

> THE PATIENT

38-year-old man

> SIGNS & SYMPTOMS

- Chest pain
- Shortness of breath
- Fever and nausea

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*The authors reported no
potential conflict of interest
relevant to this article.*

> THE CASE

A 38-year-old Hispanic man was brought to the emergency department (ED) after losing consciousness and falling at home, striking his elbow, head, and neck. For the past week, he'd had palpitations, shortness of breath, mild swelling of the lower extremities, fever, nausea, and fatigue. He had also been experiencing squeezing chest pain that worsened with exertion and was only partially relieved by nitroglycerin.

The patient did not have any rashes and denied having contact with anyone who was sick. He said that he'd been bitten by mosquitos during recent outdoor activities. His medical history included hypertension, hemorrhagic basal ganglia stroke, hyperlipidemia, sleep apnea, metabolic syndrome, and gout. The patient denied smoking or using illicit drugs.

In the ED, his temperature was 101°F, heart rate was 112 beats/min, blood pressure was 175/100 mm Hg, and respiratory rate was 18 breaths/min. His head and neck exam was normal, with no neck stiffness. A lung exam revealed bilateral basal crackles, and a neurologic exam showed residual right-sided weakness due to the hemorrhagic stroke one year ago.

Lab test results revealed the following: white blood cell (WBC) count, 13,000/mm³ with relative monocytosis (14%); lymphocytosis (44%) with normal neutrophils and no bands; hemoglobin, 12 g/dL; hematocrit, 36/mm³; and platelets, 300,000/mm³. Liver function tests were within normal limits. Urinalysis was unremarkable. His troponin I level was elevated at 1.385 ng/dL. In addition to the tachycardia, his electrocardiogram (EKG) showed left axis deviation, left atrial enlargement, left anterior fascicular block, and diffuse nonspecific ST and T wave abnormalities. Chest x-ray was unremarkable except for cardiomegaly. A computed tomography (CT) scan of his head showed residual changes from the previous stroke.

The patient was admitted with a provisional diagnosis of systemic inflammatory response syndrome (SIRS), syncope, non-ST elevation myocardial infarction (NSTEMI), and acute heart failure. The patient had continuous EKG monitoring and serial assessments of his troponin levels. He was also given aspirin, metoprolol 25 mg BID, lisinopril 10 mg/d, furosemide 40 mg IV, isosorbide mononitrate 60 mg/d, and atorvastatin 40 mg/d.

The patient's cardiac enzymes subsequently decreased. A left heart catheterization was performed, which showed minimum irregularities of the left anterior descending artery (< 20% narrowing) and an ejection fraction (EF) of 35%, without any evidence of obstructive coronary artery disease (CAD). An echocardiogram revealed systolic dysfunction, with an EF of 35% to 40% and global hypokinesis without any apical ballooning or pericardial effusion. (An echocardiogram performed 6 months earlier had shown normal systolic function, an EF of 60% to 65%, and no wall motion abnormalities.) Blood, urine, and fungal cultures were negative; stool studies for ova and parasites were also negative. A lower extremity venous Doppler was negative for deep vein thrombosis.

THE DIAGNOSIS

Because our patient had SIRS, troponinemia, acute systolic dysfunction, and global hypokinesia without any evidence of obstructive CAD, we considered a diagnosis of viral myocarditis. Serologic studies for echovirus, coxsackievirus B, parvovirus B19, adenovirus, and human herpesvirus 6 (HHV-6) all came back negative. However, an enzyme-linked immunosorbent assay (ELISA) for West Nile virus (WNV) was positive. WNV infection was confirmed with a positive plaque reduction neutralization test and a positive qualitative polymerase chain reaction (PCR) assay, which established a diagnosis of WNV myocarditis.

