



Asymptomatic Children Might Transmit Human Parechovirus Type 3 to Neonates and Young Infants

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Abstract

Background: Human parechovirus type 3 (HPeV3) epidemics occur worldwide and can lead to severe disease in neonates and young infants. Little is known about the source of HPeV3 infection.

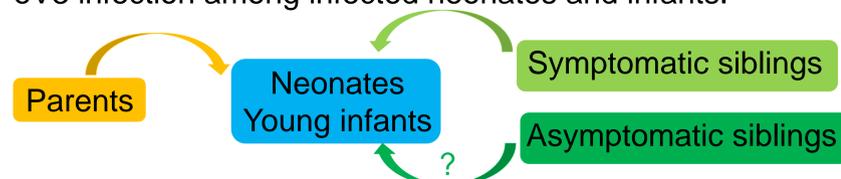
Methods: To investigate the source of HPeV3 infection and the role of asymptomatic children in the families of infected children, during a 2014 HPeV3 epidemic in Niigata, Japan, we analyzed (1) clinical information on sick contacts for 43 neonates and young infants with HPeV3-related disease diagnosed by PCR analysis of serum and/or cerebrospinal fluid and (2) stool samples from symptomatic and asymptomatic siblings/cousins of index patients.

Results: Sick contact with family members was confirmed for 51% (n = 22) of patients. Among the 30 symptomatic family members, 67% (n = 20) were siblings, 20% (n = 6) were mothers, and 13% (n = 4) were other relatives. Cough and/or rhinorrhea were more frequent in children (14/22, 64%) than in adults (2/8, 25%) (P = 0.101). Fever was more frequent in adults (6/8, 75%) than in children (9/22, 41%) (P = 0.215). Stool samples from symptomatic and asymptomatic siblings/cousins of 4 HPeV3-infected patients yielded positive results for HPeVs on PCR analysis. Furthermore, the P1 and 3D^{pol} nucleotide sequences of family members were 100% identical to those of the respective index cases.

Conclusions: Identification of genetically identical virus from HPeV3-infected patients and asymptomatic children in their families suggests that the latter are a source of infection in neonates and young infants with HPeV3-related diseases.

Background

- Like enteroviruses, HPeVs replicate mainly in the gut and are transmitted via the fecal–oral route, although the virus is also shed from the nasopharynx.
- In general, infection with HPeVs is asymptomatic or causes mild disease, including respiratory tract infections and gastroenteritis in children, and the virus is frequently detected in stool samples from such patients.
- HPeV3 (HPeV type 3) is an emerging pathogen that can cause sepsis and meningoencephalitis in neonates and young infants.
- Little is known about the source of HPeV3 infection. During a 2011 Japanese epidemic, approximately half of patients had sick contacts.
- Determining the source of HPeV3 transmission could help control HPeV3 epidemics.
- We tested the hypothesis that asymptomatic siblings are a source of HPeV3 infection among infected neonates and infants.



Patients & Methods

Patients and samples

- Forty-three HPeV3-infected neonates and young infants (median age, 32 days; range, 4–113 days) hospitalized for sepsis or sepsis-like syndrome at the hospitals in Niigata, Japan, during 2014
- The diagnosis of HPeV3 was confirmed by a positive result for HPeVs in PCR analysis of serum and/or cerebrospinal fluid.
- Stool samples were collected from symptomatic and asymptomatic siblings and/or cousins of the index case.
- Information on Japanese general population was obtained from Vital Statistics in 2013 from Japanese Ministry.

Genetic analyses of the virus

- Detection of HPeVs: Real-time RT-PCR targeting the conserved 5'-UTR.
- Genotyping; RT-PCR assays and sequencing for the P1 (VP0, VP3, and VP1, 2,313 bp) and 3D^{pol} (697bp) regions

Statistical analysis

- The χ^2 test: comparing the likelihood of a sibling being present in the household between patients and children in the Japanese general population. Fisher's exact test: comparing the frequencies of clinical findings among symptomatic family members of the patients.

