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TITLE OF CASE

Fulminant Immune-Mediated Necrotizing Myopathy (IMNM) mimicking Myocardial Infarction with Nonobstructive Coronary Arteries (MINOCA)

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SUMMARY

A 74-year old man, with inflammatory arthritis recently commenced on adalimumab, presented with a four-week history of left-sided chest pain, malaise and shortness of breath. Admission electrocardiogram showed age-indeterminate left bundle branch block. Troponin-T was 4444 ng/L (normal range <15 ng/L) and acute coronary syndrome treatment was commenced. Catheter angiogram revealed mild-burden non-obstructive coronary disease. Cardiac magnetic resonance (CMR) was performed to refine the differential diagnosis and demonstrated no myocardial oedema or late gadolinium enhancement (LGE). Extra-cardiac review highlighted oedema and enhancement of the left shoulder girdle muscles consistent with acute myositis. Creatinine kinase was subsequently measured and significantly elevated at 7386 IU/L (normal range 30 – 200 IU/L in men). Electrophoresis clarified this was of predominantly skeletal muscle origin. Myositis protocol MRI revealed florid skeletal muscle oedema. The MR findings, together with positive anti-Scl-70 antibodies, suggested fulminant immune-mediated necrotizing myopathy (IMNM) presenting as a rare mimic of myocardial infarction with nonobstructive

coronary arteries (MINOCA), diagnosed by careful extracardiac CMR review.

BACKGROUND

The idiopathic inflammatory myopathies (IIM) encompass a heterogeneous group of multisystem disorders characterised by inflammation (muscle, skin and joints), vasculopathy and fibrosis. Cardiac involvement in IIM is rare but potentially life-threatening. The term MINOCA is applied to patients with a clinical diagnosis of myocardial infarction and no evidence of obstructive coronary artery disease on angiography. The prevalence of MINOCA has been estimated at approximately 6%.[1] It is a distinct clinical entity, which requires further investigation in order to find the cause of each patient's presentation so that targeted treatment can be instigated.[2]

We report a case of IMNM in which cardiac magnetic resonance (CMR), autoimmune serology and careful analysis of serum biochemistry were instrumental in making the diagnosis that was masquerading as MINOCA.

CASE PRESENTATION

A 74-year-old man presented with four-week history of general malaise with chest pain, shortness of breath and peripheral oedema. Past medical history included inflammatory arthritis that had recently been treated with adalimumab. The admission electrocardiogram (Figure 1) demonstrated age-indeterminate left bundle branch block, with QRS interval 140ms. troponin-T was elevated (4444 ng/L, normal range <15ng/L) in the context of serum creatinine of 91 μmol/L and an eGFR of 71 ml/min/1.73m^2.

INVESTIGATIONS

A presumptive diagnosis of acute coronary syndrome was made and usual treatment commenced alongside intravenous diuretics. However, an urgent coronary angiogram demonstrated no obstructive coronary artery disease (Figure 2). His echocardiogram demonstrated good biventricular function, abnormal septal motion consistent with LBBB and no significant valve abnormality. The diagnosis was revised to MINOCA and a CMR study performed to distinguish a spontaneously re-canalised myocardial infarction (MI) from acute myocarditis.

The CMR protocol included oedema-sensitive (T2-STIR) and late gadolinium enhancement (LGE)

sequences. The CMR confirmed normal biventricular volumes and ejection fractions. There was dis-coordinated right ventricular contraction with a septal regional wall motion abnormality consistent with the known LBBB. A small pericardial effusion was demonstrated. No convincing myocardial oedema (Figure 3a, 3b 3c) or late gadolinium enhancement (Figure 3e, 3f, 3g) was present, suggesting recent/prior MI and/or myocarditis was unlikely. However, extra-cardiac review, demonstrated high signal return on STIR from the visualised left shoulder girdle muscles (Figure 3d) and some patchy enhancement on LGE in these appendicular muscles, in keeping with shoulder girdle myositis. The initial creatinine kinase (CK) was significantly elevated at 7386 IU/L (normal range 30 – 200 IU/L in men). Subsequent CK electrophoresis, to differentiate between the various isoforms, indicated the elevated CK was predominantly of skeletal muscle origin with CK-MM contributing 89.2%, CK-MB 6%, and macro-CK type 1 (4.8%). No CK-BB was detected. Troponin-I was elevated (534 ng/L, NR <0.04ng/ml) but proportionately much lower than the troponin T, suggesting some cardiac involvement (despite reassuring CMR).

