our tertiary care centre with chief complaint of intermittent substernal chest pain and acute vision loss. The chest pain began during an argument, lasted for only a few minutes, and was noted to be centrally located with right shoulder radiation. The visual deficit was described as a

'burnt foil' covering the patient's left eye. Of note, the patient had recently received a diagnosis of peripheral neuropathy at an outside hospital for which she was started on gabapentin therapy. Our patient's family history was significant for hypertension in her mother and alcohol dependence and cardiovascular disease in her father. She denied any history of tobacco, alcohol, or illicit drug use. Upon presentation to the emergency department, she was noted to have the following vitals: afebrile, heart rate: 87–106 beats per minute (b.p.m.), blood pressure: 116–155/80–96, and oxygen saturation: 93–96% on room air. Cardiovascular exam revealed a regular rate and rhythm, normal S1 and S2 heart sounds, no jugular venous distention, and no murmurs. Pulmonary exam revealed lungs, which were clear to auscultation bilaterally. No gross deficits were noted on neurological exam and extremities did not reveal any peripheral oedema. On ophthalmological exam, the right eye revealed a large area of whitening of the retina with a cherry red macula and left eye was largely unremarkable. Laboratory results were significant for white blood cell (WBC): 18.85 bil/L (ref: 3.4–10.8 ×10E3/μL), haemoglobin (Hgb): 13.5 g/dL (ref: 11.1–15.9 g/dL), platelets: 345 10E3/μL (ref: 150–450 ×10E3/μL), K: 3.3 mm/L (ref: 3.5—5.2 mmol/L), Troponin: 0.33 ng/mL (ref: ≤0.03 ng/mL), and Creatine kinase myocardial band (CKMB): 8.9 ng/mL (ref: 0.0–7.5 ng/mL). Electrocardiogram (ECG) demonstrated sinus rhythm without ischaemic changes (*Figure 1*). She was started on a heparin infusion and admitted for evaluation of non-ST-elevation myocardial infarction (NSTEMI), with a peak troponin I level of 0.45 ng/mL. A transthoracic echocardiogram (TTE) was obtained, demonstrating a left ventricular ejection fraction (EF) of 25%, with global hypokinesis with more predominant septal involvement and preserved wall thickness. A moderate decrease in right ventricular systolic function was also noted, without any signs of valvular disease (*Figure 2A* and *B*). Given these findings, the patient was referred for coronary angiography which noted normal coronary arteries (*Figure 3A* and *B*). From an ophthalmology perspective, she was diagnosed with central retinal artery occlusion of her right eye and was outside the window to undergo hyperbaric oxygen protocol. With slight improvement in her vision, additional workup including carotid ultrasound and rheumatological work up was initiated and she was advised to follow-up as outpatient. Regarding the newly diagnosed systolic heart failure, the patient's chest pain had improved, and she was medically optimized with guideline-directed medical therapy including angiotensin-converting enzyme inhibitor (ACE-i), beta blockade (BB), and statin therapy. Further diagnostic workup including multimodality imaging and laboratory work up was to be completed on an outpatient basis.

The patient was readmitted to our facility 11 days later, with recurrent complaints of shortness of breath, bilateral upper extremity rash, and generalized fatigue. Labs were again notable for a persistent leucocytosis with WBC 18.44 bil/L (ref: 3.4–10.8 ×10E3/μL), Hgb 12.3 g/dL (ref: 11.1–15.9 g/dL), an unremarkable chemistry panel, a Troponin upon presentation at 1.8 ng/mL (ref: ≤0.03 ng/mL) with peak at 2.27 ng/mL, CKMB: 22.8 ng/mL (peak) (ref: 0.0–7.5 ng/mL), and peripheral eosinophil percentage of 67.2 (ref: 0.0–6.5%). ECG during this admission showed sinus tachycardia (heart rate: 105) without ischaemic changes. In the setting of NSTEMI, unremarkable ECG, normal coronary arteries on recent angiogram, and recent diagnosis of MINOCA just 11 days prior, the patient was referred for cardiac magnetic resonance (CMR) imaging which showed an EF of 45% with global hypokinesis with regional involvement. There was predominant focal anteroseptal and inferoseptal akinesis with focal sub-endocardial delayed enhancement, indicative of myocardial infarction involving the septal branches of the left anterior descending artery (*Figure 4A* and *B*). Due to the focal findings on CMR, peripheral eosinophilia, rash, and acute vision loss, the patient was evaluated for EGPA. A multidisciplinary approach was pursued, including dermatology for biopsy of the rash and rheumatology for evaluation of possible vasculitis. Rheumatological workup was significant for

