Case Report: Myocarditis in a Traveler Returning from the Dominican Republic: An Unusual Presentation of Dengue Fever

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Abstract. Myocarditis is an uncommon manifestation of dengue fever. We describe a case of a 69-year-old Hispanic male who presented to an emergency room in New York City 3 days after returning from a trip to the Dominican Republic complaining of a 1-day history of chest pain and fever. His first electrocardiogram showed a new left bundle branch block, and initial cardiac enzymes included troponin of 5 ng/dL, creatine kinase-MB of 9 ng/mL, and myoglobin of 234 ng/mL. Dengue fever antibodies were found to be elevated: immunoglobulin M (IgM) titer was 2.48 (reference range < 0.9), and immunoglobulin G (IgG) titer was 4.26 (reference range < 0.9). The patient was diagnosed with myocarditis caused by dengue fever. He improved after 1 week with conservative management in a telemetry unit and was discharged home.

INTRODUCTION

Dengue is the most rapidly spreading mosquito-borne viral disease globally.¹ The manifestations of this potentially fatal infection are varied and can involve any organ system. We present a case of a traveler who presented with chest pain and was initially treated for acute coronary syndrome. The symptoms were found to be caused by myocarditis caused by dengue fever.

CASE REPORT

A 69-year-old Hispanic male presented in the month of July with a 1-day history of severe midsternal chest pain that had started at rest on the evening before admission. He described the pain as pressure-like, non-radiating, aggravated by lying down, relieved by leaning forward, and associated with fever and chills. He complained of muscle soreness and headaches and denied respiratory, gastrointestinal, or genitourinary symptoms.

The patient denied having any significant past medical history and took no medications. He was a retired factory worker, lived at home with his wife, and denied using alcohol, tobacco, or illicit drugs. Three days before presentation, he had returned from a 1-month vacation in the Dominican Republic.

On physical examination, the oral temperature was 38.4°C (101.2°F), blood pressure was 118/63, heart rate was 93 beats per minute (BPM), respiratory rate was 21 breaths per minute, and pulse oximetry on room air was 95%. The examination was significant for crackles at the lung bases.

Admission laboratory data revealed a troponin of 5 ng/mL, creatine kinase-MB of 9 ng/mL, myoglobin of 234 ng/mL, brain natriuretic peptide of 149 pg/mL, and d-dimer of 2.6 mg/L. Chest X-ray showed pulmonary venous congestion and atelectasis of the lingula. The first electrocardiogram showed sinus rhythm at 95 BPM, with a possible new left bundle branch block. A two-dimensional echocardiogram revealed an ejection fraction of 62%, mild left ventricular diastolic dysfunction, and normal right ventricular function with a

trace posterior pericardial effusion. A persantine stress test did not reveal any evidence of pre- or post-test ischemia.

The patient was treated empirically with intravenous azithromycin and ceftriaxone for possible community acquired pneumonia. Multiple blood, sputum, and urine cultures were sent and showed no bacterial or fungal growth. Additional laboratory data revealed negative results for human immunodeficiency virus (HIV), influenza A and B antigens, H1N1 polymerase chain reaction (PCR), nasopharyngeal swab, mycoplasma antibodies, malaria smear, coxsackie A antibodies, and legionella urinary antigen. Dengue fever serologies were sent.

During the hospital course, the patient continued to have fevers, with the highest recorded temperature of 39.5°C (103.2°F). Antibiotics were discontinued. The troponin level peaked at 7.34 ng/mL. Telemetry monitoring was notable for multiple pauses, with the longest pause recorded to be 5.42 seconds, although the patient remained asymptomatic. On the sixth hospital day, the temperature normalized. The patient was discharged on the eighth hospital day with a diagnosis of myocarditis.

One week later, the dengue fever antibody titer results were found to be elevated, with immunoglobulin M (IgM) of 2.48 (reference range is < 0.9) and immunoglobulin G (IgG) of 4.26 (reference range is < 0.9), suggestive of a recent or current infection.

