

Hypoxemic Respiratory Failure Secondary to Zika Virus Infection

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An 80-year-old man experienced general weakness, myalgias, arthralgias, fever, chills, and diarrhea for one week. He had hypotension and tachycardia. He also had leukocytosis, thrombocytopenia, increased creatinine levels, elevated liver enzymes, elevated creatine phosphokinase (CPK) levels, and metabolic acidosis with hypoxemia, for which he was admitted to the Intensive Care Unit (ICU). His chest x-ray showed decreased lung volumes. Ceftriaxone and levofloxacin were empirically started to cover leptospirosis and community acquired pneumonia, respectively. The patient continued with clinical deterioration and the antibiotic therapy was changed to linezolid, cefepime, and doxycycline. He required endotracheal intubation and mechanical ventilation support due to progressive hypoxemic respiratory failure. A bronchoscopy showed no evidence of bacterial infectious process. The patient developed clinical improvement with successful extubation afterwards (4 days after initial intubation). He was later discharged home with physical therapies. A serum specimen was tested with real-time polymerase chain reaction (RT-PCR) technique, producing a positive result only for Zika virus. Confirmatory molecular diagnostic testing was performed at the Center for Disease Control (CDC). [*P R Health Sci J* 2018;37(Special Issue):S99-S101]

Key words: Zika Virus, Respiratory Failure, Viral Syndrome

Zika is an arthropod-borne virus. “Arbovirus” is a RNA virus transmitted by arthropods, notably mosquitos and ticks. Zika virus was discovered incidentally in Uganda in 1947 in the course of mosquito and primate surveillance (1). The virus circulated predominantly in wild primates and arboreal mosquitoes such as *Aedes africanus*. In 2016, the virus disseminated in areas known to be infected with *Aedes* mosquitos (2-3). Recent reports from the World Health Organization shows the Zika virus has spread through the Americas, including Puerto Rico (2). Although most infections are asymptomatic, Zika virus has been identified as a cause of adverse outcomes of pregnancy, including microcephaly and other congenital brain defects, and has been linked to Guillain-Barré syndrome, and severe thrombocytopenia (3-4).

Case Report

An 80-year-old man with hypertension, diabetes mellitus, hyperlipidemia, peripheral vascular disease, chronic kidney disease stage III, and one coronary artery bypass graft in 2000 was brought to the Emergency Room (ER) after he complained of diffuse myalgia, diffuse arthralgia, general weakness, unquantified fever, chills, and watery diarrhea of one week of evolution. He was found with hypotension (blood pressure: 100/57 mmHg) not responsive to volume expansion. He was tachycardic (110 beats per minute), oriented (in person,

time, and place), and with dry oral mucosa. Laboratories showed the presence of leukocytosis (14,000/ μ L) and new onset thrombocytopenia (101,000/ μ L). Creatinine level increased from 1.6 mg/dl to 2.9 mg/dl and there was presence of hyponatremia (127 mEq/L). Aspartate aminotransferase (AST) levels were 86 units/L, while alanine aminotransferase (ALT) levels were 60 units/L. Creatine phosphokinase (CPK) level was elevated at 2,348 units/L. Lactic acid was 1.6 mmol/L. Arterial blood gases showed the presence of hypoxemia (pO₂: 65 mmHg) despite a venturi mask at 50% of fraction of inspired oxygen.

An initial radiograph showed the presence of diminished lung volumes and vascular crowding (Figure 1). The patient was empirically started on ceftriaxone for suspected leptospirosis (in view of possible contact with rodents at his house) and levofloxacin for possible community acquired pneumonia. He was later admitted to the Medical Intensive Care Unit (MICU). Blood and sputum cultures, as well as dengue, chikungunya, leptospira titers and atypical bacteria work-up were collected. Despite these interventions, the patient continued with

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The author/s has/have no conflict/s of interest to disclose.

