Case Report

Detection of chikungunya infection in a dengue-endemic region: A case report of NS1-negative patient managed initially as dengue

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Abstract

This case report examines the diagnostic challenges in distinguishing chikungunya fever from dengue fever in a 25-year-old male living in a dengue-endemic area. This patient presented with high-grade fever, severe arthralgia, and myalgia, exhibiting symptoms which are common to both diseases. At the initial stage, despite being negative for dengue nonstructural protein 1(NS1) antigen test, the patient was managed as having dengue fever. However, the persistence of symptoms led to additional testing, and the results of chikungunya-specific polymerase chain reaction (PCR) testing became positive, confirming the diagnosis of chikungunya virus infection. The patient was subsequently managed for chikungunya. This case emphasizes the significance of maintaining a heightened suspicion for chikungunya, especially in instances with negative dengue NS1 antigen tests.

Keywords: Chikungunya, Sri Lanka, dengue

Introduction:

Chikungunya is a debilitating mosquito-borne disease caused by the chikungunya virus that belongs to the genus Alphavirus in the family Togaviridae. Sri Lanka experienced a chikungunya outbreak in mid-October 2006, coinciding with outbreaks in the Maldives and Andaman and Nicobar Islands.[1] Over 100,000 chikungunya cases were diagnosed in Sri Lanka during this period.[2,3] Although the same Aedes mosquitoes transmit both chikungunya and dengue, absence of chikungunya outbreaks in Sri Lanka after 2007, despite the continued prevalence of dengue outbreaks in the region, raises intriguing questions about the factors contributing to this disparity.

Case Presentation

In July 2020, a 25-year-old previously healthy man developed high fever (>39 °C), myalgia, arthralgia, headache, cough and chills and was admitted to the hospital on the third day of fever. An NS1 antigen test was conducted on the same day. Laboratory investigations at the time of presentation showed a total leukocyte count of 5.0 x 10^3 /µL (neutrophils 67%). His

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haemoglobin was 15.5 g/dL, and thrombocyte count was 94,000/mm.[3] His FBC's during the admission are shown in Figure 1. He had no travel history to known chikungunya virus affected areas. Laboratory evaluations were unremarkable and NS1 serology for dengue virus infection was negative. Even with the negative NS1 antigen results, he was managed as dengue fever according to the national dengue management guidelines. Even though not routine, on the second day of admission, molecular diagnosis targeting the amplification of dengue virus, chikungunya virus and Zika virus nucleic acid sequences for research purposes was carried out. Real-time reverse transcription polymerase chain reaction (RT-PCR) was carried out using a commercially available VIASURE Real-time RT-PCR kit (CerTest Biotec, S.L., Zaragoza, Spain), which yielded negative results for Zika and dengue viruses and positive results for chikungunya virus with a cycle threshold of 0.04. As a result, acute chikungunya viral infection was diagnosed. Over the ensuing 7 days, the patient continued to have fever, abdominal pain and body aches and was managed conservatively. The patient recovered by the seventh day and was discharged from the hospital. The time line of the index case is shown in Figure 2.