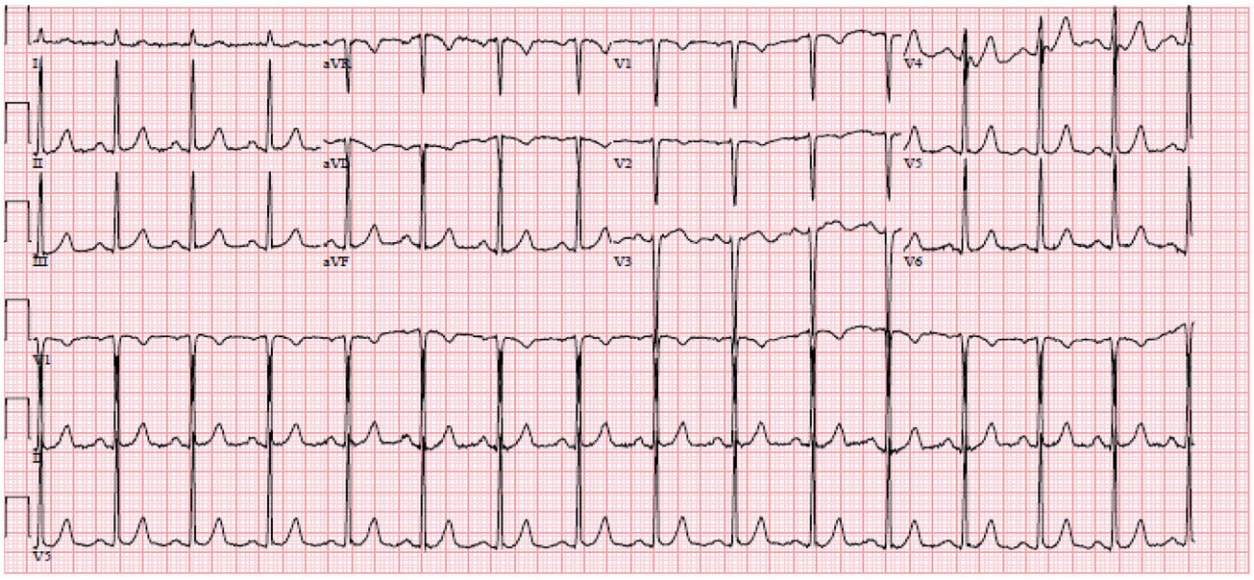


**Figure 1** Electrocardiogram showing sinus rhythm without acute ischaemic changes.

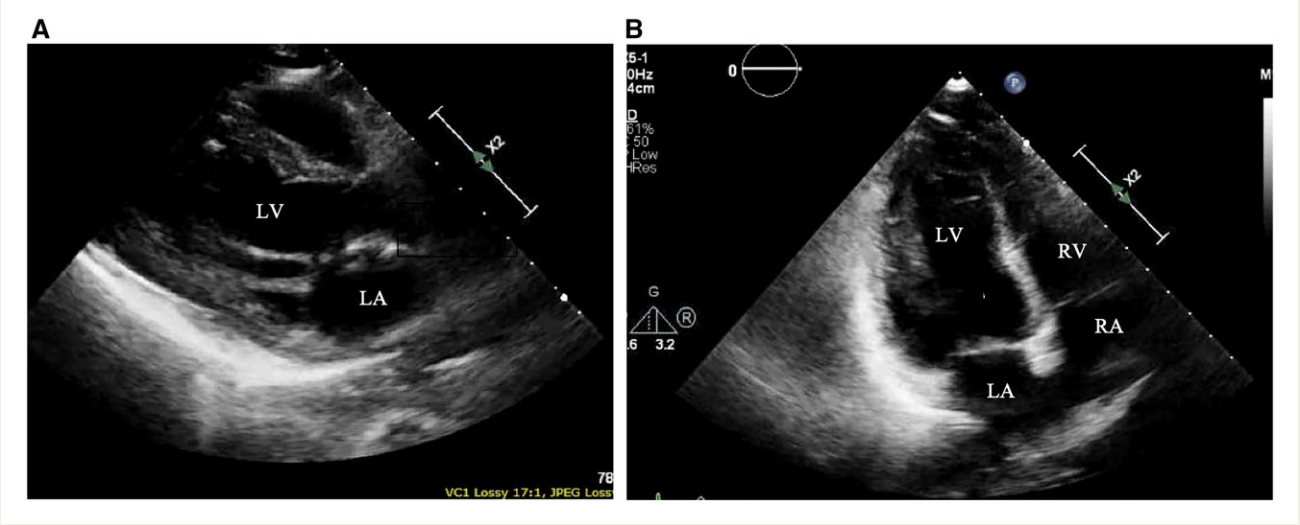


**Figure 2** (*A*) Parasternal long-axis cardiac view. (*B*) Four-chamber cardiac view. (*A* and *B*) Non-dilated, non-hypertrophied left ventricle. Akinetic basal to mid anterolateral, inferolateral, inferior wall with preserved wall thickness. Left ventricular ejection fraction ~25%. Moderate decrease in right ventricular systolic function. No significant valvular disease and normal filling pressures.

