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Commentary

Detection of Jingmen tick virus in human patient specimens: Emergence of a new tick-borne human disease?

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Jingmen tick virus (JMTV) is a new tick-borne segmented RNA virus detected in *Rhipicephalus microplus* ticks in the Jingmen region of Hubei province in China in 2010 and was first described by Qin et al. in 2014 [1]. The viral genome is composed of four segments: two which encode non-structural proteins are genetically related to the NS3 and NS5 sequences of the genus *Flavivirus*, and the other two segments, which encode structural proteins, are completely unique suggesting that they might have originated from a yet uncharacterized virus. Subsequently to this report, Shi et al. and Webster et al. reported the detection of JMTV-like virus genomes in insects in China and in England and Kenya, respectively [2,3]. In 2016, Guaico Culex virus (GCXV), a virus genetically close to JMTV was detected in *Culex* spp. mosquitoes collected in Central America and South America [4]. They also reported the detection of JMTV genome in red colobus monkey in Uganda. Mogiana tick virus, which is 88–90% identical to JMTV in nucleotide-level, was detected in ticks and cattle infested with ticks in Brazil [5,6]. As described above, JMTV and JMTV-like viruses have been detected around the world. A previous paper reported the detection of JMTV genome in fatal cases of Crimean-Congo haemorrhagic fever (CCHF) in Kosovo [7]. However, whether or not JMTV causes disease in humans remains unclear.

In an article in *EBioMedicine*, Jia *et al.* propose for the first time that JMTV is one of the causative agents of human diseases [8]. The authors identified four JMTV-infected patients by high-throughput sequencing of skin biopsies and blood samples. The four patients all had an itchy or painful eschar at the site of tick bite, which the authors remark as one of the distinct clinical presentations of JMTV infection. Two patients showed lymphadenopathy and one showed headache and asthenia. Some patients showed laboratory abnormalities such as the rise of AST and ALT levels, and a low neutrophil count. Furthermore, a retrospective serological test was performed and identified eight JMTV-infected patients from 509 patients with a history of tick-bite. These eight patients showed more severe manifestations: four patients were hospitalized and one patient whose acute phase serum was positive for JMTV genome presented seizure. These findings suggested that JMTV could be a causative agent of human disease.

The study by Jia et al. provide novel tools and insights into future JMTV studies. To date, JMTV genome has been detected in several kinds of arthropods and cattle [1–3,6,9] and Jia et al. detected JMTV genome in four tick species in their study. Further investigation such as elucidation of unknown human febrile diseases and field studies must be performed not only in areas where JMTV has been detected but also in all areas where these arthropods inhabit. In addition, Jia et al. succeeded both in isolating JMTV from *Amblyomma javanense* and sustaining JMTV in BME/CTVM23, an embryo-derived tick cell line. A previous study by Qin et al. could only succeed in the isolation of JMTV with C6/36 and DH82. This discovery will enable future studies to investigate the biological properties of JMTV *in vitro*.

Furthermore, results of FISH experiments suggested that the four segments of JMTV might be packaged in a single viral particle. A previous study revealed that GCXV was a unique multicomponent animal virus whose genome was composed of five segments. It may be interesting to see the characteristic difference between JMTV and GCXV in future studies. In this regard, the establishment of JMTV cultivating system in mammalian cell lines and reverse genetics system is the next challenge.

Since JMTV may cause severe symptoms in infected patients, screening for anti-JMTV drug candidates should be performed in the future. Currently there is no approved therapy for flaviviral infection, but some drug candidates which showed anti-flavivirus, especially anti-Dengue virus, activity have been reported [10]. Among them, there are several compounds which act as NS2B/3 or NS5 inhibitor. It would be interesting to test the potential of these compounds as anti-JMTV drugs, since two segments of JMTV genome are genetically close to the NS3 and NS5 sequences of typical flavivirus. However, it must be noted that only a limited number of patient specimens was used in the study by Jia et al., suggesting that this research still does not completely exclude the possibility that the patients were infected with not only JMTV but also other tick-borne pathogens, which were the actual cause of the diseases. More in-depth laboratory studies and long-term epidemiological studies are needed to clarify the pathogenicity of JMTV in humans and the global distribution of JMTV. Nonetheless, public concern about JMTV must be heightened especially in the areas where JMTV and JMTV-like viruses have been detected.

Disclosure

The author declared no conflicts of interest.

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