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Brief report

Outbreak of coinfection with human metapneumovirus and measles virus resulting in the death of a child at a hospital in China



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Two children with different digestive diseases were admitted to the gastroenterology department of a children's hospital in Hangzhou, Zhejiang Province, China, in May 2010. They manifested successively acute lower respiratory tract infection symptoms during their stay in the hospital. The epidemiologic and experimental evidence supports that one child acquired nosocomial coinfection with measles virus and human metapneumovirus from another child while they shared the same ward.

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Respiratory tract infection is a leading cause of morbidity and mortality in children worldwide.¹ Recently, we identified an outbreak of coinfection with human metapneumovirus (hMPV) and measles virus (MV) in 2 children who manifested acute respiratory tract infection symptoms during their stay at a children's hospital in Hangzhou, Zhejiang Province, China. The research informed consents were obtained from the parents of these 2 children.

On May 27, 2010, we were informed by the children's hospital that a 2-month-old child (child A) suffered from pneumonia with unknown cause. Before he was admitted to this hospital, he had been diagnosed as having cytomegalovirus hepatitis and had received treatment at a local hospital in Hangzhou in April 2010. He was taken by his parents to visit a doctor at the outpatient clinic of the children's hospital on May 3, where he was initially diagnosed as having infant hepatitis syndrome. On May 5, the child was admitted to the children's hospital with the diagnosis of neonatal intrahepatic cholestasis and was kept at a ward (room X, zone 10) in the gastroenterology department. However, the child developed a fever and started to cough on May 25. On the following day, red

maculopapules were found on his face and trunk, and white spots were found on his oral mucous membrane. His body temperature became normal on May 28. He was diagnosed clinically as having acute bronchitis, measles, and neonatal intrahepatic cholestasis in a consultation on May 29. He started to recover on June 5 and was discharged from the hospital on June 7 (Figs 1 and 2).

During this investigation, we found that 2 children had been kept in the same ward with child A (room X, zone 10). One of them, a 5-month-old child (child B) whose bed was adjacent to the bed of child A, had similar respiratory symptoms. However, the other child whose bed was near the window of the room, had not. It was reported that child B suffered from infected eczema and received outpatient treatment at a hospital in Hangzhou on May 1, 2010. This child developed diarrhea with fever up to 39.4°C and was admitted to the gastrointestinal department of the children's hospital with the diagnosis of enteritis and infective eczema on May 6. He was initially kept at a ward (room Y, zone 10) for 7 days, when he had diarrhea about 10 times a day, vomiting, fever (body temp = 38.8°C), and red maculopapules on his face and trunk. He successively received anti-infective treatment with aztreonam and symptomatic treatment. Then, he was transferred to room X, zone 10 to share the ward with child A on May 13 (Figs 1 and 2).

Child B started to cough on May 14 and quickly developed tachypnea on May 15. Bronchopneumonia was indicated in his chest radiograph on May 16. Then he was transferred to the intensive care unit of the hospital. The pathologic changes of pneumonia were observed in both lungs, and mechanical ventilation was initiated on May 17. This child was discharged from the hospital at the request of his parents on June 13. The death of the boy was reported in a telephone interview later (Figs 1 and 2).