TREATMENT

In the absence of any overt myocardial damage and following clinical improvement, the patient was discharged from the acute cardiology ward with urgent outpatient Rheumatology follow-up arranged (pending CK electrophoresis, troponin-I and autoimmune serology). At Rheumatology review two weeks following hospital-discharge, the patient was noted to be unwell with a cough and hypoxia. He was readmitted to hospital with suspected aspiration pneumonia.

The patient's autoimmune profile identified the presence of anti-Scl70 antibodies. No overt cutaneous features of connective-tissue disease were present. CK remained elevated at 6255 IU/L (normal range 30 – 200 IU/L in men) and the troponin-T rose to >9999 ng/L (normal range <15 ng/L).

A myositis-protocol MRI demonstrated abnormal increased signal intensity on STIR from the proximal thigh muscles, with no evidence of atrophy on T1, consistent with an acute myositis (Figure 4). The constellation of cardiac and skeletal muscle MR findings, together with positive anti-Scl-70 antibodies, led to a diagnosis of fulminant Immune-Mediated Necrotizing Myopathy (IMNM). IMNM is characterised by proximal muscle weakness, grossly elevated muscle enzymes, autoantibodies and inflammatory change on muscle biopsy.[3] In IMNM, in contrast to other inflammatory myopathies, myofibre necrosis is a prominent feature rather than the per-vascular lymphocytic infiltration typically identified on histological assessment of uncomplicated idiopathic inflammatory myopathy. Muscle prognosis is worse in IMNM and many patients have persistent weakness despite aggressive immunosuppressant treatment. [3] Cardiac involvement is a rare but important cause of morbidity in IMNM.

Treatment was commenced with intravenous antibiotics and high dose intravenous corticosteroids; however, the patient continued to deteriorate and was transferred to higher acuity ward-based care, where treatment with intravenous immunoglobulin (IVIg) was commenced. Due to the rapid deterioration, a muscle biopsy was not possible.

OUTCOME AND FOLLOW-UP

The patient continued to deteriorate with Type 1 respiratory failure, requiring emergency intubation on the ward and he was transferred to the Intensive Care Unit. Treatment was continued with intravenous corticosteroids and antibiotics and intravenous immunoglobulin (IVIg) therapy. Several attempts to extubate were unsuccessful due to profound respiratory muscle weakness. Following a small improvement in clinical condition and successful extubation, the patient together with his family decided to cease active management. He was transferred home for best supportive care with palliative team input, where he subsequently died.

DISCUSSION

Our case illustrates the value of CMR and careful analysis of serum biochemistry in differentiating a suspected case of MINOCA from fulminant (IMNM. CMR has a leading role in the diagnosis of alternative causes of symptoms in patients with non-obstructed coronaries.[4] Non-infarction differential diagnoses of elevated troponin can be classified as either ‘coronary causes’, ‘non-coronary cardiac causes’ and ‘non-coronary non-cardiac causes’, and include pathology ranging from plaque rupture, myocarditis and pulmonary embolism.[5] A meta-analysis of MINOCA patients demonstrated that, following CMR, cardiac myocarditis and an occult subendocardial infarct are the most common diagnoses.[1]