DISCUSSION

Dengue is the most rapidly spreading mosquito-borne viral disease around the world. In the last 50 years, its incidence has increased 30-fold with increasing geographic expansion to new countries, and in the present decade, it has moved from urban to rural settings. It affects 50–100 million people every year, and 2.5 billion people are at risk.¹ The disease is caused by any of the four serotypes of dengue virus and transmitted by the mosquito species *Aedes aegypti* and *Ae. albopictus*. The World Health Organization (WHO) changed the clinical classification of the disease—dengue fever (DF) and dengue hemorrhagic fever (DHF)—to dengue with/without warning signs and severe dengue. Cases with significant organ involvement are now classified as severe dengue^{1,2} (Tables 1 and 2). Our patient presented with myocarditis associated with dengue virus infection, which represents a manifestation of severe dengue.

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TABLE 1
Criteria for probable dengue

Case
Probable dengue
Live in/travel to dengue endemic area; fever (2 or more days) and two of the following criteria
Nausea and vomiting
Rash
Aches and pains
Tourniquet test positive
Leukopenia
Any warning sign: abdominal pain or tenderness, persistent vomiting, clinical fluid accumulation, mucosal bleed, lethargy, restlessness, liver enlargement > 2 cm, laboratory finding of an increase in hematocrit
Severe dengue
Criteria for dengue and at least one of the following criteria
Plasma leakage leading to shock or respiratory distress
Severe bleeding
Severe organ involvement: liver, aspartate aminotransferase (AST) or alanine aminotransferase (ALT) $\geq$ 1,000; central nervous system, impaired consciousness; heart and other organs

Adapted from the WHO.¹

Cardiac manifestations of dengue are varied and include myocarditis, pericardial effusions, atrioventricular blocks, atrial fibrillation, and ectopic ventricular beats.³ Although the incidence of dengue myocarditis is unknown, several cases describing the clinical association between dengue virus and myocarditis have been reported.^{4–7} Most reports of dengue describe patients with 2 or more days of fever, which is consistent with the current classification of dengue. The work by Salgado and others⁸ showed direct dengue virus invasion of cardiomyocytes, myocardial interstitial cells, and endothelial cells in a patient who died of myocarditis. Salgado and others⁸ also found increased proinflammatory markers and abnormal calcium homeostasis in myocardial endothelial cells infected with dengue virus. They proposed abnormal calcium homeostasis as a possible cause of myocardial dysfunction secondary to dengue virus infection.⁸

Most cases of dengue myocarditis have resolved spontaneously with supportive care.^{5,6,8} However, fatalities have occurred, especially when a prompt diagnosis was not made.^{7,8} Premaratna and others⁹ reported a patient with dengue myocarditis who was in shock and recovered after receiving a single dose of intravenous methylprednisolone. Although some studies have been done comparing supportive therapy with pharmacologic therapies in patients with shock secondary to dengue infection, no randomized studies have been done comparing treatment modalities in patients with dengue myocarditis.^{10,11}

Our case is of importance, because it illustrates the difficulty in diagnosing dengue infection in a patient with myocarditis who has fevers but lacks other manifestations

TABLE 2
Criteria for confirmed dengue

Laboratory-confirmed dengue
IgM seroconversion or fourfold increase and IgG increase in paired samples or single positive Ig (in this particular case, it is considered highly suggestive of dengue)
Reverse transcriptase PCR (RT-PCR)
Virus isolation from tissue

Adapted from the WHO.¹

suggestive of dengue. The diagnosis was based on a history of recent travel to an endemic area, fever, exclusion of other diagnoses, and an elevated IgM antibody titer for dengue virus. This type of antibody usually remains positive in the serum for only 3–6 months.¹ Although our patient was born in an endemic region, he was not living in the area, and before his recent trip, he had last visited the Dominican Republic 2 years before.

