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CASE REPORT

INTERMEDIATE

CLINICAL CASE

Toxin-Mediated Myocarditis From a Brown Recluse Spider Bite

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ABSTRACT

We describe a case of myocarditis associated with a brown recluse spider bite in a 31-year-old man. Cardiac magnetic resonance revealed late gadolinium enhancement in the lateral wall and inferior wall. There was also regional elevation of the myocardial T2 and extracellular volume indicative of myocardial edema. (**Level of Difficulty: Intermediate.**)
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HISTORY OF PRESENTATION

A 31-year-old man who presented with a diffuse erythematous rash and fever and chills 3 days after a spider bite was found to have hemolysis, acute kidney injury, and mild rhabdomyolysis. A diagnosis of loxoscelism was made based on the patient's report of a brown spider found immediately after the bite, in a region where brown recluse spiders are endemic, and the presence of classic signs and symptoms. On hospital day 3, he developed chest pain and diffuse ST-segment elevation on electrocardiogram (ECG). Given a rising troponin I (peaked at 24 ng/mL, normal <0.04 ng/mL), he was taken to the cardiac catheterization lab, which revealed diffuse nonobstructive coronary disease. Cardiac magnetic resonance (CMR) was performed to further characterize suspected myopericarditis.

LEARNING OBJECTIVES

- To identify the CMR patterns associated with acute myocarditis (T1 and T2 mapping, late gadolinium enhancement, extracellular volume).
- To understand the clinical manifestations, differential diagnosis, and treatment of systemic loxoscelism.

PAST MEDICAL HISTORY

The patient reported being in good health, with no medical history, prior to this hospitalization.

DIFFERENTIAL DIAGNOSIS

The constellation of acute kidney injury, hemolysis, and rhabdomyolysis in the setting of a known spider bite was strongly supportive of a diagnosis of systemic loxoscelism. Brown recluse spiders are endemic to middle Tennessee, where the patient was bitten.

The differential diagnosis included frank sepsis, systemic inflammatory response syndrome, metabolic derangements, hemolytic uremic syndrome, thrombocytopenic thrombotic purpura, cytokine release syndrome, and certain ingestions or intoxications.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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ABBREVIATIONS AND ACRONYMS

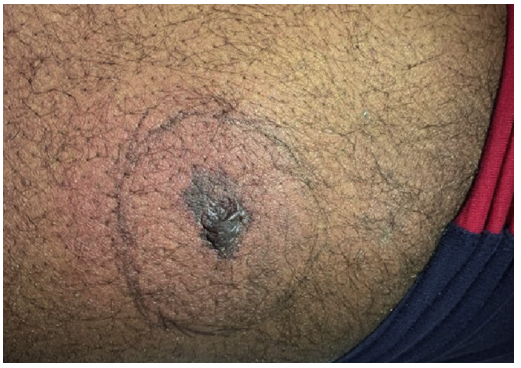
CMR = cardiac magnetic resonance

ECG = electrocardiogram

The appearance of the localized necrotic ulceration characteristic of brown recluse envenomation can vary over time and normally takes up to 7 to 10 days to develop. Other conditions with lesions of similar appearance include bacterial cellulitis, *Pseudomonas* infection or ecthyma gangrenosum, primary Lyme disease, deep fungal and parasitic infections, herpes simplex viral infection, chemical or thermal burns, cutaneous vasculitis, cryoglobulinemia, and calcium deposition disorders.

The differential for myocardial infarction with nonobstructed coronary arteries is broad and includes myocarditis, thrombotic or embolic coronary occlusion with recanalization, coronary vasospasm, and stress cardiomyopathy.

FIGURE 1 Skin Lesion on Hospital Day 1



Patient's left thigh.

INVESTIGATIONS

Review of systems on presentation was notable for chills, malaise, diffuse myalgias, decreased appetite, diarrhea, and swelling of hands and feet. His vital signs were the following: body temperature 39 °C (102.5 °F), heart rate 103 beats/min, blood pressure 154/82 mm Hg, respiratory rate 16 breaths/min, and oxygen saturation 98% on ambient air. A faint holosystolic murmur was present. He had a 2 cm × 2 cm necrotic patch with surrounding erythema on his left medial thigh (**Figure 1**). The lactate dehydrogenase was elevated and haptoglobin was undetectable, indicative of hemolysis. Rhabdomyolysis (creatinine phosphokinase elevated at 681 U/L) and acute kidney injury (creatinine 1.63 mg/dL) were present. Troponin was elevated to 13.6 ng/mL on day 3 of hospitalization and peaked at 24 ng/mL (normal <0.04 ng/mL).

