Case Report

First introduction of dengue virus type 3 in Niger, 2022

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A R T I C L E   I N F O

A B S T R A C T

Dengue fever is the most important mosquito-borne viral disease of humans, with a significant disease burden in tropical and subtropical countries. The disease is caused by four distinct dengue virus (DENV) serotypes, DENV-1 to -4, all of which belong to the family Flaviviridae, genus *Flavivirus*. Approximately 3.6 billion people live in areas where they are at risk of transmission of DENVs, resulting in up to 390 million infections and 96 million symptomatic cases annually. Although the disease is highly endemic in the West Africa region, little is known about the prevalence and distribution of DENVs in Niger. We hereby report the first laboratory-confirmed case of dengue in Niger.

Introduction

Dengue fever is a global public health concern, with an estimated 390 million infections occurring each year (95% credible interval 284–528 million), of which 96 million are symptomatic (95% credible interval 67–136 million) [1]. The disease's severity varies from a self-limitng, potentially debilitating illness to hypovolemic shock, with a mortality rate as high as 20% if untreated [2]. With no specific treatment available, the only way to mitigate the risk of acquiring dengue fever is by controlling its mosquito vectors [2].

The causative agent, dengue virus (DENV), is a mosquito-borne single-stranded RNA virus belonging to the *Flavivirus* genus. DENVs exist as a variety of genotypes within four genetically diverse serotypes (DENV-1 to -4) [3]. All four serotypes are present in Africa [4] where many countries lack a national surveillance system and active reporting mechanism [5]. Therefore, virological surveillance should be considered as the most important strategy for early warning and monitoring the circulation of different serotypes [6]. However, cases can be reported in endemic and non-endemic countries due to importation of viremic travelers, made possible by international travel [7]. In Niger, little was known about the prevalence and distribution of dengue viruses, although the disease is highly endemic in the West Africa region [8,9]. This report describes the first ever laboratory-confirmed case of DENV infection detected in Niger.

Case presentation

On August 17, 2022, a 47-year-old man traveling from the Republic of Cuba, where dengue is still circulating, was hospitalized with febrile symptoms, including a temperature of 39.8°C, headache, physical debility, rhinorrhoea, and muscle and joint pain, at the Clinic Gamkallé in Niamey, the capital city of Niger. The symptoms began on August 15, 2022, during his trip to Niger. Upon admission, the patient tested negative for malaria and COVID-19, using specific rapid diagnostic tests. He presented no severe complications, but experienced moderate thrombocytopenia and leucocytosis, for which he received only compensatory treatment with paracetamol and ceftriaxone. He was discharged on August 21, 2022.

In view of his travel history, a blood sample was collected to test for suspected dengue, and sent to the Centre de Recherche Médicale et Sanitaire (CERMES), the national reference laboratory testing for hemorrhagic fever viruses. Dengue was confirmed on August 18, using qRT-PCR with specific primers and probes for detecting any of the four serotypes, as previously described [10]. An aliquot of serum sample was sent to the Institut Pasteur de Dakar (IPD) for confirmation and further analysis, including molecular typing and genome sequencing, using an enrichment library preparation method [11]. The sample was identified as DENV-3 serotype and a nearly complete genome sequence was obtained (GenBank [GB] no. OQ132878). The new DENV-3 sequence
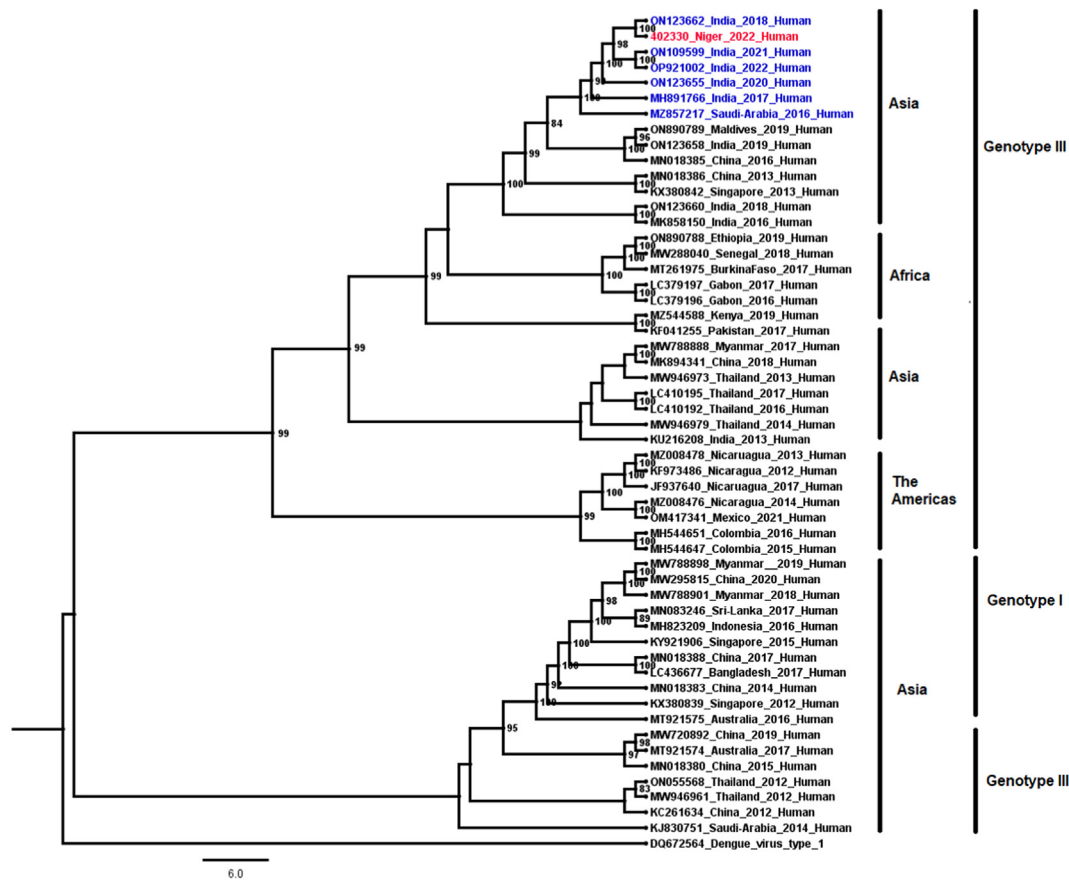

