First imported case of Zika virus infection into Jiangsu Province, China, returning from Ecuador

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Abstract: We report a case of laboratory-confirmed Zika virus (ZIKV) infection imported into China from Ecuador. This is the first documented imported case with ZIKV infection into Jiangsu, and the first imported case into China from Ecuador nationwide. The patient developed fever, rash, conjunctivitis and joint pain after returning. However, due to the less specific clinical symptoms and lack of quick diagnostic methods in elementary healthcare facilities, this imported case was not identified during her first two medical consultations. ZIKV RNA was detected in the urine sample rather than serum sample of the case, and anti-ZIKV IgM was detected from her serum samples collected 4 and 6 days after her onset of symptom. Case isolation and clearance of mosquito-breeding places were implemented instantly when the case was identified. No more human infections were found during a follow-up of 14 days since the case's isolation. This incident highlights the important role of urine sample in the diagnosis of ZIKV infection and the urgent need for efficient rapid diagnostic method for clinical healthcare providers.

Keywords: Zika; imported; China; Ecuador; Jiangsu

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Introduction

Zika virus (ZIKV) is a mosquito-borne virus transmitted by Aedes mosquitoes across tropical and subtropical regions around the world. It is a reemerging flavivirus historically known to be present in much of Africa and Asia, occasionally causing outbreaks among the local populace (1). ZIKV infections in humans are mostly asymptomatic, only a small percentage of patients may show clinical symptoms such as headache, muscle and joint pain, mild fever, rash, and inflammation of the underside of the eyelid, which are less differential. Recently, viral infection of women during pregnancy have been associated with microcephaly in their offspring (2), and neurological disorders such as Guillain-Barré syndrome (GBS) have also been associated with prior ZIKV infections (3). In addition, persistence of ZIKV in the semen of infected patients (4) and sexual transmission of the virus were observed (5). These suggest that this virus may be more dangerous than initially thought. According to the report on ZIKV transmission released by World Health Organization (WHO) on 24 May 2017, a total of 85 countries or territories or subnational areas are suffering or has been suffered from ZIKV worldwide. Among them, Ecuador which is situated at South America, is reported to be an area with ongoing transmission of ZIKV (6). As of 5 April 2016, a total of 13 ZIKV cases have been reported to be imported into China by travelers from South America or Oceania, excluding Ecuador (7). Here, we report the first imported case of ZIKV returning from Ecuador into China, as well as the first imported case into Jiangsu Province of China.

Table 1 Testing results of case's serum and urine samples

Samples and detected items	Samples taken after onset of symptom (days)*		
	4	6	7
ZIKV-RNA			
Serum	Negative[1]	Negative	Negative
Urine	Weakly positive[1]	Negative	Negative
DENV-RNA			
Serum	Negative	Negative	NA
Urine	Negative	Negative	NA
Anti-ZIKV-IgM[2], serum	Weakly positive	Positive	NA
Anti-ZIKV-IgG[2], serum	Negative	Negative	NA
Anti-DENV-IgM[3], serum	Weakly positive	Weakly positive	NA

ZIKV, Zika virus; DENV, dengue virus. Viral RNA was tested by RT-PCR method, viral antibody was tested by Immune colloidal gold technique. [1], confirmed by Jiangsu Entry-Exit Inspection and Quarantine Bureau, Jiangsu CDC and Chinese CDC respectively. All other tests in the table were conducted by Jiangsu CDC; [2], Zika virus IgM/IgG antibody test kit (LumiQuick Diagnostics); [3], Panbio Dengue Duo Cassette (Panbio Diagnostics); *, patient's samples were not available during day 1–3 or after day 7.