Chest pain, elevated troponin, and diffuse ST-segment elevation on ECG (**Figure 2**) prompted coronary angiography, which demonstrated no obstructive disease and an elevated left ventricular end diastolic pressure of 29 mm Hg (**Figures 3 and 4,** Videos 1, 2, and 3). Transthoracic echocardiography on hospital day 4 showed a left ventricular ejection fraction of 40% to 50% with lateral and inferolateral hypokinesis and a small pericardial effusion (Videos 4, 5, 6, and 7). CMR was performed on hospital day 7 using a 1.5-T magnetic scanner (Avanto Fit, Siemens). CMR revealed a left ventricular ejection fraction of 51% with regional hypokinesis of the basal lateral wall. There was regional increased T2 signal (basal lateral segment 55.6 ms; normal range 40-50 ms) and extracellular volume in the lateral wall (35.3%; normal range 22%-28%) (**Figure 5**). Dense, patchy, midmural late gadolinium enhancement was present in the basal to distal lateral wall, and the basal inferior wall (**Figure 6**). There was mild mitral regurgitation and mild-to-moderate tricuspid regurgitation by flow analysis. A trivial pericardial effusion was noted.

MANAGEMENT

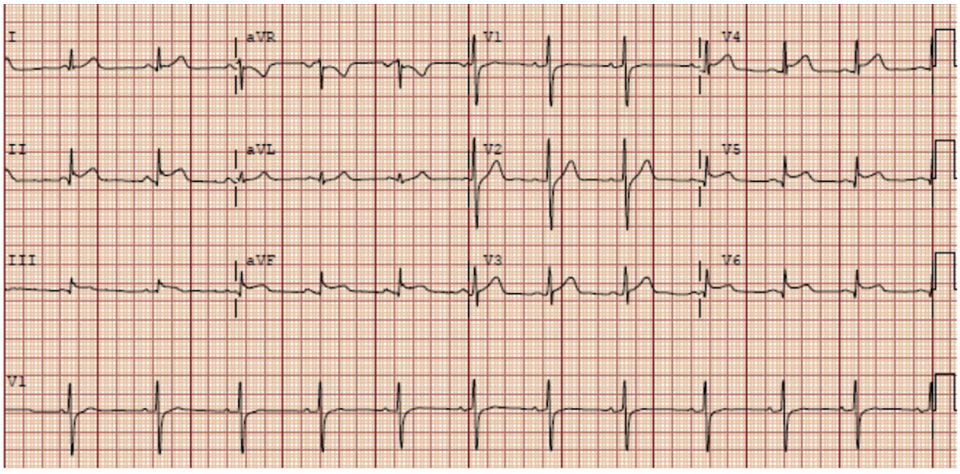
The treatment for systemic loxoscelism is predominantly supportive, with blood transfusion often necessary if significant hemolysis is present. Antivenom may be effective but must be administered within 12 hours of the bite and is not available in the United States (1).

Our patient was briefly monitored in the intensive care unit for hemolysis, but he did not require transfusion of blood products. Prior to discharge, he was initiated on metoprolol and lisinopril for a mild cardiomyopathy and colchicine for acute pericarditis. Guideline-appropriate tetanus prophylaxis was ensured.

DISCUSSION

Loxoscelism, or systemic brown recluse envenomation, was first described in the United States in 1879 in Tennessee. The two arachnid genera most known in the United States to produce significant morbidity and mortality are *Latrodectus* (black widow) and *Loxosceles* (brown recluse). Although black widow–associated myocarditis has been previously described (2,3), we could not identify a prior report of myocarditis due to a brown recluse bite. The clinical syndrome of cutaneous brown recluse spider bite includes a single, small erythematous lesion that develops induration and central necrosis

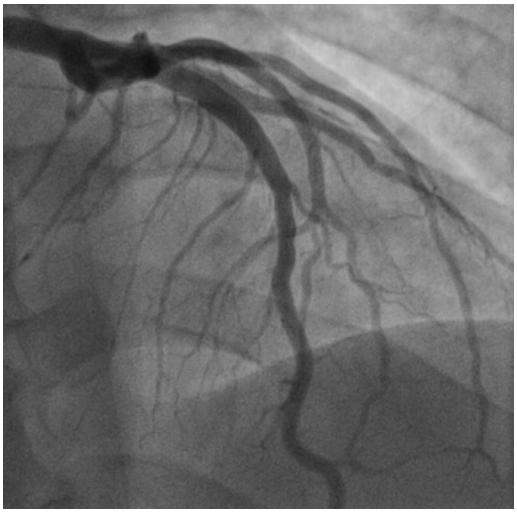
FIGURE 2 **Electrocardiogram**



Electrocardiogram showing diffuse ST-segment elevation and PR depression, suggestive of pericarditis.

