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High Dose Intravenous Vitamin C Treatment for Zika Fever

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Abstract

The Zika Fever is a viral disease caused by a single-stranded RNA virus from the Flavivirus genus, Flaviviridae family, from the Spondweni group. Its transmission occurs through mosquito vectors, principally Aedes Aegypti. The most common symptoms of Zika are fever, rash, joint pain, and conjunctivitis (red eyes). Other common symptoms include muscle pain and headache. As of now, no vaccine exists for the virus and no official treatment has been developed aside from standard procedures of the use of acetaminophen (paracetamol) and non-steroidal anti-inflammatory drugs. This is a case report of a 54 year-old Hispanic female who arrived at the clinic with symptomatology congruent with the Zika fever. The patient was treated with high doses of intravenous vitamin C over three days. The symptoms resolved after the infusions without any side effects at day four. Recovery from this viral infection takes normally around two weeks. Based on the positive outcome in this case, we propose that intravenous vitamin C should be studied further as a potential treatment for acute viral infections.

Introduction

Zika virus (ZIKV) is a member of the virus family Flaviviridae and the genus Flavivirus (Knipe et al, 2007). Like other flaviviruses, Zika virus is enveloped and icosahedral and has a nonsegmented, single-stranded, positive-sense RNA genome. It is spread by daytime active Aedes mosquitoes, such as A. Aegypti and A. Albopictus (Knipe et al, 2007). Its name comes from the Zika Forest of Uganda, where the virus was first isolated in 1947 (European Center for Disease Prevention and Control, 2015). Zika virus is related to dengue, yellow fever, Japanese encephalitis, and West Nile viruses (European Center for Disease Prevention and Control, 2015). As of February 2016, there are three reported cases indicating that Zika virus could possibly be sexually transmitted (World Health Organization, 2016a).

The infection, known as Zika fever, often causes none or only mild symptoms, similar to a mild form of dengue fever (Knipe et al, 2007). The illness cannot be prevented by medications or vaccines and is treated mainly by rest (Chen et al, 2016). Zika fever in pregnant women is associated with microcephaly but it is unclear whether the virus is the cause (Knipe et al, 2007; Cable News Network, 2015; Centers for Disease Control

and Prevention, 2016a). There is a link between Zika fever and neurologic conditions in infected adults, including cases of the Guillain–Barré syndrome (World Health Organization, 2016b; Oehler et al, 2014; Cao-Lormeau et al, 2016). Common symptoms of infection with the virus include mild headaches, maculopapular rash, fever, malaise, conjunctivitis, and joint pains. Within two days, the rash may start fading, and within three days, the fever is generally resolved and only the rash remains.

As of 2016, no vaccine or preventive drug is available. Symptoms can be treated with rest, fluids, and paracetamol (acetaminophen), while aspirin and other nonsteroidal anti-inflammatory drugs should be used only when dengue has been ruled out to reduce the risk of bleeding (Sikka et al, 2016). It is difficult to diagnose Zika virus infection based on clinical signs and symptoms alone due to overlaps with other arboviruses that are endemic to similar areas (Centers for Disease Control and Prevention, 2016b). In small case series, routine chemistry and complete blood counts have been normal in most patients. A few have been reported to have mild leukopenia, thrombocytopenia, and elevated liver transaminases (Centers for Disease Control and Prevention, 2016c; Waggoner et al, 2016).

Zika virus can be identified by reverse transcriptase PCR (RT-PCR) in acutely ill patients. However, the period of viremia can be short and the World Health Organization (WHO) recommends RT-PCR testing be done on serum collected within 1 to 3 days of symptom onset or on saliva or urine samples collected during the first 3 to 5 days (Waggoner et al, 2016; Faye et al, 2008; Ayers et al, 2006).

Later on, serology for the detection of specific IgM and IgG antibodies to Zika virus can be used. IgM antibodies can be detectable within three days of the onset of illness (Waggoner et al, 2016). Serological cross-reactions with closely related flaviviruses such as dengue and West Nile virus as well as vaccines to flaviviruses are possible (Waggoner et al, 2016; Faye et al, 2008). Commercial assays for Zika antibodies are now available but have not yet been FDA approved (Centers for Disease Control and Prevention, 2016). During the first seven days of these illnesses, viral RNA can often be identified in serum, and RTPCR is the preferred test for Zika, chikungunya, and dengue viruses.

