Japanese Encephalitis Virus RNA Not Detected in Urine

TO THE EDITOR—The mosquito-borne flaviviruses, including West Nile virus (WNV), dengue virus (DENV), Japanese encephalitis virus (JEV), and yellow fever virus (YFV), are emerging and re-emerging globally, posing a significant public health threat [1]. In Asia, JEV represents as the most important cause of arboviral encephalitis responsible for childhood morbidity and mortality, and approximately 3 billion people are at risk for JEV infections. Although several JEV vaccines are now commercially available [2], at least 50,000 cases with 10,000 deaths were reported annually [3].

The diagnosis of JEV infection is commonly confirmed by detection of specific antibodies or viral RNAs in blood or cerebrospinal fluid samples. WNV and YFV genome RNA was detected in urine from patients with both acute and persistent infections [4, 5]. Detection of viral RNAs in urine by real-time polymerase chain reaction (PCR) has been indicated as an easy, noninvasive diagnosis tool for DENV infection [6]. For JEV infection, pathological changes in kidney in patients [7] and viral shedding in the urine of JEV-infected mice have been described [8]. However, whether JEV RNA was present in urine of Japanese encephalitis patients remains unknown.

During 2011, a total of 52 fresh urine specimens were collected from Japanese encephalitis patients in Chongqing city, China. All the patients were laboratory-confirmed with JEV-specific immunoglobulin M antibodies in serum or cerebrospinal fluid samples. The median age was 60.4 months (range, 11–142 months), and 18 of 52 patients (35%) were female. The urine specimens were collected from 3 to 9 days after onset. The study was approved by the Beijing TCM Hospital and Children’s Hospital of Chongqing Medical University review boards, and all the participants provided informed consent before enrollment.

All the urine specimens were tested for JEV-specific RNA by using both reverse transcription (RT) PCR and real-time RT-PCR as previously described [9, 10]. Urine samples from healthy children were set as negative control. Total RNA was extracted from each urine specimen by using the QIAamp Viral RNA Mini Kit (Qiagen, Valencia, California), according to the manufacturer’s instructions. The results showed that all urine specimens from 52 patients tested negative for JEV RNA by either RT-PCR or real-time RT-PCR. Testing of urine specimens from healthy children yielded negative results as expected. Virus isolation in mosquito C6/36 cells was also negative. These results strongly demonstrated that viral RNA was not present in human urine during acute JEV infection, which is significantly different from other flavivirus members.

To our knowledge, this is the first study to examine urine in humans for presence of JEV RNA. The lack of JEV RNA in urine is distinct from other mosquito-borne flaviviruses including DENV, WNV, and YFV. Urine specimens should not be further employed in any molecular diagnosis for JEV infection. Renal dysfunction has been observed in Japanese encephalitis patients [7]; however, it has not clearly been determined whether JEV replication occurs in human kidney. The pathological mechanism corresponding to the lack of JEV genome in urine needs to be elucidated in the future.

Notes

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