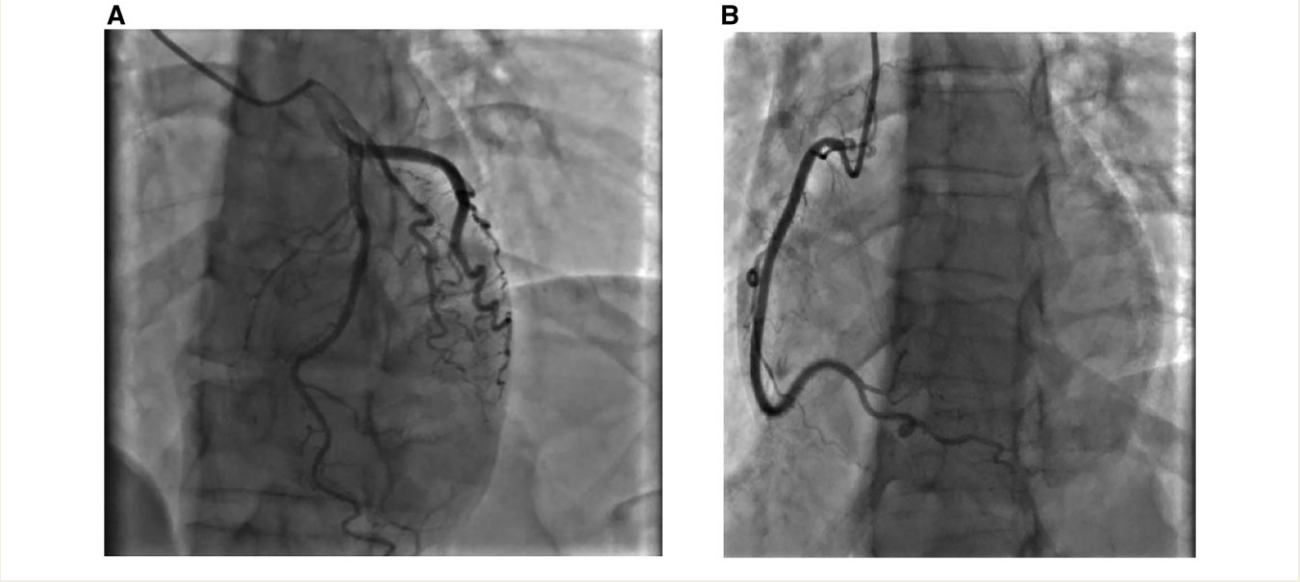


**Figure 3** (*A*) Radial approach of coronary angiography showing normal coronary arteries. (*B*) Right anterior oblique view displaying patent right coronary artery.

elevated inflammatory markers including erythrocyte sedimentation rate 44 mm/h (ref: 0–30 mm/h) and C-reactive protein 5.5 mg/dL (ref: 0–0.8 mg/dL). Serum IgE was also elevated at 772 IU/mL (ref: 0.0–100.0 IU/mL), along with rheumatoid factor 46.8 IU/mL (ref: 0–20 IU/mL). Skin biopsy of the peripheral rash demonstrated leucocytoclasis, which was indicative of small vessel vasculitis. An enhanced diagnosis of EGPA involving multiple systems including coronary vasculature leading to MINOCA was made. Patient was initially treated with methylprednisolone 16 mg intravenous every 8 