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Letters

Letters commenting on recent articles as well as letters reporting cases, outbreaks, or original research are welcome. Letters commenting on articles should contain no more than 300 words and 5 references; they are more likely to be published if submitted within 4 weeks of the original article’s publication. Letters reporting cases, outbreaks, or original research should contain no more than 800 words and 10 references. They may have 1 Figure or Table and should not be divided into sections. All letters should contain material not previously published and include a word count.

Hand, Foot, and Mouth Disease Caused by Cox sackievirus A6, Japan, 2011

To the Editor: Coxackievirus A6 (CVA6) belongs to human enterovirus species A of the genus Enterovirus. According to a Japanese Infectious Agents Surveillance Report, this virus is one of the major causes of herpangina, an acute febrile disease characterized by vesicles, ulcers, and redness around the uvula, which occurs mainly in young children and infants. (1)

In June 2011, a sudden increase in cases of hand, foot, and mouth disease (HFMD) at pediatric sentinel sites (>3,000 pediatric hospitals and clinics) was reported to the National Epidemiologic Surveillance of Infectious Diseases System in Japan. Compared with past numbers of cases over 30 years of surveillance, the number of cases of HFMD per sentinel site peaked in week 28 (July) of 2011 (10.97 cases per sentinel), particularly in western Japan (2). According to the Infectious Agents Surveillance Report (as of September, 18, 2011), CVA6 was detected in 709 HFMD cases and 156 herpangina cases throughout Japan (1).

Clinical samples (throat swab specimens and feces) obtained from sentinel sites in Shimane, Hyogo, Hiroshima, and Shizuoka, Japan, were screened for enteroviruses by using an enterovirus-specific reverse transcription PCR and sequence analysis of the partial viral protein (VP)4/VP2 or VP1 region (3). Among 93 clinical samples from 108 HFMD case-patients, we identified 74 case-patients as CVA6 positive by sequence analysis.

On the basis of sequence analysis of the entire VP1 region (GenBank accession nos. AB649286–AB649291), the consensus sequence

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had 82.3%–82.5% nt identity (94.8%–
95.4% aa identity) with the prototype
CVA6 Gdula strain (GenBank
accession no. AY421764). CVA6 was
not isolated from clinical samples
in a cell culture system. Therefore,
most CVA6 strains were identified
by molecular detection directly from
clinical samples and sequence analysis.
Some CVA6 strains were grown and
isolated in suckling mice; these strains
were antigenically identified as CVA6
by a neutralization test with specific
antiserum against CVA6 (4).

In Japan, HFMD and herpangina
are classified as category V infectious
diseases. On the basis of clinical
diagnosis, suspected infections were
reported by pediatric sentinel sites on a
weekly basis to the Infectious Disease
Surveillance Center of the National
Institute of Infectious Diseases
(Tokyo, Japan). Typical clinical signs
and symptoms of HFMD cases caused
by CVA6 were fever, mild vesicles
in oral mucosa, and skin blisters on
hands, arms, feet, legs, buttocks, and
nail matrixes (Figure). Some patients
with HFMD had onychomadesis
(periodic shedding of the nails) 1–2
months after onset of HFMD. Most
cases of HFMD were self-limited.
However, additional follow-up
may be necessary for patients with
onychomadesis who are treated at
dermatology clinics.

As in other countries in the Asia–
Pacific region, major causes of HFMD
in Japan were CVA16 and enterovirus
71. In 2010, enterovirus 71 was
identified as a major cause of HFMD
(1). In contrast, CVA6 was consistently
associated with herpangina, as were
CVA2, CVA4, CVA5, and CVA10, but
CVA6 was occasionally detected in
HFMD case-patients. CVA6 was the
major cause of herpangina in 2007,
but an increase in the detection rate
of CVA6 in HFMD case-patients was
reported in Japan in 2009 (1).