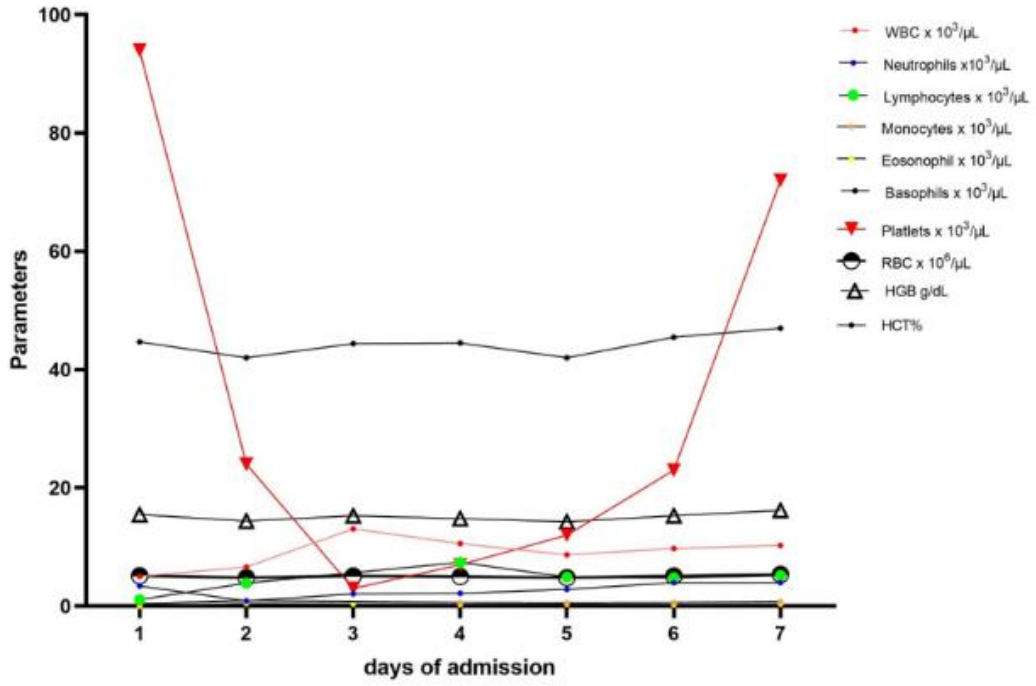

Figure 1: Laboratory parameters from day 1 of admission to day 7

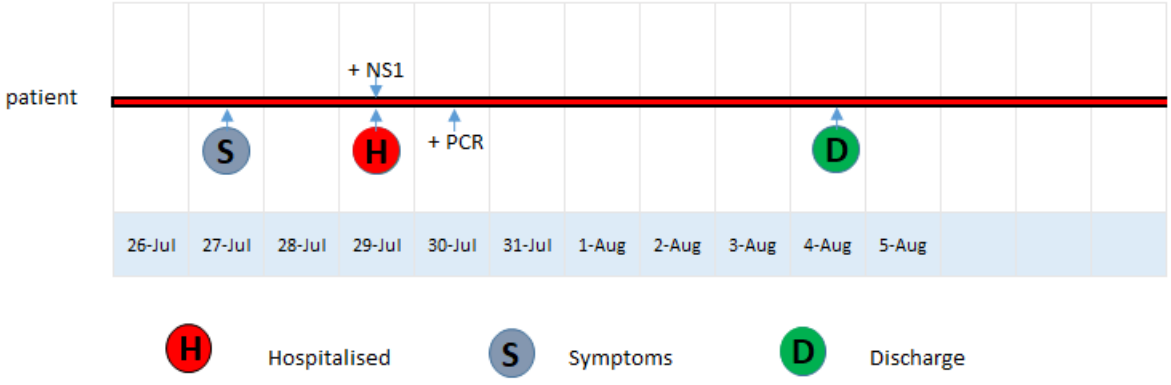

Figure 2: Time line of the index case

Discussion

The most important sign of chikungunya fever is severe joint pain that arises with almost every clinical case. Arthralgia is most frequently noted in the ankles, toes, fingers, elbows, wrists and knees. The joints show extreme tenderness and swelling with patients often reporting incapacitating pain lasting for weeks or months.[1] Most symptoms/signs recover totally within weeks or months but there are reported cases of chikungunya fever induced arthralgia continuing for several years. In an occasional case, the rheumatic signs have resulted in joint destruction. Unlike dengue, chikungunya is believed to be more nonthreatening although death has been reported in earlier epidemics in Reunion and India.[4] In Sri Lanka, two deaths have been reported among chikungunya infected patients but it is not confirmed that the reason for these deaths was chikungunya. [2]

The signs of chikungunya infection can be related to those caused by many other infections in endemic areas. One specific difficulty in identifying infection is its overlapping clinical symptoms/signs with dengue infection. Many cases of chikungunya infection may be misdiagnosed and in practice, the rate of chikungunya infection may be much greater than reported. This could be due to the limitation of relying solely on NS1 antigen testing and serology tests for dengue in regions where both chikungunya and dengue coexist. Clinicians should maintain a high index of suspicion of chikungunya in patients with compatible symptoms, especially when the dengue tests are negative. Timely and accurate diagnosis is crucial for appropriate management and public health interventions of the disease condition.

This reported case of chikungunya infection in July 2020 in Sri Lanka raises important considerations about the ongoing prevalence of the virus in the region.

Despite both dengue and chikungunya viruses sharing the same mosquito vector, dengue outbreaks have been extensively reported, whereas chikungunya outbreaks in Sri Lanka remain notably absent. This discrepancy may be due to the lack of available diagnostic tools for detecting the chikungunya virus, leading to underreporting or misidentification of outbreaks. The high prevalence of dengue fever in Sri Lanka has led to a focus on investigations primarily geared towards identifying dengue infections.

The presence of IgG antibodies for chikungunya in community studies conducted in Sri Lanka[5,6,7] without any recent reported chikungunya cases raises questions about the interpretation of these serological findings. The hypothesis that the detected antibodies may be remnants from the 2006 and 2007 outbreaks is a plausible explanation as infection with the chikungunya virus provides lifelong immunity. The co-circulation of multiple arboviruses in the same region complicates the diagnostic landscape. The potential cross-reactivity of antibodies in serological tests designed for one virus with another virus, such as dengue and chikungunya, could contribute to misinterpretations of results. To ensure accurate and reliable diagnostics, it becomes imperative to enhance the specificity of tests and implement more sophisticated methods that can differentiate between these viruses. Additionally, ongoing surveillance efforts and clear clinical differentiation between dengue and chikungunya cases are essential to provide a more accurate picture of the current epidemiological situation. Therefore, we suggest conducting a chikungunya rapid antigen test as a routine test if the NS1 is negative and the patient is suffering from severe joint pain.

Conclusion:

This case highlights the importance of expanding diagnostic capabilities to encompass a broader spectrum of mosquito-borne diseases. It highlights the need for clinicians to consider alternative diagnoses, such as chikungunya, when evaluating febrile patients in dengue-endemic areas, especially if the NS1antigen and serological tests results are negative. Comprehensive diagnostic approaches, including specific serological tests for multiple arboviruses, are essential to guide appropriate treatment and public health strategies in regions with overlapping mosquito-borne diseases.

Declaration

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