

A Case of Triple-Infection with SARS-CoV-2, Chikungunya, and Dengue Fever in a Returning Traveler

Sally Arif, PharmD^{1,*}, Milena Murray, PharmD, MSc², Brian Harting, MD³ and Sarah Siddiqui, DO⁴

¹ Rush University Medical Center, Northwestern University College of Pharmacy, Downers Grove, IL 60515, USA

² Northwestern Medicine, Northwestern University College of Pharmacy, Downers Grove, IL 60515, USA; mmurra@northwestern.edu

³ Metro Infectious Disease Consultants, LLC, 901 McClintock Dr, Suite 202, Burr Ridge, IL 60527, USA; hartingafc@gmail.com

⁴ Amita Medical Health Group, 5201 Willow Springs Rd Ste. 160, La Grange, IL 60525, USA; sarah.n.siddiqui@gmail.com

* Corresponding author: sarif@northwestern.edu

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Abstract: Chikungunya (CHIKV) and dengue (DENV) fever are caused by arboviruses with a shared vector and often overlap in tropical endemic areas. COVID-19, caused by the SARS-CoV-2 virus, has a similar presentation to CHIKV and DENV. The case of a 39-year-old woman with a triple viral infection (DENV, CHIKV, and SARS-CoV-2) is presented. Co-infection with endemic viruses post-travel is likely underreported due to overlapping clinical presentations and timelines. Awareness of illness in returning travelers and prompt co-infection diagnosis are needed to optimize patient outcomes.

Keywords: SARS-CoV-2; dengue fever; chikungunya

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Introduction

Between 43% and 79% of international travelers return home with a travel-related illness; diarrhea is the most commonly reported symptom [1]. While Europe remains a common destination, regions

with emerging economies such as Asia, Africa, Latin America, and the Middle East are seeing an increase in travel and are associated with specific endemic viruses [1]. Chikungunya (CHIKV) and dengue (DENV) fever are caused by arboviruses that share the same *Aedes* mosquito vectors and often overlap in tropical endemic areas [2,3]. There are five known serotypes of DENV (DENV1–5) and three known strains of CHIKV (Asian–West African; East–Central; South African) [4]. DENV is most commonly characterized by fever, nausea or vomiting, myalgia or arthralgia, headache with retro-orbital pain, petechia, and leucopenia [5]. CHIKV is associated with sudden-onset fever, arthralgia, or severe arthritis not explained by other causes. Coinfections with CHIKV and DENV may be observed because of overlapping endemic territories. COVID-19 is associated with severe acute respiratory syndrome caused by the SARS-CoV-2 virus circulated through respiratory droplets in the air [6,7]. Due to travel, COVID-19 spread globally.

The introduction of the COVID-19 pandemic and SARS-CoV-2 virus into areas with ongoing viral epidemics introduces a new challenge: the diagnosis of multiple concomitant viral infections with overlapping symptoms. Due to their similar clinical manifestations, diagnosis is complex, and misdiagnosis may delay appropriate care and disease management. This case describes a scenario of triple viral infection with CHIKV, DENV, and SARS-CoV-2 after international travel.

Case Presentation

A 39-year-old woman presented to the emergency department (ED) four days after returning from a 5-day-long trip to The Gambia in West Africa with complaints of fever, nausea, anorexia, and fatigue. The onset of symptoms started two days after her return to the United States. The patient recalled being bitten by mosquitoes daily during her trip, did not take any malaria prophylaxis, and had heard that several of her travel mates tested positive for SARS-CoV-2 upon return to the United States. The patient had a positive COVID-19 antigen test confirmed using a rapid home antigen test 2 days before presentation to the ED, despite being triple vaccinated against SARS-CoV-2 (a booster was given 10 weeks before presentation). She had no significant past surgical history and a past medical history of asthma, for which she did not need any rescue inhalers. The patient's self-reported high-grade fevers, ranging from 101 to 104 °F, were associated with rigors and chills for the 4 days before admission. The only other complaint included multiple small petechiae on the abdomen that resolved within 24 h of returning from the trip abroad. The patient denied having a sore throat, chest pain, shortness of breath, or diarrhea and had stable vital signs besides slight tachycardia (HR 105 bpm).

Upon physical exam, she was oriented to person, place, and time. Laboratory baseline findings in the ED were within reference ranges except for a low WBC of $1.92 \times 10^9/L$ (with a differential that included an absolute neutrophil count of 1200, platelet count of $145,000 \times 10^9/L$) and elevated liver function tests (highest AST 148 IU/L, ALT 199 IU/L, alkaline phosphatase 111 IU/L). The Infectious Disease service was consulted, and empiric antibiotic therapy was started with ceftriaxone 2 grams IV daily and doxycycline 250 mg PO twice daily.

