

Elevated cardiac troponin in a patient with coronary artery disease: why look harder?

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Abstract

Cardiac involvement in systemic lupus erythematosus (SLE) is common and often unsuspected. We report a case of a female patient presenting with an acute coronary syndrome, but without target lesions on coronary angiography. As the presentation was not typical of non-ST-segment elevation myocardial infarction (NSTEMI), cardiac magnetic resonance imaging (MRI) was used to reveal alternative diagnoses. We discuss a list of conditions that can cause elevated cardiac troponin (cTn) and represent a common diagnostic challenge, in particular in patients with a previous history of coronary intervention. This case also illustrates the importance of taking into account coexistent medical conditions when interpreting cTn results and that cardiac MRI can be a valuable diagnostic tool when alternative differential diagnoses exist. ■ *Heart Metab.* 2015;67:30-33

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A 62-year-old woman presented to the emergency department with left-sided chest pain and exertional breathlessness. Her past medical history included systemic lupus erythematosus (SLE), chronic obstructive pulmonary disease (COPD), hypertension, hyperlipidemia, and stable angina. She had previously undergone percutaneous coronary intervention (PCI) to her first obtuse marginal (OM1) branch of the circumflex artery. A subsequent angiogram revealed in-stent restenosis in the OM1 of 60% to 70%, without significant functional obstruction based on a fractional flow reserve of 0.82.

On current presentation, her electrocardiogram (ECG) did not reveal any acute ischemic changes; however, her previous cardiovascular history and her symptoms raised the suspicion of non-ST-segment elevation myocardial infarction (NSTEMI). Her high-sensitivity cardiac troponin I (cTnI) levels were elevated at 843 ng/L (99th percentile cutoff of 40 ng/L) and she was started on dual antiplatelet therapy. Her renal function was normal. Inpatient coronary angiography was performed; however, no obstructive coronary lesions were identified and she was discharged. Her echocardiogram showed preserved

Abbreviations

CAD: coronary artery disease; **COPD:** chronic obstructive pulmonary disease; **cTn:** cardiac troponin; **LGE:** late gadolinium enhancement; **MRI:** magnetic resonance imaging; **NSTEMI:** non-ST-segment elevation myocardial infarction; **PCI:** percutaneous coronary intervention; **SLE:** systemic lupus erythematosus; **OM1:** first obtuse marginal

left ventricular function, with no regional wall motion abnormalities.

At routine follow-up she continued to report ongoing chest pain associated with breathlessness and palpitations on minimal exertion. Her medications consisted of doxazosin, isosorbide mononitrate, losartan, ivabradine, amlodipine, aspirin, clopidogrel, atorvastatin, domperidone, hydroxychloroquine, lansoprazole, fluticasone, and salmeterol inhalers. There was limited scope for increasing her antianginal medications, because she had experienced symptomatic hypotension, and 24-hour ambulatory ECG monitoring revealed bradycardia with intermittent pauses of 2.5 seconds.

Dobutamine stress echocardiography showed evidence of reversible ischemia laterally, so coronary angiography was repeated. The repeat angiogram showed de novo lesions in her mid-right coronary artery (*Figure 1*), for which she underwent PCI and stenting with no significant residual stenoses.

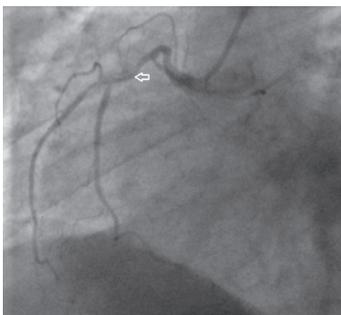


Fig. 1 Coronary angiogram, showing a lesion in the mid-right coronary artery.

At her follow-up clinic visit she reported ongoing exertional chest pain and also joint problems. Although objectively she had coronary artery disease (CAD), with a previous episode of reversible ischemia, treating this had not fully alleviated her symptoms. In view of her ongoing symptoms and the absence of target lesions on angiography, it was felt that an isch-

emic episode might not fully explain her symptoms, therefore cardiac magnetic resonance imaging (MRI) was used to further clarify the heart disease.

Cardiac MRI showed normal left ventricular volume and function. Tissue characterization revealed increased T2 signal in anterior apical segments and in inferior and inferoseptal basal segments, in keeping with myocardial edema and inflammation. In addition, there was late gadolinium enhancement (LGE) in the anterior mid-segment of the left ventricle (*Figure 2*), signifying either myocardial scar or extracellu-

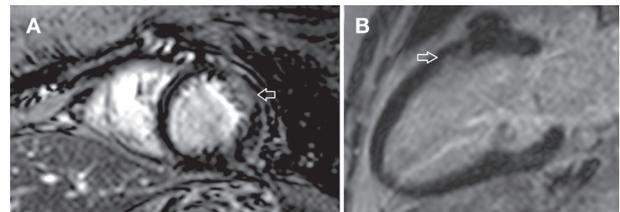


Fig. 2 (A) Short-axis view of left ventricle showing late gadolinium enhancement (LGE) in the anterior myocardium, demonstrated by cardiac magnetic resonance imaging (MRI). (B) Two-chamber view of left ventricle showing LGE in the anterior myocardium, demonstrated by cardiac MRI.

lar edema. A repeat cardiac MRI study 6 months later showed no interval change in function and volumes, with homogeneous signal on T2 imaging. The previously noted focal LGE in the anterior mid-segment was unchanged in its extent and transmural. It was concluded that the myocardial edema could be consistent with a diagnosis of lupus-related inflammatory cardiomyopathy. She was treated medically, and at her latest outpatient visit her symptoms had improved; however, episodes of exertional chest pain remained.

