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Clinical Pictures of Children with Human Metapneumovirus Infection: Comparison with Respiratory Syncytial Virus Infection

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Since the discovery of human metapneumovirus (hMPV) in 2001, acute respiratory tract infections with hMPV have been reported in Europe, North America, Australia, and Asia (1), including Japan (2,3). Now hMPV is considered a ubiquitous virus causing respiratory tract diseases among children in the winter/spring seasons (1).

Figure 1 shows the incidence of acute respiratory tract infections from September of 2002 to August of 2003 among pediatric outpatients of Mazda Hospital. Adenovirus and *Mycoplasma pneumoniae* infections persisted throughout the year. A sharp increase of influenza A infection was seen in December (influenza B antigen was detected in only a few cases from January to March). The hMPV case first appeared in March. Its incidence peaked in April and then disappeared in August. The epidemic of hMPV appeared to follow that of respiratory syncytial virus (RSV) (Fig. 1), while a previous study indicated that the epidemic patterns of hMPV and RSV were similar (1). We report here the clinical data of 27 children with acute lower respiratory tract infections from September of 2002 to July of 2003.

Nasopharyngeal specimens were used to detect hMPV RNA by reverse transcription-polymerase chain reaction (RT-PCR)(2) and RSV antigen using a commercially available kit. The hMPV RNA was positive in 16 cases and RSV antigen in 11 cases. The phylogenetic analysis of F gene indicated that hMPV strains from these patients belonged to the same lineage (3).

The 16 hMPV cases occurred in March-July of 2003. The patients' sera were negative for IgM antibody for *M. pneumoniae* except for case 1. Table 1 shows the patients' ages, sex, clinical diagnoses, and underlying diseases. Table 2 shows their symptoms and laboratory data. All had a fever exceeding 38°C, productive cough, and rales. Rhinorrhea was absent among the patients older than 3 years. About 70% (6/8) of those patients younger than 3 years developed wheezing. All three infants under 1 year old had acute bronchiolitis, while four cases out of eight patients older than 3 years developed acute pneumonia. The clinical figures appear to differ depending on the ages of the affected children.

Table 3 compares the symptoms and laboratory data of hMPV and RSV infections among children younger than 3 years old. All the patients had fever, rhinorrhea, and cough. We found no significant difference in arterial oxygen saturation and hospitalization days between the hMPV and RSV infections. However, in the hMPV infection, fever tended to

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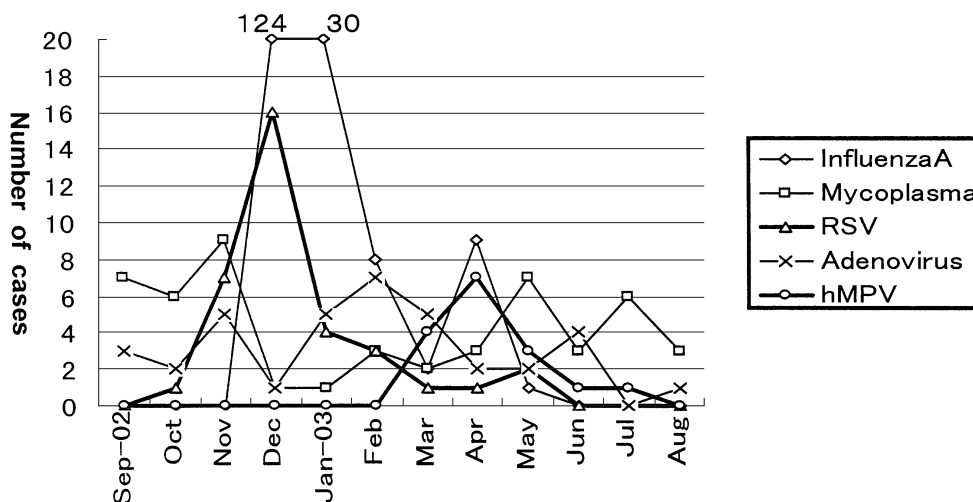


Fig. 1. Seasonal distribution of etiologic agents among outpatients with acute respiratory tract infections. Virus antigens in the nasopharyngeal specimen of each patient were identified by Capillia Flu A, B (Nippon Becton Dickinson Co. Ltd., Tokyo) for influenza A and B viruses, the check Ad (AZWELL Inc., Osaka) for adenovirus, and the Test Pack RSV (Abbott Japan Co. Ltd., Tokyo) for RS virus. IgM antibody for *Mycoplasma pneumoniae* in the patient's serum was tested using ImmunoCard Mycoplasma (TFB Inc., Tokyo). hMPV-RNA were detected by RT-PCR as previously described (2).