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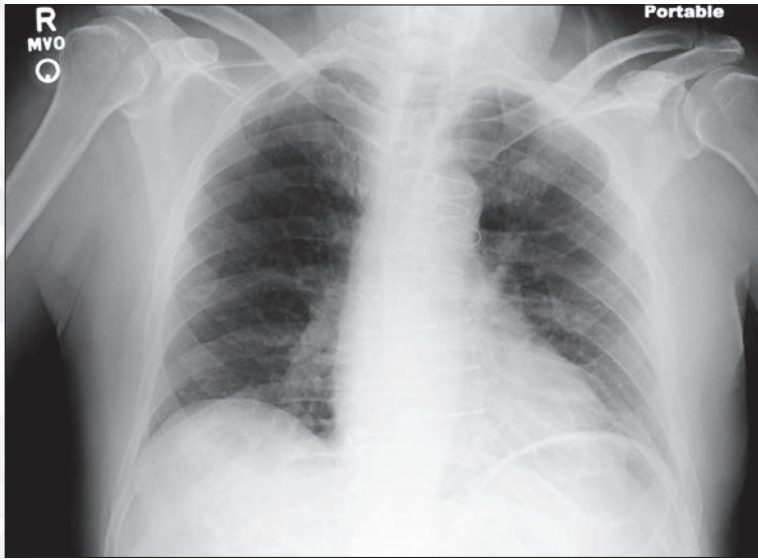


Figure 1. Initial chest x ray showing no acute cardiopulmonary process.

clinical deterioration, presenting progressive hypoxemia and worsening leukocytosis. Follow-up chest imaging showed the presence of bilateral confluent reticulonodular opacities and air bronchograms more conspicuous in the right upper lung, perihilar regions, and left pulmonary base (Figure 2). Intravenous antibiotics were changed to linezolid, cefepime, and doxycycline. Nonetheless, the patient continued deteriorating with progressive hypoxemia, for which endotracheal intubation and mechanical ventilation were required. A bronchoscopy was remarkable for whitish secretions in all the bronchial tree, as well as mild erythematous, edematous, and friable bronchial mucosa from the carina to all segments. Fungal, viral cultures, and acid-fast bacilli smears/cultures were performed, but did not grow any organism.

The patient's clinical condition improved after 4 days of mechanical ventilation and broad spectrum intravenous antibiotics. He was extubated and transferred to the regular ward after being 8 days at MICU. His clinical status continued to improve during the next week, after which he was discharged home with physical therapies due to generalized weakness. A serum sample previously collected was positive for anti-dengue virus IgM, negative for anti-chikungunya virus IgM as well as negative for detection of dengue and chikungunya virus RNA. Because a hospital-based enhanced surveillance protocol was in place for the detection of Zika virus, the same serum specimen was tested using real-time polymerase chain reaction (RT-PCR) technique, which produced a positive result only for Zika virus. Confirmatory molecular diagnostic testing was performed at the Center for Disease Control (CDC). Detection of anti-dengue virus IgM

antibody was most likely the result of cross-reactivity with anti-Zika virus IgM antibody. No other pathogen besides Zika virus was identified. To our knowledge, this is the first reported case of Zika virus causing hypoxemic respiratory failure due to pneumonia.

Discussion

Zika virus is transmitted to people primarily through the bite of an infected *Aedes* species mosquito (*Ae. aegypti* and *Ae. albopictus*). Although Zika is a vector-borne disease, there is some evidence of sexual and perinatal transmission, and a theoretical possibility of transmission via blood transfusion. The symptoms of Zika may be similar to those of dengue and chikungunya, diseases that spread through the same mosquitoes that transmit Zika (1). Symptoms that may be caused by Zika

are fever, prostration, maculopapular rash, arthralgia, myalgia, conjunctivitis, and headache. However, many people infected with Zika will not develop symptoms or will only have mild symptoms, which can last for several days to a week after infection (estimated incubation period of Zika virus is 3-14 days) (5). Because Zika is closely related to dengue, serologic samples may cross-react in tests for either virus. Gene-detection tests such as the polymerase-chain reaction assay can reliably distinguish the three viruses, but Zika specific tests are not yet widely available (1). The management for Zika viral infection is mainly supportive. There is no vaccine to prevent or medication to treat Zika infections. Zika virus has been associated with development of Guillain-Barré syndrome and other neurologic conditions (1).