For many years, it has been widely known that ascorbic acid (vitamin C) has a variety of physiological functions with clinical efficacy. Vitamin C is a water-soluble vitamin, and has been used to prevent many diseases and/or infections like the common cold and other viral infections (Mikirova et al, 2012; Padayatty et al, 2010; Byun et al, 2011; Harakek et al, 1990; Zhang et al, 2014). Ascorbic acid scavenges reactive oxygen species (ROS), increases vascular and connective tissue integrity, improves immune function (increases interferon) and assists in leukocyte phagocytic functions (increases hydrogen peroxide, number and aggressiveness of white blood cells) (Gonzalez et al, 2014).

Vitamin C supplemented orally has its limitations in achieving high blood (i.e., plasma) levels, whereas the use of intravenous vitamin C (IVC) can reach blood levels that possess distinct clinical and pharmacological advantages. Oral vitamin C is absorbed in the gastrointestinal tract, where the body metabolizes a limited amount and the rest is excreted through the kidneys. However, if the vitamin is administered intravenously it can

reach plasma concentrations that are 30 to 70 times higher than the oral route, which seems necessary for the antiviral activity (Chen et al, 2016).

Ascorbic acid is also a nutrient for the immune system. Treatment of ascorbic acid in vitro resulted in an increase in T-cells and natural killer (NK)-cells, which constitute one of the main components of the adaptive immune system, which fights against viruses and intracellular bacteria (World Health Organization, 2016). It has been suggested the same effect can be achieved by IVC administration. Here we report a case of Zika fever, treated with high doses of IVC in a period of three days without any negative side effects.

Case Report Presentation

Three days after suffering several mosquito bites the patient noted the onset of intermittent periods of fever and chills (day one). Two days later, her mouth became sore and oral blisters developed. On day five, a papular rash developed, which spread to her extremities. The rash lasted three days, and in conjunction with a retro-orbital headache and fever and mild non-purulent conjunctivitis, significant joint and muscle tenderness developed which prompted a visit to the physician.

Blood, nasopharyngeal swab, and urine samples were collected for investigation of measles and/or other possible infectious causes as the differential work-up. Initial laboratory investigations showed a hemoglobin level, leukocyte count, platelet count and levels of creatinine, electrolytes, alanine aminotransferase, and alkaline phosphatase were all within reference ranges.

A reverse transcription polymerase chain reaction (RT-PCR) described by was performed resulting positive for flaviviruses. Since the clinical signs and symptoms of infection with Zika virus can be easily confused with dengue and/or Chikungunya, mainly because of the fever, headache, and generalized rash-like presentation this test was relevant to diagnosis.

Vitamin C was applied after a G6PD test in escalating doses of 25g (Day 1 of Treatment), 50 g (Day 2 of Treatment) and 75 g (Day 3 of Treatment). The symptoms improved substantially in 24 hours and were absent by the third day.

Discussion

Mounting evidence has suggested a close correlation between oxidative stress and viral infectious disease. The elevated oxidants induced by viral infection include nitric oxide radicals, superoxide anions, hydroxyl radicals and their by-products, which may all contribute to viral pathogenesis, the modulation of cellular responses, the regulation of viral replication and the host defense (Epstein & Weiss, 1989). Many of these oxidants may be harmful to the host cells if they are released into the extracellular medium (Smith, 1994; Kim et al, 2013).

Vitamin C is an efficient antioxidant and possesses anti-viral activity. For example, it has been shown that vitamin C is an essential factor in the production of the anti-viral immune response during the early phase of viral infection through the production of type I

interferons, which up-regulates NK cell and cytotoxic T-lymphocyte activity (Madhusudana et al, 2004). Also, studies have indicated that ascorbic acid can be used as an inactivating agent for both RNA and DNA viruses, impacting viral infectivity (Byun et al, 2011). In addition, ascorbic acid can detoxify viral products that produce pain and inflammation (Harakek et al, 1990). All this evidence confirms the effectiveness of ascorbic acid against viral infections, and against Zika fever, as suggested by the patient's swift response to IVC. Furthermore, no negative side effects resulted during or after the treatment. Based on the positive outcome in this case, we propose that IVC should be studied further as a potential treatment for acute viral infections.

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