The patient was admitted to a COVID-19 isolation room for a workup of malaria, DENV fever, and CHIKV. Serological evidence was positive on enzyme-linked immunosorbent assay (ELISA) for dengue-specific IgM with a value of 5.66 (IgG 1.04) and positive for chikungunya-specific IgM with a value of 4.28. All other blood cultures, HIV antigen screening, malaria smears, and *Leptospira* IgM antibodies were negative. The patient was treated with acetaminophen 650 mg every 6 hours as needed for fever and with a one-liter infusion of normal saline at 83 mL/hour. On the third day of admission, the Hematology service was consulted as the platelets count was $107 \times 10^9/L$ and the PTT was elevated, for which mixed studies were ordered. There was a subsequent clinical improvement, and the patient was discharged with normalized blood counts and laboratory findings.

Two days post-discharge, laboratory findings showed a WBC of $4.68 \times 10^9/L$ (ANC 900) and a platelet count of $210 \times 10^9/L$. The patient reported developing an itchy rash on the palms of her hands and soles of her feet and severe bilateral hip joint pain, which resolved within 48 h of discharge. The only other symptoms occurring during the week post-discharge included headache, retro-orbital

pain, and diarrhea, which all resolved within seven days. The patient had sacroiliac joint pain that started in week 3 post-discharge and required NSAID therapy, physical therapy, and a short course of methylprednisolone. Two weeks after the initial presentation, follow-up laboratory findings showed the resolution of platelet counts ($584 \times 10^9/L$) and liver function enzymes (AST 64 IU/L, ALT 96 IU/L, alkaline phosphatase 106 IU/L).

Discussion

Healthcare professionals should be aware of potential co-infections with diseases that manifest similarly. SARS-CoV-2, DENV, and CHIKV have similar clinical symptoms and laboratory features in early disease [8]. The absence of a diagnosis may impact patient outcomes as the clinical management of patients with COVID-19 and arboviruses differs. Therefore, co-infection may go undiagnosed once the first positive test results. There may also be cross-reactivity between serological tests for DENV and SARS-CoV-2 [8]. It should be noted that both COVID-19 and CHIKV are associated with lasting manifestations after infection (biphasic), whereas DENV is monophasic [7]. It has been noted that post-CHIKV disorders took 10 years to be described and have been described in both general and mental disorders, as well as impaired quality of life. Guidelines for management are still just recently emerging for COVID-19 and should be continued to follow a similar trajectory to CHIKV. Joint pain associated with CHIKV may be debilitating and last for months to years [9].

Viral outbreaks differ in the individuals with the most significant risk, transmission vectors, fatality rates, and likelihood of transmission. Geographic spread via air travel should also be considered with infectious diseases [6]. Knowledge of endemic areas is needed to ensure appropriate testing and diagnosis of viral diseases in returning travelers. Another triple infection has been reported in the literature, with DENV, Zika virus, and malaria [10]. In this report, malaria was first diagnosed, and viral vectors were not tested until one month after the first presentation. Dual viral infection with dengue myocarditis and COVID-19 in a returning traveler from Northern India was also reported [11]. A study of 176 patients with confirmed COVID-19 from Guerrero, Mexico, provided evidence of co-infection with select arboviruses [12]. Samples from each patient were sent for testing of seven arboviruses (CHIKV, DENV 1-4, West Nile Virus, and Zika virus). There were 18 patients with CHIKV IgM, 10 patients with DENV, and 3 patients with Zika virus present in their sera [12]. A study of 105 subjects with SARS-CoV-2 in Luanda, Angola, revealed 13.3% with concomitant malaria and 27.6% with concomitant DENV. The overall co-infection rate in this cohort was 11.4% [13]. It should be noted that the co-infection, in this case, may be due to the altered immune response that may be seen with SARS-CoV-2 infection and that there is the potential for positive serology cross-reactivity between SARS-CoV-2 infection and arboviral infections [14,15]. Serological tests should always be correlated with clinical symptoms and travel history.

International travel is expected to increase with a projected annual 1.8 billion travelers by 2030 [1]. The most commonly reported symptoms include diarrhea, headache, fatigue, cough, skin manifestations, vomiting, and sore throat. Awareness of illness related to international travel assists healthcare providers with pre-travel clinical advice and should inform post-travel evaluations. Emergency room triage protocols should include decision support based on travel history to provide appropriate infectious disease risk screening and infection prevention measures [16]. Selection of criteria such as fever and shortness of breath should prompt the masking of the patient. A travel history plus fever should prompt appropriate workup based upon travel location. These measures will decrease the likelihood of unwanted exposures and ensure proper patient care.

Conclusions

This case highlights the need for a high index of suspicion for infection with multiple viruses in returning travelers. Several viral infections present with similar clinical manifestations and timelines. Measures

should ensure appropriate, timely diagnosis for the best patient outcomes. Further epidemiological studies on returning travelers are needed to assess the magnitude of co-infections, including triple viral infections.

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