Journal of Infection (2017) **75**, 356–367

BIAM British Infection Association

www.elsevierhealth.com/journals/jinf

Returning ex-patriot Chinese to Guangdong, China, increase the risk for local transmission of Zika virus

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Accepted 6 July 2017
Available online 14 July 2017

KEYWORDS
Zika virus;
Imported case;
Ex-patriot Chinese;
Guangdong;
China

Summary *Objectives:* Fast expansion and linkage to microcephaly and Guillain Barre syndrome have made Zika virus (ZIKV) track attention of global health authority concerns. The epidemiology, virological characteristics and genetic evolution of introduced ZIKV to Guangdong, China, were investigated.
Methods: Analyses of the epidemiological characteristics and genetic diversity of ZIKV isolates were performed.
Results: A total of twenty-eight confirmed ZIKV infection cases were imported into China in 2016, of which 19 were imported into Guangdong, China from Venezuela (16), the Samoa Islands (1), Suriname (1) and Guatemala (1). Serial sampling studies of the cases indicated longer shedding times of ZIKV particles from urine and saliva samples than from serum and conjunctiva swab samples. Seven ZIKV strains were successfully isolated from serum, urine and conjunctiva swab samples using cell culture and neonatal mouse injection methods. Genomic

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http://dx.doi.org/10.1016/j.jinf.2017.07.001

analysis indicated that all viruses belonged to the Asian lineage but had different evolutionary transmission routes with different geographic origins. The molecular clock phylogenetic analysis of the ZIKV genomes indicated independent local transmission that appeared to have been previously established in Venezuela and Samoa. Additionally, we found 7 unique non-synonymous mutations in the genomes of ZIKV that were imported to China. The mutations may indicate that ZIKV has undergone independent evolutionary history not caused by sudden adaptation to Chinese hosts.

Conclusion: The increasing number of ex-patriot Chinese returning from ZIKV hyper-endemic areas to Guangdong combined with the presence of a variety of *Aedes* species indicate the potential for autochthonous transmission of ZIKV in Guangdong.

Introduction

Zika virus (ZIKV) is an arbovirus belonging to the family Flaviviridae, genus *Flavivirus*. ZIKV was first isolated from a sentinel rhesus monkey from the Ziika forest of Uganda in 1947. In 1948, the virus was isolated from *Aedes africanus* mosquitoes originating from the same forest.[1] Subsequent studies found that ZIKV was also likely transmitted by *Aedes aegypti*, *Aedes albopictus*, *Aedes hensilli*, and other mosquito species.[2] Although serological studies in Uganda indicated that humans could be infected,[3] only sporadic human cases were reported in Asia and Africa from the 1960s until 2007, when the first large outbreak of ZIKV was reported on Yap Island, Federated States of Micronesia.[4] Since that time, ZIKV infection has been frequently detected outside of Africa. More than 70 countries have reported ZIKV cases worldwide, and autochthonous cases have been reported in New Caledonia, Easter Island, the Cook Islands, Southeast Asia, and French Polynesia and recently in South America and North America, the Caribbean islands, Singapore, Thailand and the Philippines[2,5,6] (http://ecdc.europa.eu/en/healthtopics/zika_virus_infection/zika-outbreak/Pages/Zika-countries-with-transmission.aspx and https://wwwnc.cdc.gov/travel/page/world-map-areas-with-zika). Additional transmission routes, such as sexual, maternofetal, and blood transfusion, were also found to contribute to the onward transmission of ZIKV.[6] Due to its wide transmission and the presence of competent vectors, including *Ae. aegypti* and *Ae. albopictus*, ZIKV is predicted to expand globally following the transmission routes of other flaviviruses, such as the dengue and chikungunya viruses.[6]

More than 80% of ZIKV infections are asymptomatic. Symptomatic cases may develop a maculopapular rash, fever, malaise, fatigue or myalgia, arthralgia, and conjunctivitis, whereas hemorrhagic or fatal cases are rarely reported. Severe neurologic complications, including microcephaly and Guillain–Barre syndrome, are suspected to be associated with ZIKV infection[7–10] and have been confirmed in case control studies in French Polynesia[7] and Colombia.[11] However, microcephaly and Guillain–Barre syndrome may only be the tip of the iceberg of complications caused by ZIKV infection. Other unapparent complications may also occur because other neurological, ophthalmologic, and auditory complications have been reported.[6,12–14]

Archived reports indicate that ZIKV cases may spread internationally through travel between endemic areas and local countries. From February 12 to September 16, 2016, 28 confirmed ZIKV infection cases were imported into China, of which 19 were imported into Guangdong Province from Venezuela (16 cases), the Samoa Islands (1 case), Suriname (1 case) and Guatemala (1 case). The epidemiological and virological characteristics of the 19 cases summarized in this study indicate that the large returning ex-patriot Chinese population to the Guangdong province increases the risk of autochthonous ZIKV transmission in Guangdong, China.

Materials and methods

Ethics statement

The procedures for clinical sample and data collection were performed in accordance with humanitarian regulations and were approved by the Ethics Committee of the Guangdong Provincial Center for Disease Control and Prevention.

Epidemiological data and sample collection

The data were obtained from the Notifiable Infectious Disease Report System (a passive surveillance system of notifiable infectious diseases in China, NIDRS). The age, gender, address, date of entry, date of symptom onset, origin, and travel history for each case were collected and recorded by the local CDC. The serum, urine, saliva, semen and conjunctival swab samples were collected by the local CDC and delivered to the Guangdong provincial CDC.

Case definitions

The cases were classified according to the diagnostic criteria for Zika virus disease (WS259-2016) from the Ministry of Health of the People's Republic of China. Suspected cases of ZIKV infection should have either a travel history in a ZIKV-endemic area within 14 days prior to symptom onset or cohabitation with an infected individual and more than two of the following symptoms: acute onset of fever, rash, arthralgia and conjunctival congestion.