Figure 1. Maximum likelihood (ML) phylogenetic tree based on 54 dengue virus type 3 polyproteins, including 52 sequences previously available from the US National Institutes of Health National Institute of Allergy and Infectious Diseases Virus Pathogen Database and Analysis Resource (http://www.viprbrc.org), and representative of dengue virus type 3 genetic diversity over the last decade. The ML tree was inferred with the IQ-TREE web server for 1000 ultrafast bootstrap replicates under the GTR+F+I+G4 substitution model, as estimated by ModelFinder and rooted on midpoints. Dengue virus type 1 was used as the outgroup. The topology was visualized by FigTree (v.1.4.2) (http://tree.bio.ed.ac.uk/software/figtree/). Only bootstrap values ≥ 80 were shown on the tree. The genome highlighted in red corresponds to the newly characterized DENV sequences from Niger, clustering with recent isolates from India.

from Niger was analyzed using maximum-likelihood (ML) phylogenetic inference, built using the IQ-TREE web server for 1000 ultrafast bootstrap replicates [12], which revealed that it belonged to genotype 3 and was most closely related to the sequence of an isolate identified from a human in India in 2018 (GB no. ON123662). All the sequences in this cluster originated from a sequence isolated from Saudi Arabia in 2016 (GB no. MZ957217) (Figure 1).

Following the case confirmation, a public health intervention, based on a case investigation, was jointly conducted by the Ministry of Health and CERMES, supported by the WHO country office.

Discussion

This introduction of dengue to Niger from the Republic of Cuba highlights the potential for viral spread through international travel [7]. From January 1 to November 17, 2022, Cuba reported a total of 3036 laboratory-confirmed cases, including 18 severe cases and one death [13]. With the presence of an *Aedes aegypti* mosquito population in Niger [14], dengue importation constitutes an emerging public health security threat. Moreover, rapid urbanization could create favorable conditions for increased transmission, as a result of increases in the vector population and also changes in the ecological balance among different strains [4].

Officially, no confirmed dengue case has been reported by the Niger's health authorities, although previous studies have reported dengue outbreaks and epidemics in all regions of Africa and involving all four dengue virus serotypes [4]. Moreover, dengue infection is highly endemic in all neighboring countries, including Burkina Faso, Mali and Nigeria [9,15]. Therefore, the lack of data on dengue infection in Niger is perhaps due to poor knowledge on the disease and misdiagnosis with malaria or other febrile diseases [15]. Thus, it is important to raise awareness among healthcare professionals regarding the need for rapid identification and diagnosis of dengue cases in Niger.

The link between the 2022 isolate from Niger and a sequence from India could be attributable to long-maintained relations supporting greater trade, commerce, and travel between India and countries of Latin America, including Cuba. Previous phylogeographical studies have suggested that the earliest introduction of DENV to Africa probably occurred through exportation from South East Asia [3]. Furthermore, according to previously reported data on global dengue importation, 76.3% of imported dengue cases were attributed to Asia [7].

Conclusion

Our findings highlight the urgent need for Niger's Ministry of Health to implement an integrative arbovirus surveillance program, for better understanding of dengue epidemiology and transmission. Strengthening laboratory diagnostic capacity could also improve early case management. Furthermore, improved border control measures, based on the International Health Regulations, could enable rapid identification of suspected cases.

Competing interests

The authors declare no competing interests.

Acknowledgments

Author contributions

AL, MF, GF1, GF2, OF, and RJ conceived and designed the study. AL, MF, MMD, SA, and SS performed the study. AL, ETI, SA, LI, HO, and HS performed the field investigations. AL, MF, and GF2 analyzed the data. AL and MF wrote the paper. AL, MF, GF1, GF2, ETI, SA LI, HS, OF, and RJ revised the manuscript. All authors read and approved the final version of the manuscript.

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Ethical approval

The Niger National Ethical Committee at the Ministry of Health approved the surveillance protocol as research with a less-than-minimal risk, while written consent forms were not required. Oral consent was obtained from the patient. All methods, including the use of human samples, were performed in accordance with the Declaration of Helsinki.

Availability of data and materials

All data generated or analyzed during this study are included in this published article. The newly characterized dengue virus type 3 sequence from Niger has been deposited in GenBank under accession number OQ132878.

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