h for 2 days and then transitioned to Prednisone 60 mg per oral for 1 month with directions to decrease by 10 mg every 2 weeks until on 30 mg daily. The patient was also started on Rituximab 375 mg/m$^2$, which she continues to receive on a weekly basis. During follow-up at approximately 6 months, the patient reported improvement in exercise tolerance and orthopnoea but continued to report intermittent chest pain. Two years later, the patient underwent a subsequent CMR to

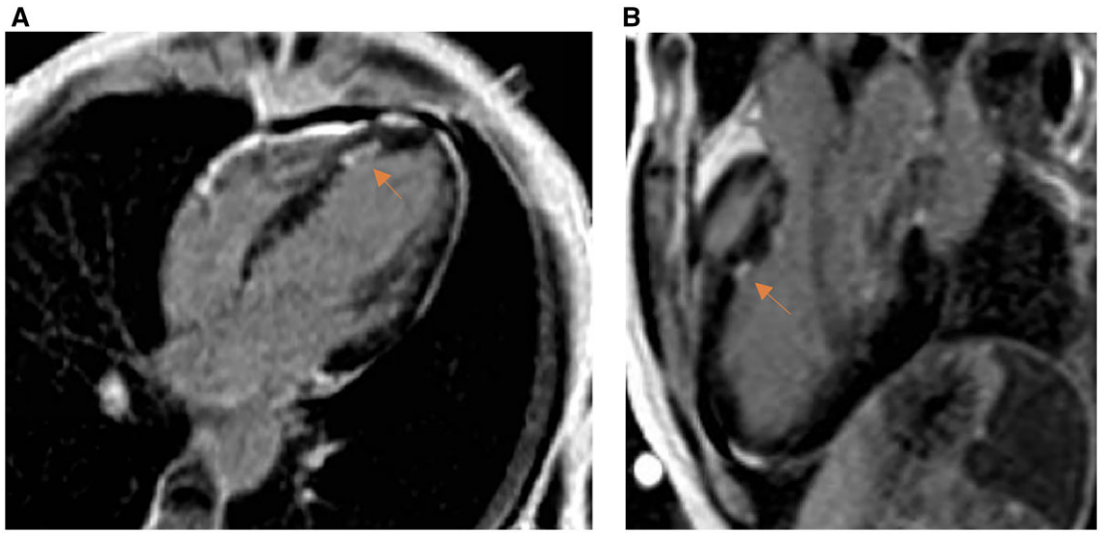


**Figure 4** (*A*) A four-chamber delayed enhancement image showing focal subendocardial delayed enhancement in the distal inferoseptal region. (*B*) A three chamber delayed enhancement image showing focal subendocardial delayed enhancement in the mid anteroseptal region.