Case presentation

The case is a 28-year-old Chinese Nantong (a municipality in Jiangsu Province of eastern China) native woman, who traveled to Ecuador around mid-July, 2016 to take over her home business of bed linings trading there. She returned China in the morning of 29 April 2017, with skin rash (red small pimples) developed one day before. The case presented to dermatology clinic of the Tongzhou District Chinese Traditional Medicine Hospital in the afternoon of the same day, where she was diagnosed as skin allergy. During the night of that day, she developed fever (38 ℃) and mild joint pain. The case then visited a nearby community clinic and received a treatment of clindamycin and dexamethasone there during the next two days. Four days after her onset of symptom (2 May), she was free of fever but developed conjunctivitis and more severe skin rash and joint pain. The case then went to the Nantong center of Jiangsu Entry-Exit Inspection and Quarantine Bureau and reported her travel history to Ecuador. Her serum and urine samples were collected that day and tested using fluorescence quantitative RT-PCR. Results showed that ZIKV RNA was detected in urine sample only taken on 2 May (confirmed by Jiangsu Entry-Exit Inspection and Quarantine Bureau, Jiangsu Provincial Center for Disease Control and Prevention (JSCDC), and Chinese Center for Disease Control and Prevention), and ZIKV IgM antibody was detected in serum samples taken on 2 and 4 May (by JSCDC) (*Table 1*). The case was notified to Jiangsu CDC on 4 May, and was treated in isolation in The Third Hospital of Nantong the same day, while her symptoms such as conjunctivitis and joint pain had almost disappeared and no abnormal laboratory testing results were found, including blood routine test, liver function, renal function, serum myocardial enzyme and electrolyte, except for elevated C-reactive protein (29.20, reference range: 0–8 mg/L). Mosquito-breeding places in an area of 200 m radius around the case's home and the hospital she was treated in isolation in Nantong were cleared the next day. ZIKV RNA was not detected in her serum and urine samples taken on 4, 5 and 6 May (*Table 1*). The case was then discharged and no more human infections were identified during a 14 days follow-up since the isolation of the case.

Discussion and conclusions

This is the first documented imported case with ZIKV infection into Jiangsu, and the first imported case into China from Ecuador nationwide. Due to the less specific clinical symptoms of ZIKV infection and lack of quick diagnostic methods in elementary healthcare facilities, this imported case was not identified during her first two medical consultations. Given the ongoing transmission of ZIKV in many tropical and sub-tropical areas in the world, China, including Jiangsu Province, is at high risk for more imported ZIKV cases.

Aedes aegypti and Aedes albopictus are the two major vectors for ZIKV transmission. In China, Aedes aegypti is mostly distributed in Hainan, southern Guangdong and Guangxi, whereas Aedes albopictus, a potential competent vector, is widespread in southern and central China, including Jiangsu Province (8). In order to prevent seeding of ZIKV into local mosquito populations, identifying and managing imported ZIKV cases as soon as possible are critical. For this purpose, the awareness of ZIKV infection of healthcare providers and of the public calls for being promoted, and efficient quick diagnostic methods, especially for primary health care providers, need to be developed and implemented.

Urine sample, as a less invasive sample collection, was reported to have a longer period of RNA detection and higher RNA levels, which should be considered as an important alternative to serum or plasma for the detection of ZIKV RNA (9,10), and as the target sample for quick diagnostic methods. In this report, ZIKV RNA was detected in case's urine sample rather than serum sample three days after her onset of symptom, indicating the important role of urine sample in ZIKV diagnosis again.

Serological test is more challenging due to cross-reactions to other Flaviviruses infection or vaccination, such as dengue (IgG or IgM) (11). In this report, we also found that patient's serum samples taken 4 and 6 days after her onset of symptom were both weakly positive to dengue (IgM).

In this incident, public health response, such as clearing mosquito-breeding places, management of patient and follow-up of close contacts, were instantly implemented when Jiangsu Provincial CDC being notified. This incident highlights the importance of close collaboration between CDC and Entry-Exit Inspection and Quarantine Bureau, and the need for screening of febrile returning travelers for arboviral infections, especially in the summer months.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/jphe.2017.09.01). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Verbal informed consent was acquired from the imported case. According to the Prevention and Control Scheme on ZIKV released by the National Health and Family Planning Commission, samples of suspected imported case of ZIKV infection were required for testing and the following disease control. The remainder serum and urine samples, which were collected following medical institutions' approved procedures for clinical use, were used for diagnosis of ZIKV infection.

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