Human metapneumovirus infection among children in Taiwan: a comparison of clinical manifestations with other virus-associated respiratory tract infections

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ABSTRACT

This study compared the clinical, laboratory and radiological features of infections caused by human metapneumovirus (hMPV) with other respiratory viruses. Nasopharyngeal aspirates and throat swabs were obtained from children during a 9-week period. hMPV was the virus isolated most frequently, followed by adenovirus, influenza virus A, respiratory syncytial virus and influenza virus B. hMPV-infected children were younger, and were more likely to be female, to present with feeding difficulties, a rash, tachycardia and a longer duration of fever, and to cough less frequently. Increasing interstitial infiltrates and hyperinflation were the most common radiological findings. None of the children required mechanical ventilation.

Keywords Bronchopneumonia, children, human metapneumovirus, respiratory tract infection, Taiwan

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Acute respiratory tract infection (RTI) is the most common disease among individuals of all ages worldwide [1]. RTIs are a major cause of childhood morbidity and mortality in the developing world [2], but despite sensitive diagnostic methods, an aetiological agent can be identified in only 35% of children with acute RTIs [3]. Human metapneumovirus (hMPV) was first isolated in The Netherlands in 2001 from nasopharyngeal aspirates obtained from young children suffering mild-to-severe RTIs [4]. hMPV is related closely to respiratory syncytial virus, but can be clearly differentiated by its cytopathic effect on tertiary monkey kidney cells, an absence of haemagglutinating activity, and its morphology on electron-microscopy. hMPV has been detected in respiratory specimens from patients of all ages in Canada, Australia, the UK, Finland and Hong Kong [5–11].

During the spring of 2004, clusters of RTIs in children were larger and more numerous than seen previously at the National Cheng Kung Hospital, located in southern Taiwan, indicating a possible change in viral aetiology. The present study aimed to determine the most common aetiological agents associated with this outbreak, and to compare the clinical symptoms, laboratory findings and radiological features of hMPV-infected children with those of children who were infected with other respiratory viruses (RVs).

The study included 1824 children aged <16 years who visited the hospital between 1 March and 2 May 2004. Cases of RTI were defined as children who presented with signs and symptoms of acute RTI, and who had a nasopharyngeal aspirate or a throat swab collected at admission. Peripheral blood was collected as warranted by the clinical circumstances. Nasopharyngeal aspirates or throat swabs were inoculated into cell cultures, including MDCK, Vero, A549 and rhabdomyosarcoma cells, and were then incubated for 14 days. A positive cytopathic effect was confirmed by immunofluorescent staining with monoclonal antibodies or, in the case of hMPV, by RT-PCR using a OneStep RT-PCR kit (Qiagen, Hilden, Germany) with antisense primer MPVF1r (5′-GTCTTCCTGTGCTAACTTTG) and sense primer MPVF1f (5′-CTTTGGACTTAATGACAGATG) to detect the fusion protein gene [5,12]. Rapid viral antigen detection by immunofluorescence was performed using commercial assays (Chemicon International, Temecula, CA, USA).

RVs were identified in 78 (23.0%) of 339 children with RTI. hMPV was the most frequent

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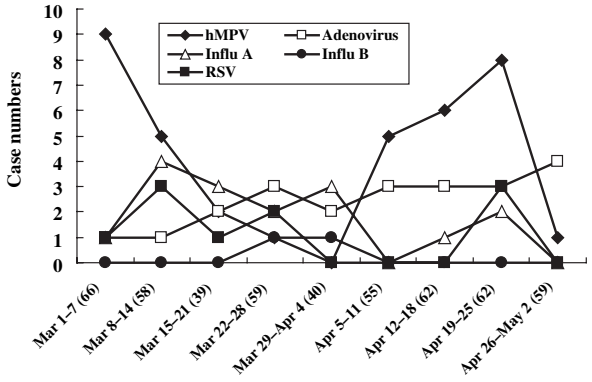

Fig. 1. Weekly prevalence of human metapneumovirus (hMPV), adenovirus, influenza virus A (Influ A), influenza virus B (Influ B) and respiratory syncytial virus (RSV) infections between 1 March and 2 May 2004. Numbers in parentheses are the number of cases examined per week.

virus isolated (n = 37, 47.4%), followed by adenovirus (n = 18, 23.1%), influenza virus A (n = 12, 15.4%), respiratory syncytial virus (n = 9, 11.5%) and influenza virus B (n = 2, 2.6%). The weekly prevalence of patients infected with hMPV, adenovirus, influenza and respiratory syncytial virus is shown in Fig. 1.