DISCUSSION

While most individuals infected with WNV are asymptomatic, 20% to 40% of patients will exhibit symptoms.¹⁻⁴ Typical presentations of WNV infection include West Nile fever and neuroinvasive disease. West Nile fever is a self-limited illness characterized by a low-grade fever, headache, malaise, back pain, myalgia, and anorexia for 3 to 6 days.² Neuroinvasive disease caused by WNV may present as encephalitis, meningitis, or flaccid paralysis.⁵ Atypical presentations of the virus include rhabdomyolysis,⁶ fatal hemorrhagic fever with multi-organ failure and palpable purpura,⁷ hepatitis,⁸ pancreatitis,⁹ central diabetes insipidus,¹⁰ and myocarditis.¹¹

Although WNV has been linked to myocarditis in animals,¹² few human cases of WNV myocarditis^{11,13} or cardiomyopathy¹⁴ have been reported. Viral myocarditis often leads to the development of dilated cardiomyopathy, and myocardial damage may result from direct virus-induced cytotoxicity, T cell-mediated immune response to the virus, or apoptosis.¹⁵ Some research suggests that immune-mediated mechanisms play a primary role in myocardial damage. Caforio et al¹⁶ found that anti-alpha myosin antibodies were present in 34% of myocarditis patients. In a follow-up study, these antibodies were shown to persist for up to 6 months, which far surpasses the viral cardiac replication timeline of 2 to 3 weeks,¹⁷ suggesting that

damage occurring after that time is primarily an autoimmune process.

■ **The differential diagnosis for WNV myocarditis** includes myocardial stunning from demand ischemia related to SIRS, Takotsubo cardiomyopathy (stress cardiomyopathy), and Dressler's syndrome. For our patient, myocardial stunning from demand ischemia was less likely because he had no obstructive coronary disease or focal hypokinesia. In addition, the persistence of left ventricular systolic dysfunction and global hypokinesia demonstrated in a repeat echocardiogram during follow-up 6 months later reinforced the likelihood of myocarditis.

The patient's chest pain with syncope, elevated troponin level, and nonspecific EKG changes in the absence of obstructive CAD raised the possibility of Takotsubo cardiomyopathy. The characteristic echocardiogram finding in Takotsubo cardiomyopathy is transient apical ballooning with akinesis or hypokinesia in the apical and/or mid ventricular regions (typical variant) or isolated midventricular hypokinesia (apical sparing variant). Our patient's echocardiogram did not show any of these focal wall motion abnormalities, but instead showed global hypokinesia. In addition, the persistence of systolic dysfunction during the repeat echocardiogram and the patient's lack of psychological distress made the diagnosis of Takotsubo cardiomyopathy unlikely.

Dressler's syndrome, which is also known as post-myocardial infarction (MI) syndrome, typically presents weeks to months after MI as pleuritic chest pain with a pericardial rub, elevated inflammatory markers, typical EKG changes (diffuse ST-segment elevation and PR-segment depression), and pericardial effusion. This did not fit our patient's presentation.

Supportive care for heart failure is the mainstay of treatment

The standard treatment for WNV myocarditis is supportive care. Diuretics are used as needed for fluid overload, along with angiotensin-converting enzyme inhibitors and beta-blockers for cardiomyopathy with decreased EF.



Although West Nile virus has been linked to myocarditis in animals, few human cases of WNV myocarditis or cardiomyopathy have been reported.

CONTINUED

■ **Our patient's dyspnea improved** with treatment of furosemide 40 mg IV BID, and his blood pressure was controlled with metoprolol 25 mg BID and lisinopril 10 mg BID. His chest pain and fever resolved when his blood pressure improved. He was discharged home after 7 days on the furosemide, metoprolol, and lisinopril, in addition to isosorbide mononitrate 30 mg/d, atorvastatin 40 mg/d, and aspirin 325 mg/d. An echocardiogram performed 6 months later showed persistent systolic dysfunction, with an EF of 35% and global wall motion abnormalities.

THE TAKEAWAY

In addition to acute coronary syndrome, consider alternate etiologies in patients who present with chest pain and elevated cardiac biomarkers, particularly if diagnostic work-up is negative for obstructive coronary artery disease. WNV myocarditis should be considered as a diagnosis when a patient's symptoms suggest acute coronary syndrome but are accompanied by fever, headache, and other constitutional symptoms, especially during mosquito season or a WNV outbreak.

JFP

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