Table 1. Summary of patients hospitalized with hMPV infection

Case no.	Year ¹⁾	Sex ²⁾	Clinical diagnosis	Underlying diseases
1	9m	F	Bronchiolitis	—
2	9m	F	Bronchiolitis	—
3	11m	M	Bronchiolitis	—
4	1y	M	Asthmatic fit	Bronchial asthma
5	1y	M	Asthmatic bronchitis	—
6	2y	F	Asthmatic bronchitis	—
7	2y	F	Bronchitis	—
8	2y	F	Asthmatic bronchitis	—
9	3y	M	Asthmatic bronchitis	—
10	4y	M	Pneumonia	—
11	4y	F	Asthmatic fit	Bronchial asthma
12	4y	F	Bronchitis	—
13	4y	M	Bronchitis	—
14	5y	M	Pneumonia	—
15	7y	M	Pneumonia	Down syndrome
16	8y	F	Pneumonia	—

¹⁾: m, month; y, year.

²⁾: M, male; F, female.

be higher, exceeding 39°C, and persist longer (3), and pulmonary rales more frequent. While Peiris et al. (4) reported that hMPV infection was more frequently associated with lower respiratory tract involvement than was RSV infection, van den Hoogen et al. (5) stated that dyspnea and hypoxemia were found more often in RSV-infected individuals than in hMPV-infected patients. Since a statistically significant difference of clinical symptoms between them was not observed in many studies (1), the differential diagnosis seems very difficult to determine.

Peiris et al. reported that the frequency of developing a febrile seizure among the patients with hMPV infection was 15.6% and higher than those with RSV and influenza A infections (4). Six of 47 pediatric patients during an endemic of hMPV infection in Hiroshima Prefecture last year developed convulsions, and a convulsion occurred in one patient without fever (manuscript in preparation). If this is the case, a clinical study of central nervous system complications such

as febrile seizures, meningitis, and encephalopathy is relevant and a potential priority.

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Table 2. Comparison of symptoms and laboratory findings of patients with hMPV infections more than and less than 3 years old

	Age groups of patients		Significant difference
	<3 years	≥3 years	
A. Clinical symptoms			
Fever	8/8 (100) ¹⁾	8/8 (100)	— ³⁾
Cough	8/8 (100)	8/8 (100)	—
Rhinorrhea	8/8 (100)	0/8 (0)	<i>P</i> < 0.05
Wheezing	6/8 (75.0)	1/8 (12.5)	<i>P</i> < 0.05
Rales	8/8 (100)	8/8 (100)	—
Diarrhea	3/8 (37.5)	0/8 (0)	—
Otitis media	2/8 (25.0)	0/8 (0)	—
X-ray infiltration	3/8 (37.5)	5/8 (62.5)	—
Duration of fever (days)	5.1 ± 0.9 ²⁾	4.3 ± 1.7	— ⁴⁾
Duration of hospitalization (days)	6.3 ± 1.5	7.1 ± 2.1	—
B. Laboratory findings			
SaO ₂ (%)	93 ± 2.4 ²⁾	95 ± 2.9	— ⁴⁾
WBC (/μl)	9033 ± 2355	9582 ± 4548	—
GPT (IU/l)	26.1 ± 16.8	32.0 ± 34.8	—
LDH (IU/l)	340 ± 64.5	323 ± 129	—
CRP (mg/dl)	1.95 ± 2.13	1.99 ± 2.16	—

¹⁾: Number of positive/total (%).

²⁾: Mean ± SD.

³⁾: Fisher exact test.

⁴⁾: Mann-Whitney test.

Table 3. Comparison of symptoms and laboratory findings of patients less than 3 years old with hMPV infection and with RSV infection

	hMPV	RSV	Significant difference
A. Clinical symptoms			
Fever	8/8 (100) ¹⁾	11/11 (100)	— ³⁾
Cough	8/8 (100)	11/11 (100)	—
Rhinorrhea	8/8 (100)	10/11 (90.9)	—
Wheezing	6/8 (75.0)	6/11 (54.5)	—
Rales	8/8 (100)	5/11 (45.6)	<i>P</i> < 0.05
Diarrhea	3/8 (37.5)	7/11 (63.6)	—
Otitis media	2/8 (25.0)	6/11 (54.5)	—
Duration of fever (days)	5.1 ± 0.9 ²⁾	3.9 ± 1.4	—
Duration of hospitalization (days)	6.3 ± 1.5	4.7 ± 2.7	—
B. Laboratory findings			
SaO ₂ (%)	93 ± 2.4 ²⁾	95 ± 2.5	— ⁴⁾
WBC (/μl)	9033 ± 2355	13860 ± 5669	—
GPT (IU/l)	26.1 ± 16.8	17.4 ± 9.95	—
LDH (IU/l)	340 ± 64.5	335 ± 31.2	—
CRP (mg/dl)	1.95 ± 2.13	3.81 ± 5.02	—

¹⁾: Number of positive/total (%).

²⁾: Mean ± SD.

³⁾: Fisher exact test.

⁴⁾: Mann-Whitney test.

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