



Brief Report

WU polyomavirus detected in respiratory tract specimens from young children in Japan

Mineyuki Okada,^{1†} Hiromichi Hamada,³ Hiromi Sato-Marui,² Yuri Shirato,³ Takafumi Honda,³ Ayako Muto,³ Kitami Hayashi³ and Masaru Terai³

Divisions of ¹Epidemiology and ²Virology, Chiba Prefectural Institute of Public Health and ³Department of Pediatrics, Tokyo Women's Medical University Yachiyo Medical Center, Chiba, Japan

Abstract Polyomaviruses (PyV) WU and KI are reportedly associated with respiratory tract disease (RTD) worldwide but their incidence is unclear in Japan. In a 2 year prospective study, WU/KIPyV were detected in 48 (13.9%) and in five (1.4%) of 345 children hospitalized with lower RTD, respectively. The seasonal distribution was observed in spring and early summer. Other respiratory viruses were co-detected in 51% of PyV-positive patients, but eight (2.3%) of the WUPyV-positive patients were negative for other known pathogens.

Key words children, KI polyomavirus, pneumonia, polymerase chain reaction, WU polyomavirus.

Molecular techniques for the search and detection of new viruses have improved recently, identifying several new viruses associated with human respiratory diseases such as human metapneumovirus (hMPV), coronavirus, and human bocavirus (HBoV). In 2007, two human polyomaviruses (PyV), polyomavirus KI (KIPyV) and polyomavirus WU (WUPyV), were identified from secretions obtained from patients with respiratory tract diseases.^{1,2} Viruses have been detected worldwide, providing serologic evidence of infection,³ but discussion of the status of WUPyV/KIPyV as a human pathogen continues because of detection in samples obtained from healthy individuals and because of the high ratio of co-detection with other respiratory viruses.^{4,5} Few reports have described the presence of these viruses in Japan.⁶ Its prevalence remains unclear.

This study was conducted prospectively to determine the prevalence of WUPyV/KIPyV in children with lower respiratory tract disease (LRTD) in Japan.

Methods

During December 2007–November 2009 at Tokyo Women's Medical University Yachiyo Medical Center, nasopharyngeal swabs were obtained from patients, all of whom were younger than 24 months old and were hospitalized with LRTD. A previous report has described the polymerase chain reaction (PCR) procedure.⁷ Nested PCR was performed with newly designed primers.

Correspondence: Hiromichi Hamada, MD PhD, Department of Pediatrics, Tokyo Women's Medical University Yachiyo Medical Center, 477-96, Owada-Shinden, Yachiyo, Chiba 276-8524, Japan. Email: h-hamada@tymc.twmu.ac.jp

[†]Present position: Section of Bacteriology, Chiba Prefectural Toso Meat Inspection Office, Chiba, Japan.

Received 29 May 2012; revised 17 April 2013; accepted 21 May 2013.

Positive samples were also determined using SYBR-Green based real-time PCR, which amplified different regions of the viral genome (Mx3005P Q; Agilent Technologies, Tokyo, Japan). Nucleotide sequences of both positive samples were determined by direct sequencing with a sequencing kit (BigDye terminator ver.1.1; Applied Biosystems, Tokyo, Japan) using a DNA sequencer (Prism 3100 Avant; Applied Biosystems). PCR was then done for respiratory syncytial virus (RSV), enterovirus (EV) including rhinovirus and coronavirus, hMPV, HBoV, adenovirus (ADV), and parainfluenza virus (PIV) as described in a previous report.⁷ Bacterial culture of nasopharyngeal specimens was done for all patients.

The LRTD were defined clinically. All patients with suspected LRTD underwent chest radiography. Pneumonia was defined according to those findings. The Ethics Committee of Tokyo Women's Medical University approved this study (no. 1492), for which the parent or guardian of each patient gave informed consent.

Results

Of 345 patients (mean age, 11.4 months; male/female, 1.68), 46 were WUPyV (+)/KIPyV (–), three were WUPyV(–)/KIPyV (+), two were WUPyV (+)/KIPyV (+), and 294 were WUPyV (–)/KIPyV (–). In total, 48 (13.9%) were WUPyV (+) and five (1.4%) were KIPyV (+). The peak of WUPyV detection was found to be April–July (Fig. 1). Of the 51 PyV-positive samples, 26 (51.0% of positive samples) were positive for one or more other respiratory tract-associated viruses as follows: HBoV, $n = 10$; hMPV, $n = 7$; RSV, $n = 5$; EV, $n = 2$; ADV, $n = 2$; and PIV, $n = 2$. All KIPyV-positive samples were co-detected with other viruses. Of the remaining 25 patients, 17 patients had complication by bacterial infection, as determined on culture from sputum. In the remaining eight patients (2.3% of 345 patients), specimens were