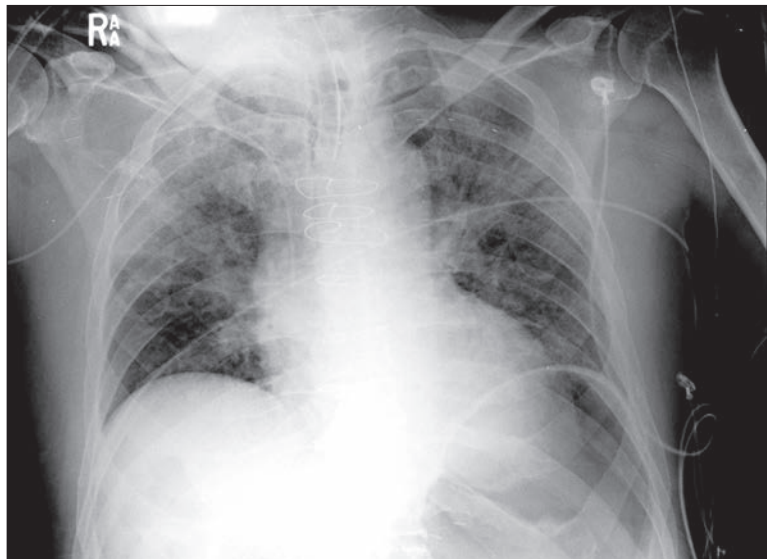


Figure 2. Chest x-ray one day after admission showing airspace and groundglass opacification of the right upper lobe and mild groundglass opacification of the left upper lobe.

The Brazilian epidemic of microcephaly, manifested by an apparent 20-fold increase in incidence from 2014 to 2015, may be caused by Zika virus infection in pregnant women (1). Zika virus infection has also been linked to severe thrombocytopenia (4). To our knowledge, the incidence of pneumonia secondary to Zika virus is unknown yet and there are no previously reported cases of Zika virus causing hypoxemic respiratory failure. Although the number of laboratory confirmed symptomatic Zika virus disease have diminished in the USA and its territories according to the CDC (6), clinicians need to be aware of the potential complications of Zika virus infection. This report illustrates that the diagnosis of Zika virus infection should be considered in patients with a similar clinical presentation and that an appropriate supportive therapy should be implemented.

Resumen

Un paciente de 80 años de edad desarrolló debilidad general, mialgias, artralgias, fiebre, escalofríos y diarrea durante una semana. Mostró hipotensión y taquicardia, además de leucocitosis, trombocitopenia, elevación de creatinina, enzimas hepáticas elevadas, nivel de creatina fosfoquinasa (CPK) elevado, y acidosis metabólica con hipoxemia, por lo cual fue admitido a la Unidad de Intensivo Médico. Una radiografía del pecho demostró volúmenes pulmonares disminuidos. Se inició ceftriaxona y levofloxacina para cubrir leptospirosis y pulmonía adquirida en la comunidad, respectivamente. El

paciente continuó deteriorando clínicamente razón y la terapia de antibióticos se modificó a linezolid, cefepime y doxiciclina. Debido a un fallo respiratorio hipoxémico progresivo, el paciente requirió intubación endotraqueal y soporte ventilatorio. Una broncoscopia no demostró evidencia de infección por bacterias. El paciente desarrolló mejoría clínica con extubación exitosa 4 días después de la intubación. Eventualmente, se le dio de alta a su hogar con terapias físicas. Las muestras de sangre examinadas con reacción en cadena de la polimerasa en tiempo real (RT-PCR) resultaron positivas solamente para el virus del Zika. La confirmación molecular de la prueba diagnóstica fue realizada por el Centro para el Control de Enfermedades.

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