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= Abstract =

Adenoviral Lower Respiratory Tract Infections in Children; Serotypes and Clinical Characteristics

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Purpose : This study was performed to characterize the epidemiologic and clinical features of acute adenoviral lower respiratory tract infections(LRTIs).

Methods : Virological analysis was done from respiratory specimens obtained from patients with LRTIs hospitalized to other hospitals and referred to the Department of Pediatrics, Seoul National University Children's Hospital(SNUCH) from June 1998 to July 2000. Viral diagnosis was made by isolation of viruses employing HEp-2 cell culture and indirect immunofluorescent staining with monoclonal antibodies. Serotypes of adenoviruses were determined by neutralization test using antiserum for types 1, 2, 3, 4, 5, 6, 7 and 11. Medical records of children admitted to the SNUCH were reviewed retrospectively.

Results : Adenovirus was isolated from 118(9.0%) of 1,305 children with LRTIs. Serotypes were 3(39.0%), 7(16.9%), 1(11.0%), 2(7.6%), 4(7.6%), 6(5.9%), 11(2.5%), and 5(0.8%) and 10 strains(8.5%) were not neutralized by antisera included in the study. Infections by type 3 and type 7 occurred in outbreaks. Male to female ratio was 1.0:0.9 and mean age was 1.95 years. The clinical diagnoses were pneumonia(83%), acute tracheobronchitis(12%) and bronchiolitis(5%). Associated symptoms, signs and abnormal laboratory findings included cough(100%), sputum(73.5%), fever(54.2%), rale(59.3%), wheezing(34%), anemia(35%) and leukopenia(15.8%). Mortality was in 13.5%. Residual radiologic sequelae was identified in 32.6% of the patients followed.

Conclusion : These data confirms that adenovirus may cause severe lower respiratory tract diseases, and infections by type 3 and 7 may occurred in outbreaks.

Key Words : Adenovirus, LRTIs(lower respiratory tract infection), Serotypes

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2~5%
2).

가 , 1995

3, 4),

51가

가

(1, 2, 3, 5),

(3, 4, 7, 21), (3, 7),

(8, 19, 37), (11,

21), (2, 3, 5, 40, 41), (1, 2,

4, 5), (7, 12, 32), Reye

(7)

5).

DNA

DNA guanine cytosine

A G . A 12, 18,

31 , B 3, 7, 11, 14, 16, 21, 34, 35 , C

1, 2, 5, 6 , E 4 , F 40,

41 , D

6).

가

1, 2, 5, 6

가

7),

8).

가

가 ,

가 9).

가

1, 2, 3, 5 ,

6, 7 . 1, 2, 5

가

. B

3, 7, 21 E 4

가

1.

1998 6 2000 7 2 2

geal aspirate)

1,305 . 651

654

(nasopharyn-

. 1

가 2

1

2.

1)

Mucus trap suction catheter

4°C

48

24 , 5)
 HEp-2 96 well plastic plate 100 TCID₅₀
 30 μ L 1 : 20
 1, 2, 3, 4, 5, 6, 7, 11
 (-70°C)¹⁰⁾ (rabbit antisera, Denka Seiken, Japan) 30 μ L
 2) HEp-2 37°C 1 ,
 American tissue culture collection(ATCC) A549 plate ,
 HEp-2 75 mm² flask(Falcon) 10 37°C 5
 % fetal calf serum Eagle's minimum es- 가
 sential medium(10% EMEM) . .
 Flask 3~15 \times 10⁴ cells/mL . .
 16 \times 125mm screw cap tube 1 mL well
 0.2 가
 mL HEp-2 2 , 가 6~
 (cytopathic effect)가 7 .
 1~2 3~4 6) 가
 3) .
 가 tube
 trypsin , , ,
 teflon-coated slide acetone 10 , , ,
 murine , , .
 (Chemicon, Temecula, CA,) 37°C (,
 30 PBS 10 3 .), (,
 Murine IgG fluorescein isothiocyanate(FITC)- , , ,
 conjugated rabbit antibody(Cappel, West Chester, , , ,
 PA,) 37°C 30 PBS 3),
 가 , ,
 4) TCID₅₀(50% Tissue , ,
 Culture Infection Dose) (, ,
 96 well, flat-bottomed, styrene plate(Falcon)) .
 well 5 \times 10⁵ cells/mL A549 5 가 1,
 100 μ L . Stock 3, 7 ,
 10⁻¹ 10⁻⁸ 10 , 2, 4, 5, 6 11
 plate . plate ‘ (O)’ , 8가
 37°C 5 , 50%
 TCID₅₀ ‘ (N)’ .
 7)