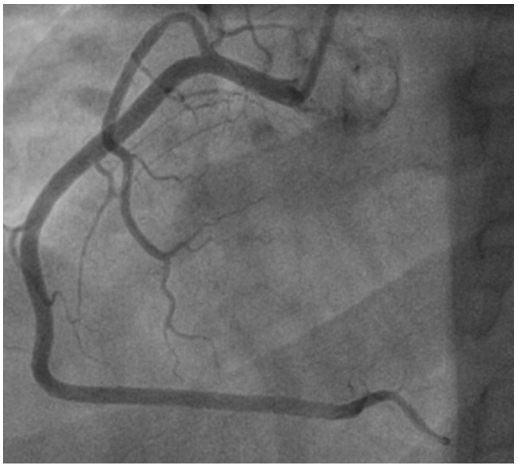
over a span of days (Figure 7). Though most patients have no systemic reaction, loxoscelism with associated hemolysis, disseminated intravascular coagulation, rhabdomyolysis, or acute kidney injury can be severe and sometimes fatal (4,5). The species of brown recluse spider (*Loxosceles reclusa*) most likely to cause morbidity is predominantly confined to an area of central and southeastern United States. The active toxin in *L. reclusa*, sphingomyelinase D, might exert its effects by direct cellular damage (hydrolysis of cell membrane phospholipids), cell-surface signaling (cascading to matrix metalloprotease release), or massive immune response with neutrophil infiltration (up-regulation of interleukin-6) (6). Hemolysis is caused by direct toxicity to erythrocytes and activation of the complement system (4). An animal study demonstrated that injection of *L. intermedia* venom and

FIGURE 3 **Coronary Angiography Left Anterior Oblique Cranial View**



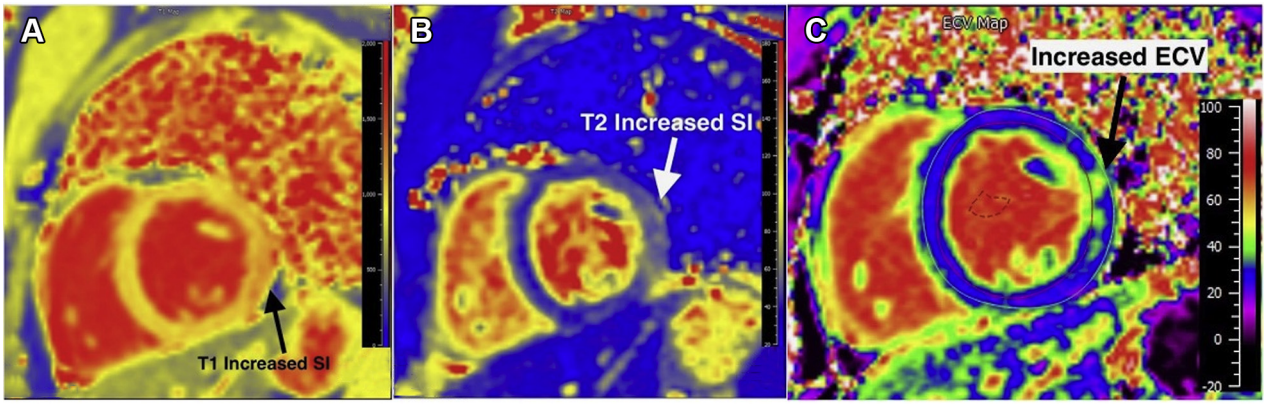
Left coronary angiography showing angiographically normal left main, left anterior descending, and left circumflex coronary arteries.

FIGURE 4 **Coronary Angiography Left Anterior Oblique Caudal View**



Right coronary artery angiography showing angiographically normal vessel.