Travelers who are originally from endemic areas but no longer live in those areas remain at risk for other mosquito-borne illnesses and other serotypes of dengue virus. For this reason, these individuals take mosquito precautions and follow Centers for Disease Control and Prevention (CDC) or WHO recommendations to minimize skin exposure by wearing pants and long sleeves, apply mosquito repellents to skin and clothing, and while indoors, use window and door screens and insecticide-treated mosquito nets.^{1,12}

The diagnosis of dengue infection remains challenging, because its manifestations are varied.^{13,14} It is important for healthcare providers to be knowledgeable about the disease to avoid potential iatrogenic complications, including unnecessary diagnostic tests and antimicrobial therapy.

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REFERENCES

- WHO, 2009. *Dengue, Guidelines for Diagnosis, Treatment, Prevention and Control—New Edition*. Geneva: World Health Organization.
- Srikiathachorn A, Rothman AL, Gibbons RV, Sittisombut N, Malasit P, Ennis FA, Nimmannitya S, Kalayanaroj S, 2011. Dengue—how best to classify it. *Clin Infect Dis* 53: 563–567.
- Gulati S, Maheshwari A, 2007. Atypical manifestations of dengue. *Trop Med Int Health* 12: 1087–1095.
- Nagaratnam N, Siripala K, de Silva N, 1973. Arbovirus (dengue type) as a cause of acute myocarditis and pericarditis. *Br Heart J* 35: 204–206.
- Kularatne SA, Pathirage MM, Medagama UA, Gunasena S, Gunasekara MB, 2006. Myocarditis in three patients with dengue type 3 infection. *Ceylon Med J* 51: 75–76.
- Lee IK, Lee WH, Liu JW, Yang KD, 2010. Acute myocarditis in dengue hemorrhagic fever: a case report and a review of cardiac complications in dengue-affected patients. *Int J Infect Dis* 14: e919–e922.
- Lee CH, Teo C, Low AF, 2009. Fulminant dengue myocarditis masquerading as acute myocardial infarction. *Int J Cardiol* 136: e69–e71.
- Salgado DM, Eltit JM, Mansfield K, Panqueba C, Castro D, Vega MR, Khaja K, Schmidt D, Martin KJ, Allen PD, Rodriguez JA, Dinsmore JH, Lopez JR, Bosch I, 2010. Heart and skeletal muscle are targets of dengue virus infection. *Pediatr Infect Dis J* 29: 238–242.
- Premaratna R, Rodrigo KM, Anuratha A, de Alwis VK, Perera UD, de Silva HJ, 2012. Repeated dengue shock syndrome and 'dengue myocarditis' responding dramatically to a single dose of methyl prednisolone. *Int J Infect Dis* 16: e565–e569.
- Srichaikul T, Punyagupta S, Sorakhunpipitkul L, Udomsubpayakul U, 2011. Adjunctive corticosteroid therapy in 149 grade II (non-shock) adult DHF patients: an analysis during January 2008–February 2010. *J Med Assoc Thai* 94: 1419–1423.

11. Tricou V, Minh NN, Van TP, 2010. A randomized controlled trial of chloroquine for the treatment of dengue in Vietnamese adults. *PLoS Negl Trop Dis* 4: e785.
12. Centers for Disease Control and Prevention, 2012. *How to Reduce Your Risk of Dengue Infection*. Available at: <http://www.cdc.gov/dengue/prevention/index.html>. Accessed June 17, 2012.
13. Halstead SB, 2013. Dengue: the syndromic basis to pathogenesis research. Inutility of the 2009 WHO case definition. *Am J Trop Med Hyg* 88: 212–215.
14. Chatterji S, Allen JC Jr, Chow A, Leo Y-S, Ooi E-E, 2011. Evaluation of the NS1 rapid test and the WHO dengue classification schemes for use as bedside diagnosis of acute dengue fever in adults. *Am J Trop Med Hyg* 84: 224–228.