Kruskal-Wallis test, Score test for trend, Chi-square test

1. 1,305 가 , 651 59 (9.0%) 가 3~4 가 1 27 . 3 46 (39.0%), 7 20 (17.0%), 1 13 (11.0%), 2 9 (7.6%), 4 9 (7.6%), 6 7 (5.9%), 11 3 (2.5%), 5 1 (0.8%) 10 (8.5%) 1, 2, 3, 4, 5, 6, 7, 11 가

59 3 18 (30.5%), 7 13 (22.0%), 1 7 (11.9%), 2 6 (10.1%), 4 6 (10.2%), 6 3 (5.0%), 5 1 (1.7%), (8.5%) 4 가 , respiratory syncytial virus(RSV) A 2 10 , *Mycoplasma pneumoniae* 5 , *Bordetella pertussis* 1 , *Streptococcus* 2 , *Enterobacter cloacae* 2 .

2. 98 6 98 11 51 , 98 12 99 5 27 , 99 6 99 11 25 , 99 12 2000 7 15 . 3 7 . 3 98 10 99 1 98 10 99 12 . 7 98 6 98 11 . 1 99 10

2000 7 (Fig. 1).

3. 가 가 59 2 13 1 11 . 2 6 12 (20.3%), 7 12 14 (23.7%), 13 24 17 (28.8%), 2 5 12 (20.3%), 6 4 (6.8%) .

($P > 0.05$). 가 31 , 가 28 1.0 : 0.9 . 24 40.7% (Table 1).

4. 1) 59 49 (83%), 7 (12%), 3 (5.0%) , 49 9 (18.4%) 2) 38°C 32 (54.2%) 39°C 30 (50.8%) , 38°C

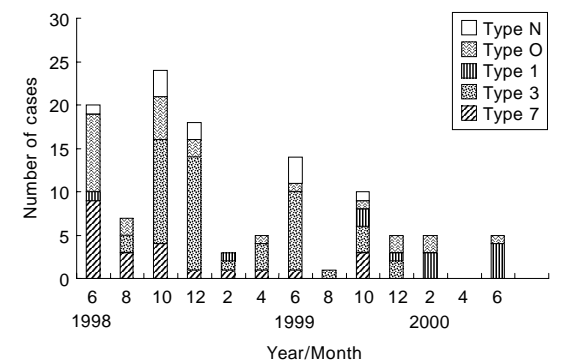


Fig. 1. Distribution of serotypes of adenovirus isolated from children with lower respiratory tract infections. Type O: serotypes 2, 4, 5, 6 and 11, Type N: serotypes not neutralized by antisera 1 through 7 and 11.

8.8 , 23 (39%) ,
 7 (P>0.05).
 11 (18.6%)
 (P>0.05). , , 23
 35 (59.3%), 20 (34%) (39%) , 가 14
 (23.7%) , 가 가

Table 1. Demographic Data of Children with Lower Respiratory Tract Infections Associated with Adenovirus by Serotypes

Characteristics	Type 1 (n=7)	Type 3 (n=18)	Type 7 (n=13)	Other type* (n=16)	Not-typed* (n=5)	Total (n=59)
Range of age	2 mo~3 yr	3 mo~10 yr	6 mo~6 yr	2 mo~13 yr	4 mo~1.75 yr	2 mo~13 yr
Mean age(yr)	1.13	2.4	1.64	2.33	1.1	1.95
Gender(M : F)	3 : 4	9 : 9	10 : 3	7 : 9	2 : 3	31 : 28
Underlying diseases	4	5	4	8	3	24
Malignancy		2	1	2	2	7
Heart diseases		1	2	3	1	7
Chronic malnutrition	1	1		1		3
Epilepsy	3	1	1	2		7

*Serotypes 2, 4, 5, 6 and 11, † Serotypes not neutralized by antisera 1 through 7 and 11

Table 2. Clinical Characteristics of Children with Lower Respiratory Tract Infections Associated with Adenovirus by Serotypes