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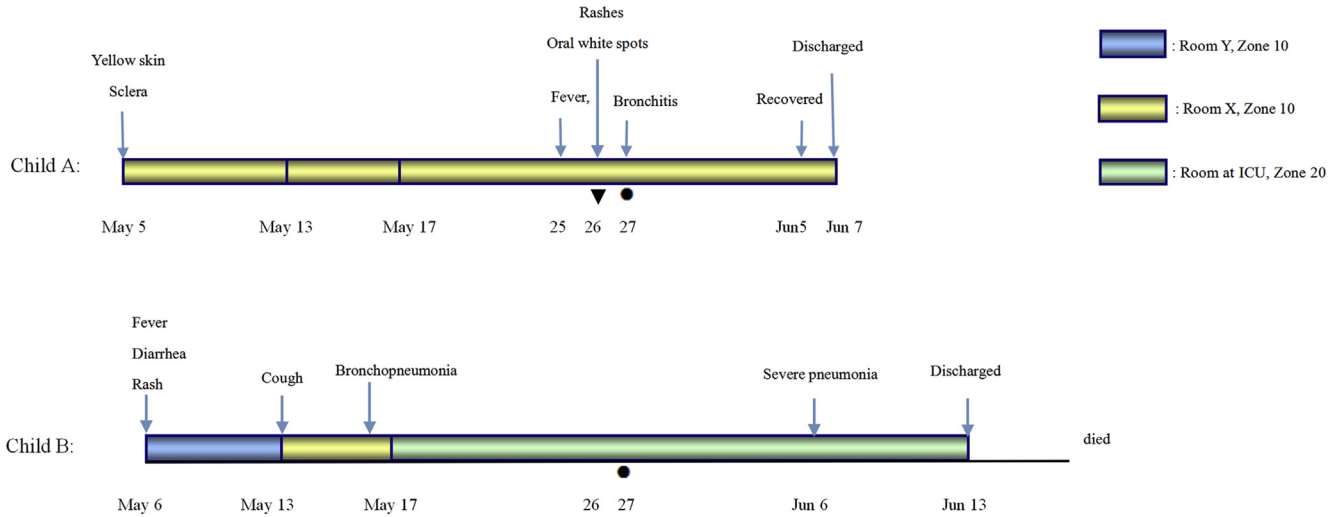


Fig 1. Timelines of 2 children's appearance of clinical symptoms and physical signs, specimen collection, and wards they stayed during hospital stay. The bars on the timelines represent the wards in which the 2 cases stayed. Black arrows show the day when blood specimen was collected; black circles show the day when respiratory tract aspirate specimens were collected. ICU, intensive care unit.

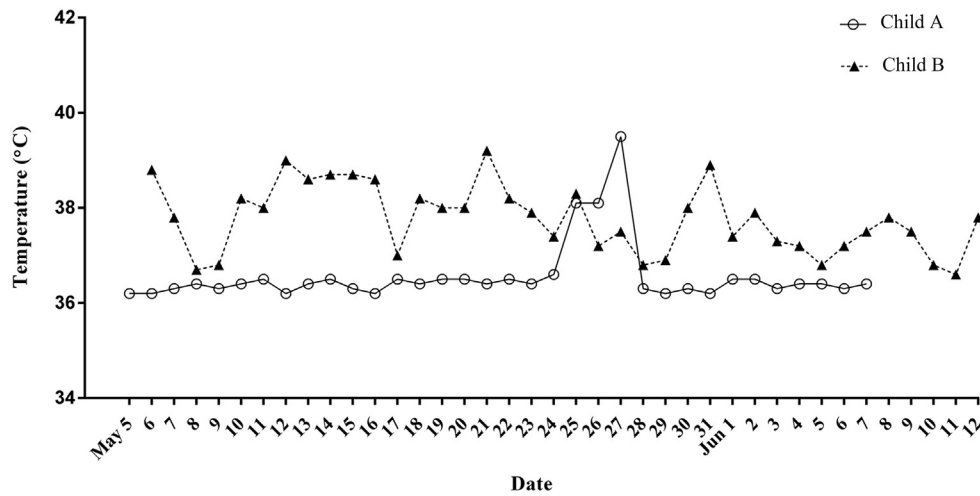


Fig 2. Temperature fluctuations for 2 children during their hospital stay.

The respiratory aspirate specimens from both of the children were collected on May 27 (Fig 1). Using real-time polymerase chain reaction (PCR) or real-time reverse transcription PCR (RT-PCR) methods published previously,²⁻⁶ both specimens tested positive for the nucleic acids of MV and hMPV but negative for the nucleic acids of the following respiratory viruses: severe acute respiratory syndrome coronavirus, influenza virus (subtypes H1N1-pdm09, seasonal H1N1, H3N2, and B), parainfluenza virus (type I, II, III, and IV), human respiratory syncytial virus, coronavirus (HKU1, OC43, 229E, NL63), adenovirus, and rhinovirus. hMPV N gene and MV N gene were detected and sequenced using RT-PCR as described previously.^{7,8} The nucleic acid sequences of hMPV N gene from child A and child B were 100% (169/169) identical, and both were very close to that of representative hMPV genotype B1, with the identity of 97.6% (165/169) (accession no. AY355328). The sequences of MV N gene segments from child A and child B had 100% identity (526/526), and both were 99.4%-99.6% similar to those of local MV isolates (data not showed). Serum specimen of child A tested positive for MV IgM antibody but negative for rubella virus IgM antibody.

