

First Report of Respiratory Syncytial Virus and Human Metapneumovirus Co-Infection in a 2-Year-Old Kawasaki Patient in Iran

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Abstract

Background: Respiratory virus infections in children are a leading cause of morbidity and mortality worldwide.

Methods: A total of 897 clinical specimens were collected from February 2007 to January 2008 and transported to the National Influenza Center. Two hundred and two samples belonged to children under the age of six from 897 specimens, described above, were selected. Then they were tested for influenza virus types and subtypes by real time PCR assay subsequently, the specimens were tested for RSV and hMPV by hemi-nested multiplex PCR and parainfluenza viruses type 1-4 by hemi-nested multiplex PCR and adenovirus by hemi-nested PCR.

Results: The throat swab was taken from the Kawasaki case with the history of chicken`s contact. The specimen was tested for all influenza subtypes especially H5N1 and the results were negative. Meanwhile PCR was done for screening of other respiratory viruses that results came out positive for RSV and hMPV.

Conclusion: In the present study, we demonstrated the possibility to detect dual infection caused by RSV and hMPV, but because of the extravagant pattern of this case, more investigation is suggested specially on Kawasaki patients.

Keywords: *RSV, hMPV, Respiratory infection, Kawasaki disease, Iran*

Introduction

Due to worldwide occurrence, substantial morbidity and mortality rates, respiratory viral infection which swiftly and easily spread, pose a serious public health problem (1). Human metapneumovirus (hMPV) is one of the etiological agents of acute respiratory tract infections (ARTIs) which can infect people in all age groups (2). It induces clinical symptoms ranging from upper to lower respiratory tract illnesses such as bronchiolitis, bronchitis and pneumonia (3-5). In 2001, HMPV was identified in samples from children with respiratory tract disease for the first time (6). In addition, it is a new member of the family paramyxoviridae, subfamily pneumovirus, genus metapneumovirus (7). RSV is one of the most important respiratory pathogens of childhood, with detection rates reaching 70-85% in hospitalized infants during seasonal winter epidemics worldwide (1, 8). RSV causes severe lower respiratory

infections like bronchiolitis or pneumonia in infants and young children (9). Coinfection of hMPV with RSV in infants has been suggested to be a factor that influences the severity of bronchiolitis (9). Phylogenetically, RSV is the closest human virus related to hMPV, and the clinical manifestations of hMPV may share an overlapping spectrum with RSV, so that these two viruses cannot be distinguished by clinical manifestations (4, 7, 9, 10). RSV and hMPV might have similar seasonal patterns, so co-infection is possible (6, 9).

This report describes a case who did not have the respiratory sign and symptoms, while was actually infected with RSV and hMPV simultaneously.

Case report

A 24 month old girl, who was originally from Tehran, Capital of Iran, was admitted to a pediatric hospital in Tehran on 29 Jan 2007 with a 2 wk history of fever and erythema of cheeks, lips, throat,

and mouth since 4 d ago. In spite of treating with antipyretics, fever still was persistent. On physical examination, the vital signs were as follow: respiration, 22 breath/min; pulse, 104 beats/min and temperature, 38° C. Cardiac, abdominal, neurological and respiratory findings were normal. Laboratory findings were as follows: WBC count, $9.9 \times 10^3/\mu\text{l}$; RBC, $3.77 \times 10^6/\mu\text{l}$; Hb, 10.6 g/dl; Hct, 34.5%; PLT, $443 \times 10^3/\mu\text{l}$; ESR, 90; CRP, +1; Wright/Widal and salmonella Para A/B, Typhi D were negative. Stool exam was normal. In the abdominal sonography, there was no problem and chest X ray was also normal. According to the findings, possible diagnosis was Kawasaki syndrome and treatment with IVIG, aspirin and acetaminophen was started. After one day, fever was resolved but dry cough started at the day four of the admission. Because of the history of contact with chickens and possibility of H5N1, throat swab specimen of the patient was collected and sent to the National Influenza Center in Tehran university of Medical Sciences for influenza surveillance. The specimen was tested for Influenza virus types and subtypes by real time PCR assay using CDC procedure, CDC Real-Time RT-PCR (r.RT-PCR) protocol for detection and characterization of influenza virus (version.2007), but the result was negative. Subsequently, as a part of a project, the specimen was tested for RSV and hMPV by hemi-nested multiplex PCR and parainfluenza viruses type 1-4 by hemi-nested multiplex PCR (11), and adenovirus by hemi-nested PCR (12). In our surprise positive results for RSV and hMPV were observed without any special respiratory sign and symptoms. The test was repeated and the results were confirmed again. The nucleotide sequence of the PCR product of the detected hMPV (the M gene fragment) was submitted to GenBank (Accession no. GQ219792).

Discussion

In the present study, we demonstrated the possibility to detect dual infection which caused by RSV and hMPV. Due to the lack of sensitivity of conventional methods detection of co-infections with different respiratory viruses had been un-

derestimated (13). Severe RSV bronchiolitis in small patient series had been recognized because of co-infection with other viral pathogens (14). Some previous studies have lighted up increased clinical severity in case of dual infection caused by RSV and hMPV (8, 9). Greensill et al. observed a 70% co-infection rate with HMPV and RSV and a 90% co-infection rate among intubated infants with hMPV and RSV admitted to their PICU (8). Although Greensill et al. did not include an appropriate control group in their study, these findings suggest that co-infection with both hMPV and RSV is common and that together the two viruses may contribute to increase the severity of disease (9, 14). Whereas in other reports hMPV did not contribute to the severity of RSV infection (15, 16). The basis of the pathogenesis of severe RSV disease is multifactorial. Since severe RSV disease may develop in apparently healthy children, known host risk factors cannot completely account for instances of severe illness. Preexisting or maternally acquired immunity, innate immunity, viral factors and genotypes and environment all likely contribute to disease pathogenesis. We detected co-infection of hMPV and RSV in Kawasaki patient without special respiratory sign and symptoms, we could not find the patient to follow up her and study more about the immunity status and other possibilities of this scenario. More investigation is suggested specially on Kawasaki patients to detect the viral pathogens.

Ethical Considerations

All ethical issues including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc have been completely observed by the authors.

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