Characteristics	Number(%) of cases					Total (n=59)
	Type 1 (n=7)	Type 3 (n=18)	Type 7 (n=13)	Other type* (n=16)	Not-typed* (n=5)	
Clinical diagnosis						
Pneumonia	3(42.8)	16(89.0)	12(92.3)	13(81.3)	5(100)	49(83.0)
Bronchitis	2(28.6)	2(11.0)	1(7.7)	2(12.5)		7(12.0)
Bronchiolitis	2(28.6)			1(6.2)		3(5.0)
Symptoms & signs						
Fever(>38℃)	3(42.0)	7(39.0)	9(69.0)	10(62.5)	3(60)	32(54.2)
Mean duration of fever(day)	7.6	8.9	11.1	7.5	8.8	8.8
Prolonged high fever(>10 days)	2(28.6)	5(27.8)	7(53.8)	5(31.0)	1(20)	20(34.0)
Dyspnea/Tachypnea	1(14.3)	4(22.2)	9(69.0)	6(37.5)	3(60)	23(39.0)
Rale	2(28.6)	10(55.5)	12(92.3)	9(56.3)	2(40)	35(59.3)
Wheeze	2(28.6)	8(44.4)	3(23.0)	6(37.5)	1(20)	20(34.0)
Decreased breathing sound	1(14.3)	5(27.8)	2(15.4)	1(6.2)	1(20)	10(17.0)
Rash	2(28.6)	2(11.0)	1(7.7)	5(31.0)	1(20)	11(18.6)
Vomiting/Diarrhea	1(14.3)	7(39.0)	6(46.0)	5(31.0)	4(80)	23(39.0)
Hepatomegaly	2(28.6)	3(16.7)	6(46.0)	2(12.5)	1(20)	14(23.7)
Seizure	2(28.6)		1(7.7)	4(25.0)		7(11.9)
Mental alteration			3(23.0)			3(5.0)

*Serotypes 2, 4, 5, 6 and 11, † Serotypes not neutralized by antisera 1 through 7 and 11

7 (11.9%) (Table 3). 9 (15.2%)
 , 5 , 3 3 , 7
 2 2 , 4 . 5
 (Table 2). , 3 2 7 2
 3) . 1,989.0±422.6 mg/
 dL, 83.6±27.5 mg/dL, LDH 2,451.0±2,020.0
 IU/L, 1,312.0±860.9 μ L
 57 25.0±23.9% . 5
 (Table 3). 20 (35%) , 5,000/mm³
 10 g/dL , 20,000/mm³ 3 2 3 7 가
 9 (15.8%), 20,000/mm³ 가 1 (1.8%)
 , 100,000/mm³ 7 (12.3%), 4)
 50,000/mm³ 2 (3.5%) 59
 . CRP 55 10 mg/L , 12 (20.3%)
 4 (7.3%) . ALT 가 25 (43.9%), 39 (66.1%)
 AST 가 14 (24.5%) , 가 , 24 (40.7%)
 16 PT 6 (37.5%), aPTT , 5 (8.5%) 가 ,
 3 (18.8%) 가 , FDP 7 (43.7%) 9 (15.2%) .

Table 3. Laboratory Findings of Children with Lower Respiratory Tract Infections Associated with Adenovirus by Serotypes

Laboratory findings	Type 1 (n=6)	Type 3 (n=18)	Type 7 (n=13)	Other type* (n=15)	Not-typed† (n=5)	Total(%) (n=57)
CBC						
Anemia(Hb <10 g/dL)	2	6	4	5	3	20(35.0)
Leukopenia(WBC <5,000/ μ L)	0	4	2	1	2	9(15.8)
Leukocytosis(WBC >20,000/ μ L)	1	0	0	0	0	1(1.8)
Thrombocytopenia(Platelet <100,000/ μ L)	0	2	3	2	0	7(12.3)
CRP						
≥0.1 mg/dL	2	13	11	14	3	43(78.2)
≥10 mg/dL	0	1	2	1	0	4(7.3)
Liver enzymes						
ALT >60 IU/L	4	5	7	4	2	22(38.6)
>300 IU/L	1	0	2	0	0	3(5.3)
AST >60 IU/L	3	2	3	4	2	12(21.0)
>300 IU/L	0	0	1	1	0	2(3.5)
Coagulation test[‡]						
Prolonged PT	0	0	3	3	0	6(37.5)
aPTT ≥40 sec	0	0	2	1	0	3(18.8)
Positive FDP	0	1	5	1	0	7(43.7)
Proteinuria	0	1	1	1	0	3(5.2)
Hematuria	0	1	1	1	0	3(5.2)

*Serotypes 2, 4, 5, 6 and 11, † Serotypes not neutralized by antisera 1 through 7 and 11, ‡n=16