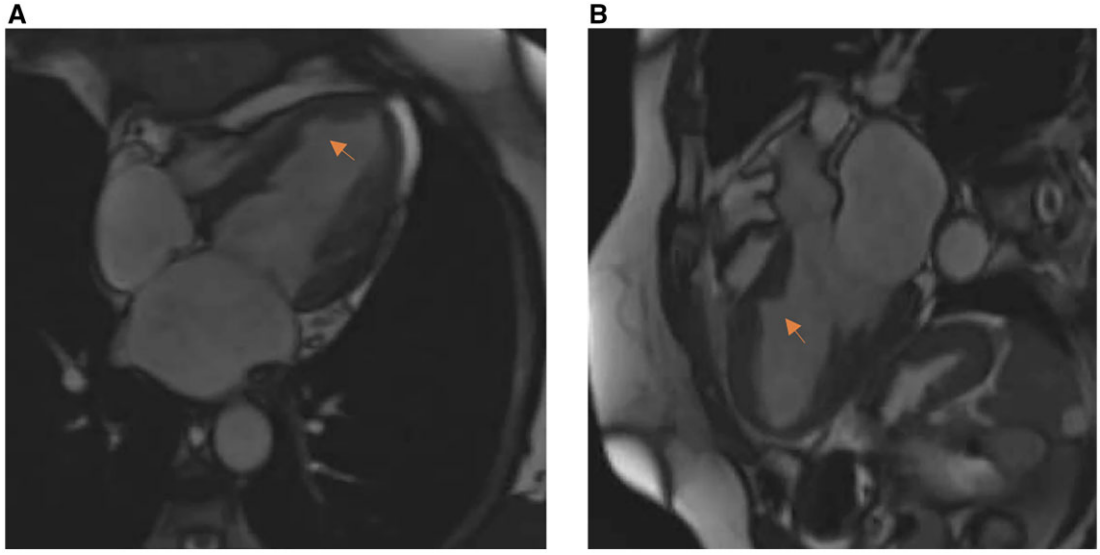


**Figure 5** (*A*) A four-chamber cine still image showing a focal aneurysm in the distal inferoseptum. (*B*) A three-chamber cine still image showing a focal aneurysm in the mid anteroseptum.

evaluate the progression of coronary artery disease and assess the EF. The CMR at follow-up demonstrated a focal aneurysm in the distal inferoseptum and mid anteroseptum, precisely at the location of the previously noted delayed enhancement and an EF of 48% (*Figure 5A* and *B*). Currently, she reports compliance with her heart failure regimen (i.e. ACE-I and BB) remains with minimal functional limitations particularly with exertion, and without subsequent readmissions or symptom recurrence.

## Discussion

While it has been established that cardiac complications are a common sequela of EGPA, we present a unique case in which the patient's initial presentation of EGPA was in the setting of MINOCA. In the present case, while echocardiogram was able to show global hypokinesis with regional wall motion abnormalities, the differential diagnosis of such findings remains broad, including myocardial