The demographical and clinical findings for the patients are summarised in Table 1. Children with hMPV were significantly younger than those with other RV infections. Most children with hMPV were aged 6–18 months, and all were aged <5 years. Children with hMPV were significantly more likely to be female, and to present with feeding difficulties, rash and tachycardia, but were noted to cough less frequently. Children with hMPV had fever lasting, on average, for 1 day longer than children with other RVs. Thirteen children had diarrhoea, and seven children with hMPV had a non-pruritic, maculopapular and transient rash on their trunk and back. Both groups frequently had underlying illness, and *c.* 60% required hospitalisation.

Table 1. Demographical and clinical data for patients infected with human metapneumovirus (hMPV) and other respiratory viruses (RVs) during a Taiwanese outbreak

Characteristic	hMPV (n = 37)	Other RVs (n = 41)	p
Demographical data			
Mean age (months)	22.9 ± 15.6	50.1 ± 46.9	0.005
6–18 months, no. (%)	14 (37.8)	5 (12.2)	0.008
>60 months, no. (%)	0	10 (24.4)	0.001
Male gender, no. (%)	13 (35.1)	26 (63.4)	0.013
Underlying illness, no. (%)	11 (29.7)	12 (29.3)	0.964
Hospitalisation, no. (%)	25 (67.6)	24 (58.5)	0.41
Clinical diagnosis			
Acute gastroenterocolitis, no. (%)	6 (16.2)	5 (12.2)	0.61
Bronchiolitis/bronchitis, no. (%)	6 (16.2)	6 (14.6)	0.847
Bronchopneumonia, no. (%)	9 (24.3)	9 (22.0)	0.804
Oral ulcer, no. (%)	2 (5.4)	2 (4.8)	0.916
Pharyngitis, no. (%)	9 (24.3)	17 (41.5)	0.109
Viral exanthems, no. (%)	5 (13.5)	0	0.015
Clinical features			
Fever			
Maximum (°C)	38.8 ± 0.6	39.0 ± 0.7	0.315
Duration (days)	4.3 ± 2.0	3.1 ± 2.4	0.046
Cough, no. (%)	26 (70.3)	39 (95.1)	0.003
Rhinorrhoea, no. (%)	17 (45.9)	25 (61.0)	0.184
Hypoxaemia, no. (%)	5 (24.3)	1 (2.4)	0.067
Feeding difficulties, no. (%)	24 (64.9)	16 (39.0)	0.023
Nausea/vomiting, no. (%)	7 (18.9)	14 (34.1)	0.13
Diarrhoea, no. (%)	13 (35.1)	11 (26.8)	0.071
Rash, no. (%)	7 (18.9)	1 (2.4)	0.017
Sore throat/injected throat, no. (%)	22 (59.5)	32 (78.0)	0.076
Tachycardia, no. (%)	21 (56.8)	5 (12.2)	0.001

The laboratory and radiological findings are summarised in Table 2. Other bacteria or viruses were detected in clinical specimens from six hMPV-infected children and four children with other RV infections. The overall rate of dual infection was 12.8%. A chest X-ray was obtained for 71.8% of the children. The most common findings in both groups were increasing interstitial infiltrates and hyperinflation. Nine children with hMPV and six with other RVs required additional oxygen. Eighteen hMPV-infected children were treated with antibiotics for a median of 5 days (range 1–14 days). The median hospitalisation period for all hMPV-infected children was 4 days (range 2–11 days). No hMPV-infected patient required mechanical ventilation or admittance to the intensive care unit.

Overall, the key findings of the current study included the following observations. First, hMPV is clearly a respiratory pathogen with an apparently unique epidemic pattern. Second, hMPV contributes substantially to acute RTI among children. Third, the respiratory symptoms and signs associated with hMPV are similar to those of other RVs. Fourth, the duration of fever, presence of a skin rash, and presentation with feeding difficulties, tachycardia and minimal cough are helpful diagnostic signs and symptoms. Fifth, a decreasing absolute lymphocyte count was not observed in hMPV-infected patients, but was encountered in other severe virus infections. Finally, the results suggest a different seasonal pattern of hMPV infection among children when compared with other RVs, although this needs to be confirmed by a longer period of observation.

Cases of severe hMPV infection among adults [10] and of re-infection among immunocompromised individuals [13] suggest that, despite universal infection in childhood, new infections can occur throughout life because of a protective