FIGURE 5 Cardiac Magnetic Resonance T1, T2, and ECV Maps

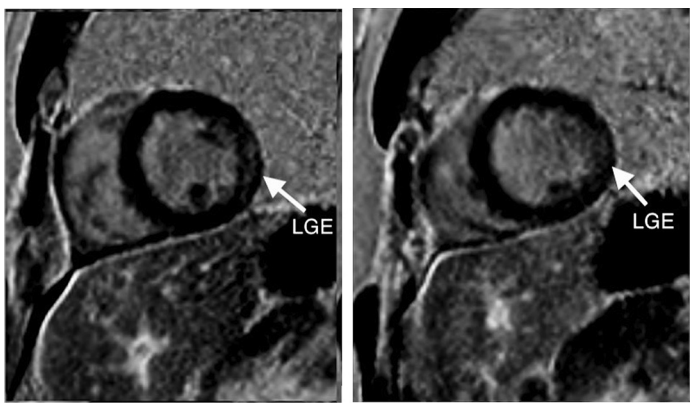


(A) Regional increase in native T1 relaxation times. Basal lateral: 1176 ms; lab normal: 940 to 1,030 ms, **(B)** Regional increase in T2 relaxation times. Basal lateral: 55.6 ms; lab normal: 40 to 50 ms. **(C)** Regional increase in extracellular volume (ECV). Lateral wall ECV: 35.3%; normal range: 22% to 28%. SI = signal intensity.

sphingomyelinase-D into mice caused cardiotoxic effects including myocardial injury with elevated creatine kinase and creatine kinase-myocardial band levels. Using immunofluorescence and microscopy, this study demonstrated binding between mouse cardiomyocytes and recombinant dermonecrotic protein derived from *L. intermedia* (7), providing biologic plausibility for the role of spider venom as the cause of myocarditis in our patient.

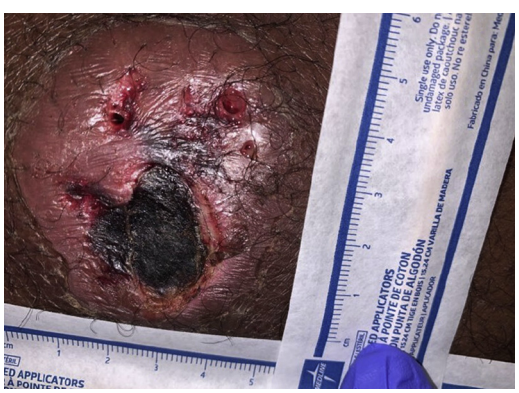
Acute myocarditis was suspected early in the patient's clinical course based on clinical presentation (atypical chest pain, dyspnea), diagnostic criteria (ST-segment elevation on ECG, systolic dysfunction on transthoracic echocardiogram, pericardial effusion on echocardiogram), and a lack of traditional atherosclerosis risk factors. After normal coronary angiography, CMR was performed for tissue characterization and to narrow the differential diagnosis of myocardial infarction with nonobstructed coronary arteries. The pattern of myocardial inflammation seen on CMR solidified the diagnosis of acute myocarditis (**Figure 8**). CMR has become an essential tool in suspected myocarditis and myocardial infarction with nonobstructed coronary arteries, providing an alternative to invasive endomyocardial biopsy, as well as informing clinical decisions, risk stratification, and prognosis (8,9). Novel parametric mapping techniques provide improved diagnostic accuracy of myocardial tissue pathology compared with traditional turbo spin echo imaging.

FIGURE 6 Cardiac Magnetic Resonance Phase-Sensitive Inversion Recovery Images (Short Axis)



Serial short-axis slices showing multifocal nonischemic late gadolinium enhancement (LGE) pattern of the left ventricle.

FIGURE 7 Skin Lesion on Hospital Day 8



Evolving induration and necrosis of left thigh lesion.

FOLLOW-UP

Transthoracic echocardiography 3 weeks after discharge showed normalization of cardiac function.

CONCLUSIONS

We report the first known case of myocarditis related to a brown recluse spider bite. CMR is essential in the noninvasive diagnosis of acute myocarditis.

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FIGURE 8 2018 Modified Lake Louise Consensus Criteria (10)

Table 1: 2018 Modified Lake Louise Consensus Criteria for CMR diagnosis of myocarditis

In the setting of clinically suspected myocarditis, CMR findings are consistent with myocardial inflammation if both of the following criteria are present:

1. Regional high T2 signal intensity (SI) *or* Global T2 SI ratio ≥ 2.0 in T2 weighted *or* Regional or global increase of myocardial T2 relaxation time in T2-based imaging
2. Regional or global increase of native myocardial T1 relaxation time or ECV *or* Areas with high SI in a nonischemic distribution pattern in LGE images in T1-based imaging

Supportive Criteria

Pericardial effusion in cine CMR images *or* High signal intensity of the pericardium in LGE images, T1-weighted or T2-weighted, *or* T-1 mapping or T-2 mapping

Systolic left ventricular wall motion abnormality in cine CMR images

CMR = cardiac magnetic resonance; LGE = late gadolinium enhancement.

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KEY WORDS acute heart failure, cardiac magnetic resonance, cardiomyopathy, chest pain, imaging, MR sequences, myocardial ischemia, systolic heart failure

APPENDIX For supplemental videos, please see the online version of this paper.