Letters to the Editor

Identification of a C2 Subgenogroup Strain of Enterovirus 71 in a Retrospective Study in Shandong Province, China, 1990-2010

Human enterovirus 71 (EV71) is an important pathogen and it can cause hand, foot, and mouth disease (HFMD), herpangina and severe neurological symptoms. There was no intensive surveillance of EV71 until May, 2008 when HFMD was classified as a category C notifiable infectious disease by the Ministry of Health of China (6). Acute flaccid paralysis (AFP) surveillance, developed for polio eradication program, can obtain non-polio enterovirus (NPEV) isolates as a side benefit. Here we report the identification of EV71 isolated from AFP cases in 1990-2010.

Altogether 768 NPEVs were isolated from AFP cases in Shandong province in this period. Primer pairs 486/488 and 040/011 were used to amplify partial VP1 sequences, and the combination of the two sequences yielded the entire VP1 coding region (2, 3). After molecular typing, 13 (1.7%) EV71 strains were identified, including 1 isolate in 1996, 1 in 2003, 2 in 2005, 2 in 2006, 1 in 2007, 1 in 2008, 4 in 2009, and 1 in 2010. The VP1 sequences were deposited in GenBank under accession numbers GQ253420-GQ253423, GQ253395, GQ253401, and JQ326297-JQ326306. Only the isolate in 1996, named 96200, was typed as C2 subgenogroup, and the others were C4 strains. According to the AFP surveillance data, strain 96200 was isolated from an 8-year-old female. The final diagnosis was Guillain-Barre syndrome (GBS), and the patient had residual paralysis at the 60-day clinical follow-up. Phylogenetic analysis
based on VP1 entire coding regions of genogroup C strains of EV71 was conducted
(Fig. 1). Shandong C4 strains all belonged to C4a, closely related to local HFMD
strains in 2007-2010. The mean p-distances within Shandong C4 branch was 8.7%.
C2 strain 96200 showed relative remote relationship with other C2 strains.
Homologous comparison revealed it had 92.5%-97.4% VP1 similarities with all C2
members available in GenBank, with the highest homology with Australia strain 2641
(AF135947) in 1995.
In China, Large-scale outbreaks of HFMD occurred repeatedly since 2007, when
the EV71 associated HFMD outbreak in Linyi city of Shandong province triggered a
nationwide epidemic. Subgenogroup C4 was thought to be the sole viral genetic
lineage circulating in mainland China since 1998 (6). This study reveals C2
subgenogroup had existed in mainland China previously. So, more retrospective study
of EV71 strains in other provinces of mainland China is needed to comprehend the
EV71 circulation before 1998.
C2 had a global distribution. Since 1998 HFMD outbreak in Taiwan, C2 had been
frequently reported in Asian, European, and American countries (1, 4, 5).
Co-circulation of various genetic subgenogroups could be frequently observed in a
given region (4). And the re-emergence of C2 in Taiwan in 2008 (1) implied we need
to closely monitor if the subgenogroup C2 outbreaks happen or not in mainland China
in the next few years.
To our knowledge this is this first report of C2 subgenogroup of EV71 in mainland
China, and this study reveals not a single EV71 subgenogroup had existed previously
in China.

This study was supported by a grant from the Health Department of Shandong province, China (2011QZ013) and the Science and Technology Development Planning Project of Shandong Province (2009GG10002055).
REFERENCES


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Fig. 1 Phylogenetic tree based on complete VP1 sequences of EV71 isolates in Shandong province and subgenogroup C reference strains. Black triangle indicated strains from local AFP surveillance (represented as YY+serial number), square indicated Shandong HFMD reference strains in 2007-2010.
Authors: Zexin Tao, Haiyan Wang, Aiqiang Xu*

Author affiliations:

Zexin Tao
Haiyan Wang
Aiqiang Xu*

Shandong Provincial Key Laboratory of Infectious Disease Control and Prevention,
Shandong Center for Disease Control and Prevention,
16992 Jingshi Road,
Jinan 250014, People’s Republic of China

*Phone: +86 531 82679606
Fax: +86 531 82620031
E-mail: aqxuepi@163.com
Fig. 1