infarction and myocarditis. CMR demonstrated focal anteroseptal and inferoseptal akinesis with classic focal subendocardial delayed enhancement, indicative of myocardial infarction involving the septal branches of the left anterior descending artery. Thus, in this case, CMR was not only helpful in establishing the aetiology of troponin rise but also, by showing the involvement of relatively small sized septal coronary branches. This allowed us to narrow the diagnosis down to small- to- medium vessel vasculitis, like EGPA. Cardiac manifestations during the presentation of EGPA have been associated with high mortality and increased rates of relapse.[10,11] A recent meta-analysis by Pakbaz and Pakbaz[12] reviewed 62 cases of EGPA between 2011 and 2018 and concluded cardiac symptoms, electrocardiographic abnormalities, abnormal biomarkers, and abnormal echocardiography in 82.3%, 68.5%, 77.4%, and 96.8% of the patient population, respectively. While clinical evidence of myocardial involvement can be uncommon in the setting of EGPA,[13] utilization of CMR has become the gold standard to properly diagnose the disease and guide appropriate therapy for individuals with underlying myocardial injury in the setting of MINOCA. A comprehensive CMR evaluation in individuals with EGPA, who were determined to be in clinical remission, noted that despite the lack of clinical findings along with normal electrocardiogram and echocardiogram, 9 out of 11 subjects had delayed late gadolinium enhancement, indicating subclinical involvement of the myocardium.[14] CMR performed in 46.8% of the patients was abnormal in all cases and findings were significant for coronary arteritis (12.9%) and endomyocardial fibrosis (30.6%).[12] Of note, angiogram was also performed in those presenting with chest pain and showed normal coronary arteries or mild coronary lesions in 63.6%.[12] Furthermore, in a systemic review by Pasupathy *et al.*[15] of approximately 1500 patients, CMR provided an identifiable basis of troponin elevation in nearly 74% of the patients and an astounding 79% when imaging was performed within 6 weeks of presentation. The validity of CMR imaging was similarly confirmed in a retrospective study by Dastidar *et al.*[16] in which CMR was able to identify the cause of troponin elevation in 74% of its patients (25% myocarditis, 25% myocardial infarction, and 25% cardiomyopathy), while CMR resulted normal findings for another 26%. It is to be noted that in the population with normal CMR, mortality rate was only 2% as opposed to 15% in the cardiomyopathy group supporting the prognostic importance of this non-invasive testing modality.

While we continue to utilize proven clinical and diagnostic modalities including physical examination, ECG, and TTE to help guide our approach to diagnosing and managing patients with EGPA, such techniques are not always reliable and appropriate diagnosis may require a deeper, more comprehensive investigation. The exposure to non-invasive techniques, can help further elucidate the cardiac anatomy and play a crucial role in optimizing management for those that are classified by the fourth universal definition of myocardial infarction, which now includes MINOCA. A diagnosis of MINOCA is entertained when (i) a patient meets the universal acute myocardial infarction criteria, (ii) has non-obstructive coronary arteries on angiography, defined as no coronary artery stenosis ≥50% in any potential infarct-related artery; and (iii) there is no clinically overt specific cause for the acute presentation.[17] Unfortunately, further workup (i.e. CMR or delayed enhancement imaging) is underutilized, because patients with MINOCA are thought to have a better prognosis.[12] Recent studies, however, have shown an all-cause mortality as high as 4.7% at 12 months.[15]

## Conclusion

Several studies have shown the reliability of CMR in the setting of MINOCA, as it has shown to provide an accurate diagnosis in 60–80% of patients.[15,16] In fact, utilization of CMR within 1 week (median delay ∼5 days) shows a 90% accuracy in diagnosing cardiac pathology, as was shown in a study of 107 MINOCA patients by Leurent *et al.*[18] Patients with NSTEMI, without any significant obstruction on cardiac catheterization, can present with heterogeneous underlying aetiologies. CMR can help establish correct diagnosis, provide further guidance to management strategy, and offer prognostic information in such patients.

## Lead author biography

Payush Chatta is an internal medicine resident in training at Loma Linda University Medical Center. He earned his Bachelor's in Science from the University of California Los Angeles after which he attended medical school at A.T. Still University School of Osteopathic Medicine in Arizona. There he was a member of Sigma Sigma Phi, a National Osteopathic Honors Society. He will now be pursuing cardiology fellowship at Loma Linda University Medical Center and hopes to further subspecialize as an advanced heart failure cardiologist.

## 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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