HFMD outbreaks caused by
CVA6 were reported in Singapore,
Finland, and Taiwan in 2007–2009
(5–8). Recent HFMD outbreaks in
Finland and Spain were associated
with cases of onychomadesis 1–2
months after onset of HFMD (6,8,9).
In Japan, cases of onychomadesis
after onset of HFMD were reported
in 2009 (10). Therefore, changes in
clinical outcomes of CVA6-associated
diseases should be investigated.

Although most HFMD cases
caused by CVA6 in Japan were
mild, CVA6 was also detected in
other clinical samples, including
cerebrospinal fluid from a patient
with acute encephalitis in Hiroshima,
which reaffirmed possible additional
clinical manifestations during an
HFMD outbreak caused by CVA6.
Careful surveillance of disease
and infectious agent activities
are crucial in monitoring CVA6-
associated HFMD, onychomadesis,
and neurologic diseases. Nucleotide
identity between CVA6 strains in
Finland (2008) (7) and Japan (2011)
was ≈95% in the partial VP1 region.
More detailed genetic, phenotypic,
and epidemiologic analyses of CVA6
are needed to determine the role of
CVA6 in HFMD outbreaks with or
without onychomadesis.

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Figure. Typical clinical manifestations of hand, foot, and mouth disease associated with
coxsackievirus CVA6 in Shizuoka, Japan, June–July, 2011. A) Hand and arm of a 2.5-year-
old boy; B) foot and C) buttocks of a 6-year-old boy; D) nail matrix of a 20-month-old boy. A
color version of this figure is available online (wwwnc.cdc.gov/EID/article/18/2/11-1147-F1.
htm).
Human and Porcine Hepatitis E Viruses, Southeastern Bolivia

To the Editor: Hepatitis E virus (HEV) genotypes 3 and 4 are considered to be primarily zoonotic (1). However, recent data indicate that both genotypes can be transmitted among humans through other routes (2,3). Observations of genetic distinctiveness between swine and human HEV strains circulating within the same region argue against exclusivity of zoonotic transmission (4). A recent report presented a remarkable example of such distinction between genotype 3 isolates in rural communities in southeastern Bolivia (5).

We examined HEV sequences obtained in that study to show the independent genetic origin of swine and human variants. Findings suggest disjunction between human and swine HEV strains in this epidemiologic setting, despite the potential for extensive cross-species exposure.

Using reference sequences from Lu et al. (6), we conducted subtype analysis of HEV open reading frame 2 sequences at nucleotide positions 826–1173 (GenBank accession no. AF060668) from isolates from 2 rural communities in southeastern Bolivia (5). Analysis showed that swine sequences belonged to subtype 3i and that the human sequences belonged to 3e.

We collected all available GenBank genotype 3 sequences covering this genomic region for which the dates of collection were documented. Sequences were used to estimate the time from the most recent common ancestor (tMRCA) by using BEAST version 1.6.1 (7). Estimated tMRCA for GenBank sequences was longer than for sequences from Bolivia alone (Table) or for all genotype 3 sequences together (Table).

To reduce the effect of close relatedness among human or swine HEV sequences from Bolivia on the tMRCA estimate, we used only 1 representative sequence per species from each community in the final analysis. This analysis identified an estimated tMRCA similar to that seen for GenBank sequences alone (Table, model F vs. model D). This estimate indicates that human and swine HEV isolates from southeastern Bolivia last shared a common ancestor ≈275 years ago (Table, model F). Thus, swine HEV strains from both rural communities belonged to subtype 3i, and the human HEV strains identified from the community of Bartolo, Bolivia, belonged to subtype 3e and shared an ancestor with swine strains almost 3 centuries ago.

This finding is surprising because the community of Bartolo has several potential risk factors for zoonotic transmission of HEV. There are ≈200 humans and ≈70 swine in Bartolo (8). Residents are mainly native Quechua and Guarani with some of mixed Spanish ancestry who subsist at a low socioeconomic level. Their main livelihood activities are agriculture and breeding of animals. Free-range pig farms are family owned. Because of its impoverished state, the community has no running water, and few houses have toilets. No facilities are suitable for safely slaughtering

References


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