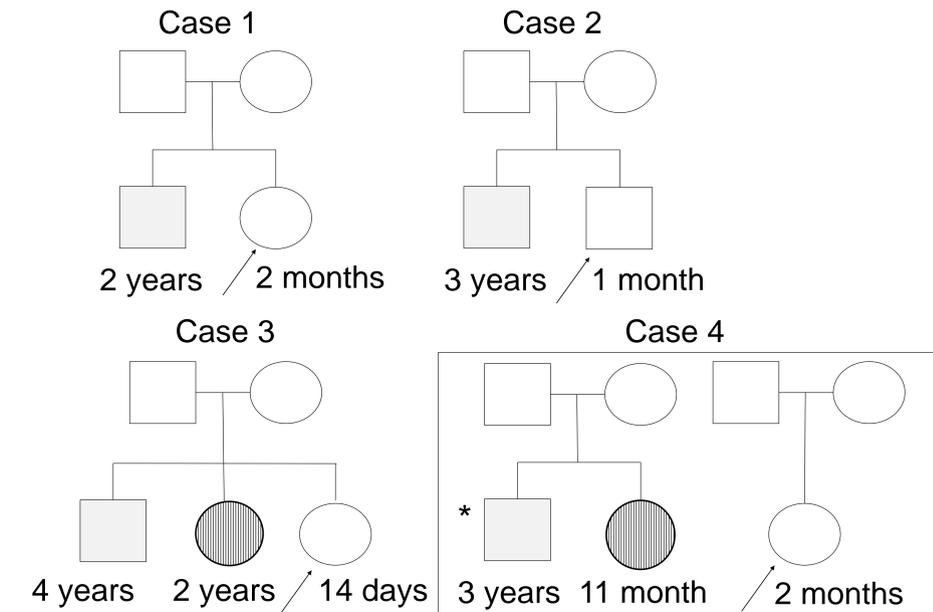
Results

Table. Information on sick contacts in families of neonates and young infants with HPeV3-related diseases.

Source of sick contact	No. (%)	
	Children (n = 22)	Adults (n = 8)
Sibling	20 (91)	
Cousin	2 (9)	
Mother		6 (75)
Grandmother		2 (25)
Symptoms in contacts		
Cough and/or rhinorrhea	14 (64)	2 (25)
Fever (>38°C)	9 (41)	6 (75)
Abdominal pain	2 (9)	1 (13)
Vomiting	2 (9)	1 (13)
Diarrhea	1 (5)	0 (0)
Sore throat	0 (0)	2 (25)
Headache	0 (0)	1 (13)
Myalgia	0 (0)	1 (13)

Among the 43 patients, 77% (n = 33) had siblings, which is a significantly higher proportion than in the Japanese general population (53%) (P = 0.002).

Figure 1. Pedigree diagrams of 4 patients with HPeV3-related diseases.



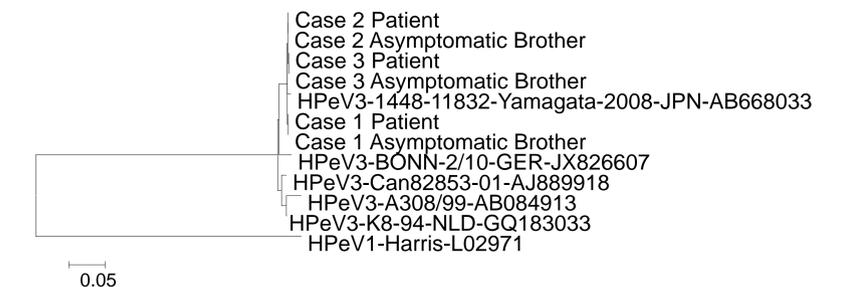
○, □ with arrows: index cases with HPeV3-related diseases.

□ : asymptomatic siblings/cousins with a positive PCR result for HPeVs.

● : symptomatic siblings/cousins with a positive PCR result for HPeV3.

- The box for Case 4 indicates that 2 related families lived together in the same house. All parents were asymptomatic.
- The P1 and 3D^{pol} nucleotide sequences were 100% identical between index cases and their respective siblings, for Cases 1, 2, and 3.
- In Case 4, the cousin (*) was positive for HPeVs; however, amplification failed in the cousin's sample.

Figure 2. Phylogenetic analysis of serum samples from patients and stool samples from asymptomatic siblings (P1 region)



Conclusion

Asymptomatic children might be a source of HPeV3 infection in neonates and young infants. Careful hand hygiene and other standard precautions are thus warranted during HPeV3 epidemics, even in asymptomatic households, to protect neonates and young infants from severe HPeV3-related diseases.

Reference: Aizawa Y, et al. *J Clin Virol* 70: 105-108, 2015