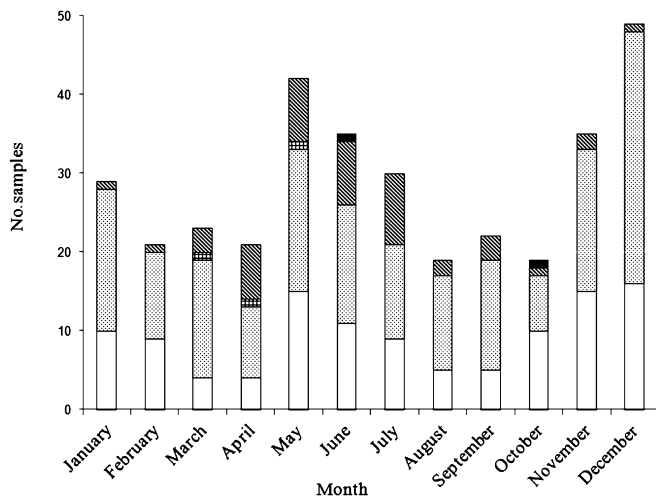


Fig. 1 Seasonal distribution of polyomavirus KI (KIPyV)- and polyomavirus WU (WUPyV)-positive samples. ■, KI + WUPyV; ▨, WUPyV; ▩, KIPyV; ▤, other viruses; □, negative.

positive only for WUPyV. Among those eight patients (pneumonia, $n=3$; bronchitis, $n=5$), the most likely symptoms were coughing (100%) and wheezing (89%). High fever ($>38.5^{\circ}\text{C}$) was found in three patients (38%). Data related to oxygen saturation (mean, 94%), number of white blood cells ($12.4 \times 10^3/\mu\text{L}$), percentage of neutrophils (55%), C-reactive protein (0.73 mg/dL), and length of hospital stay (6.0 days) were similar to those of children with other virus-positive LRTD.

Discussion

This study assessed the presence in Japan of children with WUPyV-positive LRTD, of which the prevalence is higher than that indicated in previous reports from other countries. The presence of PyV in Japanese children was recently reported:⁶ KIPyV and WUPyV were detected in 3.0% and in 16.4%, respectively, of children with respiratory infections in northern Japan. From the present study and a study conducted in northern Japan, the WUPyV-positive rate might be higher in Japan than in other countries. Moreover, the seasonality of this virus is apparently spring–early summer. Regarding KIPyV, we can provide no evidence at this point that KIPyV is a pathogen of respiratory tract disease.

Limitations

First, the virological diagnosis was done according to PCR assay alone. In children positive for WUPyV, half of the patients were found to have multiple viruses or bacteria. We must also investigate serological analysis or longitudinal PCR data showing that WUPyV is truly pathogenic in these children. Second, we did not check other microorganisms such as influenza virus and mycoplasma. We cannot confirm at this point that WUPyV is the only pathological organism in the eight children who were single-positive for WUPyV.

Conclusion

WUPyV was detected in 13.9% of hospitalized children with LRTD in Japan. Two independent studies conducted in Japan (separated temporally and geographically) have yielded similar results, suggesting a certain number of patients among Japanese children. Additional clinical and etiological studies of WUPyV as potential pathogens must be conducted to assess the characteristics of their epidemiology and pathogenicity.

Acknowledgment

This study was supported by a grant from the Chiba Serum Institute Memorial Fund, Chiba prefecture, Japan.

References

- Allander T, Tammi MT, Eriksson M *et al.* Cloning of human parvovirus by molecular screening of respiratory tract samples. *Proc Natl Acad Sci USA* 2005; **102**: 12 891–6.
- Gaynor AM, Nissen MD, Whiley DM *et al.* Identification of a novel polyomavirus from patients with acute respiratory tract infections. *PLoS Pathol.* 2007; **3**: e64.
- Nguyen NL, Le BM, Wang D. Serologic evidence of frequent human infection with WU and KI polyomaviruses. *Emerg. Infect. Dis.* 2009; **15**: 1199–205.
- Norja P, Ubillos I, Templeton K, Simmonds P. No evidence for an association between infections with WU and KI polyomaviruses and respiratory disease. *J. Clin. Virol.* 2007; **40**: 307–11.
- Wattier RL, Vázquez M, Weibel C *et al.* Role of human polyomaviruses in respiratory tract disease in young children. *Emerg. Infect. Dis.* 2008; **40**: 1466–8.
- Teramoto S, Kaiho M, Takano Y *et al.* Detection of KI polyomavirus and WU polyomavirus DNA by real-time polymerase chain reaction in nasopharyngeal swabs and in normal lung and lung adenocarcinoma tissues. *Microbiol. Immunol.* 2011; **55**: 525–30.
- Moriyama Y, Hamada H, Okada M *et al.* Distinctive clinical features of human bocavirus in children younger than two years. *Eur. J. Pediatr.* 2010; **169**: 1087–92.