Neither of these 2 children were inoculated with measles vaccines because they had not reached the age allowed for measles vaccine inoculation in China. We postulated that child A acquired MV and hMPV infections while he shared the same room with child B. The supporting evidence includes the following: (1) child A did not manifest fever, cough, eruption, or symptoms of lower respiratory infections until 20 days after admission to the children's hospital; (2) the period of time from child A's exposure to child B (sharing the same room) to child A's appearance of fever was 8-12 days, which is within the incubation periods of measles infection (8-12 days) and hMPV infection (7-9 days) reported previously⁹⁻¹¹; and (3) the nucleic acid sequences of MV N gene and hMPV N gene from child A and child B are 100% identical.

When child B was admitted to the children's hospital, skin eruption had already been observed, suggesting that the child seemed to have acquired the measles infection. However, it is difficult to determine whether the hMPV infection of child B was nosocomial or not because child B manifested symptoms of respiratory infection 8 days after admission, which is within the known range of incubation period of hMPV infection (7-9 days).⁹

The primary cause of the hospital-acquired infection event was that the possibility of measles was not considered for child B's diagnosis when he was admitted to the children's hospital, although red maculopapules and desquamation were found on his face and trunk. If he had been assigned to an isolated room for treatment, the transmission of measles infection and hMPV infection to others could have been avoided. Therefore, the improvement of diagnostic ability for respiratory virus infections and enhanced measures of isolation treatment are relevant to the control of nosocomial infection of respiratory viruses. This report sheds light on the importance of making accurate clinical diagnoses and instituting infection control measures early in the course of an illness.

References

1. Walker CL, Rudan I, Liu L, Nair H, Theodoratou E, Bhutta ZA, et al. Global burden of childhood pneumonia and diarrhoea. *Lancet* 2013;381:1405-16.
2. Yu XF, Pan JC, Ye R, Xiang HQ, Kou Y, Huang ZC. Preparation of armored RNA as a control for multiplex real-time reverse transcription-PCR detection of influenza and severe acute respiratory syndrome coronavirus. *J Clin Microbiol* 2008;46:837-41.
3. Raymond F, Carbonneau J, Baoucher N, Robitaille L, Boisvert S, Wu WK, et al. Comparison of automated microarray detection with real-time PCR assays for detection of respiratory viruses in specimens obtained from children. *J Clin Microbiol* 2009;47:743-50.
4. van de Pol AC, van Loon AM, Wolfs TF, Jansen NJ, Nijhuis M, Breteler EK, et al. Increased detection of respiratory syncytial virus, influenza viruses, parainfluenza viruses, and adenoviruses with real-time PCR in samples from patients with respiratory symptoms. *J Clin Microbiol* 2007;45:2260-2.
5. Deffernez C, Wunderli W, Thomas Y, Yerly S, Perrin L, Kaiser L. Amplicon sequencing and improved detection of human rhinovirus in respiratory samples. *J Clin Microbiol* 2004;42:3212-8.
6. Damen M, Minnaar R, Glasius P, van der Ham A, Koen G, Wertheim P, et al. Real-time PCR with an internal control for detection of all known human adenovirus serotypes. *J Clin Microbiol* 2008;46:3997-4003.
7. Mackay IM, Jacob KC, Woolhouse D, Waller K, Szymis MW, Whitley DM, et al. Molecular assays for detection of human metapneumovirus. *J Clin Microbiol* 2003;41:100-5.
8. Huang ZC, Pu XY, Zhu SF, Yu CF. Analysis of nucleotide sequence of measles virus in Hangzhou in 2006. *Zhongguo Wei Sheng Jian Yan* 2007;17:284-6.
9. Kim S, Sung H, Im HJ, Hong SJ, Kim MN. Molecular epidemiological investigation of a nosocomial outbreak of human metapneumovirus infection in a pediatric hemato-oncology patient population. *J Clin Microbiol* 2009;47:1221-4.
10. Xu WB, Xie ZD, Zuo SY. Diagnostic criteria for measles (WS296-2008). Beijing, China: Ministry of Health of the People's Republic of China; 2008.
11. Peiris JS, Tang WH, Chan KH, Khong PL, Guan Y, Lau YL, et al. Children with respiratory disease associated with metapneumovirus in Hong Kong. *Emerg Infect Dis* 2003;9:628-33.