In our case, chest pain and raised troponin-T was likely related to his shoulder girdle/chest wall skeletal myositis. Troponin-I is considered to be exclusive to myocardial tissue whereas troponin-T, the basis for high-sensitivity tests in our hospital, has been detected in healthy adults and regenerating adult skeletal muscle tissue.[6] Several studies have reported a close correlation with elevated troponin-T and CK; particularly CK-MB. This may be due to regenerating skeletal muscle tissue undergoing a phenotype switch where previously repressed cardiac troponin-T (along with CK-MB) is re-expressed in adult regenerating skeletal muscle tissue.[5] Persistently elevated serum troponin-T levels have also been diagnosed in patients with myositis where myocardial damage has been excluded.[7] Isotype analysis of serum CK and troponin in our patient demonstrated the elevations were predominantly secondary to skeletal muscle dysfunction, rather than cardiac.

The presence of a pericardial effusion in our patient, although not specific for myocarditis, raises the possibility of active inflammation despite the absence of other features of myocarditis on CMR.[7] Myocardial LGE, which can be due to acutely damaged and/or chronically scarred myocardium, has been demonstrated to be less sensitive in milder cases, which may explain why there was no myocardial oedema or LGE in our patient.[8]

CMR and serum biomarkers have an important role in the investigation of patients with a clinical diagnosis of myocardial infarction and non-obstructed coronary arteries. To our knowledge, this is the first reported case of shoulder girdle myositis secondary to IMNM mimicking MINOCA. Our case highlights the importance of careful review of CMR for extra-cardiac findings and the importance of further biochemical and rheumatological work-up of patients with suspected MINOCA and known/suspected autoimmune rheumatic disease.

LEARNING POINTS/TAKE HOME MESSAGES

- Troponin is a biomarker for myocardial damage. However, in addition to coronary causes, troponin levels can be elevated due to non-coronary cardiac causes and non-cardiac causes. A high index of suspicion is required to differentiate common causes of MINOCA from rare mimics.

- Troponin-T is released by regenerating skeletal muscles; such that levels can remain persistently raised in patients with myositis.

- CMR has a leading role in differentiating the possible alternative causes of symptoms in patients with non-obstructed coronary arteries.

- Careful review and identification of extra-cardiac findings on CMR is important: many cardiac diseases have systemic consequences and non-cardiac causes for presentation may be demonstrated.

- In immune-mediated myopathy, cardiac involvement is a rare but important cause of morbidity. Patients with suspected MINOCA and known/suspected autoimmune rheumatic disease require early rheumatological input alongside imaging and biochemical work-up.

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FIGURE/VIDEO CAPTIONS

Figure 1. Admission ECG demonstrating left bundle branch block (QRS 140ms).

Figure 2. Diagnostic coronary angiogram demonstrating with A) only mild atheroma of the left main stem, A) mild-moderate diffuse atheroma of the left anterior descending, B) unobstructed left circumflex and C) mild atheroma of the right coronary artery.

Figure 3. Cardiac magnetic resonance images. T2-weighted Short Tau Inversion Recovery (T2-STIR) images of the A) cardiac short-axis basal, C) cardiac short-axis mid and C) cardiac short-axis apical segments demonstrating no increased signal return to suggest myocardial oedema and D) trans-axial T2-STIR image of the thorax demonstrating high signal return from the visualised left shoulder girdle muscles (latissimus dorsi and serratus anterior, arrowed). Late gadolinium enhancement (LGE) images of the E) cardiac short-axis basal, F) cardiac short-axis mid and G) cardiac short-axis apical segments demonstrating no enhancement and H) trans-axial LGE image of the thorax demonstrating patchy enhancement of the left shoulder girdle muscles (latissimus dorsi and serratus anterior, arrowed).

Figure 4. Magnetic Resonance Images of the thigh: (a) coronal T1; (b) coronal STIR; (c) axial T1 and (d) axial T2, show oedema within the adductor compartments bilaterally (arrows) without substantial evidence of fatty muscle atrophy on the T1 imaging (asterisks).

PATIENT'S PERSPECTIVE

Unfortunately, the patient's perspective could not be obtained as he sadly passed away.

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Date:

DISCLOSURES/COMPETING INTERESTS

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