Discussion

Patients with SLE are prone to cardiovascular disease,^{1,2} which develops prematurely, progresses faster, and has more devastating outcomes. Cardiac manifestations of SLE include pericarditis, myocarditis, heart failure, conduction disturbances, noninfective verrucous vegetations (Libman-Sacks endocarditis), premature coronary atherosclerosis, and coronary arteritis.

The primary driver of cardiovascular disease in SLE is thought to be accelerated epicardial coronary atherosclerosis due to persistent systemic inflammation, via autoimmune complement-mediated cytotoxic injury.³ Lupus myocarditis may also contribute to

the apparent myocardial injury in SLE patients,⁴ and tends to present with atypical symptoms and cTn elevation. As illustrated by this case, the diagnosis of inflammatory lupus cardiomyopathy can be challenging, especially in older patients with traditional cardiovascular risk factors, where the coexistence of classical CAD and nonischemic inflammatory myocardial injury may lead to cardiovascular injury and confusion over the predominant clinical problem.

Anginal chest pain, with angiographically unobstructed coronaries, is not uncommon in SLE patients and is thought to be due to microvascular coronary obstruction⁵ causing ischemia. Angiographic findings may therefore be unhelpful and early use of imaging techniques, in particular cardiac MRI, has been shown to add clarity to the diagnosis.⁶⁻⁹ Interestingly, a recent study of patients with cTn-positive chest pain and unobstructed coronaries on angiography, reported that cardiac MRI established the cause for cTn elevation in 65% of cases, most commonly myocarditis (50%), followed by myocardial infarction (11.6%), and cardiomyopathy (3.4%).⁶ Furthermore, the first report of the European Cardiovascular Magnetic Resonance (EuroCMR) registry revealed that cardiac MRI leads to a change of diagnosis and management in 8.7% of patients.¹⁰ There is also evidence for a role for cardiac MRI in acute NSTEMI for diagnosis and prognosis.¹¹

Echocardiography lacks sensitivity to detect myocardial involvement in myocarditis, as the myocardial injury predominantly affects intra- or epicardial function, leading to either apparently normal function or global mild myocardial impairment. Even though endomyocardial biopsy remains the gold standard diagnostic test for myocarditis,¹² this is only reserved for severe cases. Because of an epicardial or midmyocardial site for injury, the yield of biopsy in myocarditis is notoriously low. Visualization of myocardial inflammation on cardiac MRI is now an established method to confirm the clinical diagnosis of myocarditis and to follow up on its sequelae.¹³ Current treatment strategies for lupus-related inflammatory cardiomyopathy involve optimizing treatment of the underlying SLE, which could include corticosteroids and/or immunosuppressive therapy, as well as optimizing treatment for any associated heart failure and CAD.

In this case, the myocardial edema seen on cardiac MRI, angiographically unobstructed coronar-

ies at presentation, and ongoing symptoms despite later revascularization were not typical of NSTEMI. The myocardial LGE in this patient could represent infarcted tissue, related to the previous coronary intervention. However, in nonischemic cardiomyopathy the location of LGE within the mid-wall of the left ventricle has been associated with an infectious or inflammatory pathology.¹⁴ This case illustrates the need for complementary information, to help understand the source of cardiovascular injury, in patients with both CAD and suspected myocarditis, in whom acute coronary syndrome is not confirmed. This may require advanced phenotyping, for example, by using cardiac MRI.

This present case also illustrates the importance of taking into account coexistent medical conditions when interpreting cTn results. With the routine use of high-sensitivity cTn assays in early rule-out protocols for NSTEMI, chronic cTn elevations may be detected in many other conditions, including chronic heart failure,¹⁵ stable CAD,¹⁶ atrial fibrillation,¹⁷ chronic renal failure,¹⁸ COPD,¹⁹ and sepsis,²⁰ and in healthy persons with cardiovascular risk factors and/or advanced age.²¹ The list of conditions that can cause elevated cTn is extensive and can represent a diagnostic challenge when patients present with coincident chest pain and a history of coronary intervention.

Conclusion

Cardiac involvement in SLE is common and often unsuspected. In this case, elevated high-sensitivity cTnI in the absence of target lesions on angiography and persistent symptoms after successful treatment of obstructive coronary lesions led us to think that the symptoms were not fully explained by ischemia. Cardiac MRI was crucial in highlighting an alternative diagnosis. In patients with elevated cTn, symptoms of chest pain and breathlessness, and absence of obstructive coronary disease, cardiac MRI should be considered early to exclude inflammatory cardiomyopathy. ■

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