Table 4. Treatment and Outcomes of Children with Lower Respiratory Tract Infections Associated with Adenovirus by Serotypes

	Number(%) of cases					Total (n=59)
	Type 1 (n=7)	Type 3 (n=18)	Type 7 (n=13)	Other type* (n=16)	Not-typed† (n=5)	
Mean duration of hospitalization	9.1	9.7	14.4	19.1	9.8	10.2
Oxygen inhalation	1(14.3)	6(33.0)	9(69.2)	5(31.0)	3(60)	24(40.7)
Mechanical ventilation	0	2(11.0)	4(30.8)	2(12.5)	1(20)	9(15.2)
Use of IVIG	0	1(5.5)	4(30.8)	2(12.5)	1(20)	8(13.5)
Fetal cases		1(5.5)	3(23.0)	3(16.0)	1(20)	8(13.5)
By adenoviral infection	0	1(5.5)	2(15.4)	0	0	3(5.0)
By underlying disease	0	0	1(7.7)	3(18.7)	1(20)	5(8.5)

*Serotypes 2, 4, 5, 6 and 11, † Serotypes not neutralized by antisera 1 through 7 and 11

5) 천, 가 .
15
24 (32.6%), 5 (32.6%), 3
(40.7%), (20%), 8
9, 3, 3,
(15.2%) . 9 1 가 (Table 5).
3 2, 7 4,
2, 1
10.2 2~5%
20 1 8% 20%
1 25 가 1, 2).
8 (13.5%)
가 가 5 (5%),
3 3 1, 7 2 11, 12).
9%
(Table 4). 가 7 1 7
가 ,
1 가 , 1 가 , 1 가 6 5
, 1 가 가 , 3~18
. 90%
6) 가 가
7.0 (1~22) , 가 ,
15 (32.6%) , 6 , 가

Table 5. Results of Clinical Follow Up in Children with Lower Respiratory Tract Infections Associated with Adenovirus by Serotypes

Characteristics	Number(%) of cases					Total (n=59)
	Type 1 (n=7)	Type 3 (n=18)	Type 7 (n=13)	Other type* (n=16)	Non-typed† (n=5)	
Patients followed	5	14	9	16	2	46
Mean F/U duration(months)	2.0	7.5	7.2	7.7	6.5	7.0
Persistent respiratory symptoms	2(40.0)	5(35.7)	2(22.2)	5(31.2)	1(50)	15(32.6)
Persistent abnormal radiographic findings	2(28.6)	6(42.9)	2(15.4)	3(18.7)	2(40)	15(32.6)
Infiltration		1	1	1	2	5(33%)
Hyperaeration		2		1		3(20%)
Bronchiectasis		2		1		3(20%)
Bronchiolitis obliterans	1	1	1			3(20%)
Pleural thickening	1					1(6.7%)

F/U : Follow up(during 1~22 months), * Serotypes 2, 4, 5, 6 and 11, † Serotypes not neutralized by antisera 1 through 7 and 11

(1.4%), 2
(0.5%), (0.1%)
13). 6 14 (0.9%)
% 1 가 44 ~ 50% 가 1990 11
1 2 1994 4 가
가 . 5 가 70 ~ 80%가 가 16), 1996 5
1, 2 7 7
50%가 5 14). 4, 17, 27).
1%가 1983 WHO
, 1967 1976 25,000
4% 6). 2, 1, 7, 3, 5, 6, 4, 8
1 11 5 3, 4, 8, 7, 19
가 93.2% C , 3
가 . 8~9 , 7 8 . A
가 , C ,
가 15). 3 7
B C , 4 19
가
10) 1990 11 1994 4
, 45.9% 가 1982 1993
, RSV(27.2%), 3 (7.8 40% 가
, A (3.9%), , 3, 2, 1, 5
(3.9%), 1 (1.7%), B . 9.5%

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3, 2, 1, 5 . 20%
 3, 4, 8, 37, 19 가
 7 (0.2%)
¹⁸⁾ 1996 11 1997
 1 7 가
¹⁹⁾ 8.8
 1958 1990 33 1976
 1990 15 , CRP
 Korppi ²⁵⁾ 55%
 1976 1980 7 , 1981
 1990 3 ²⁰⁾ 25%, 45%
 hex-
 on fiber 가 (30%)
 4 ,
 5 , 5
 penton base fiber 가 가 (35.7%).
 rhesus monkey X
 , 25%
²⁶⁾
⁶⁾ hexon ,
 59.3% 34%
 66.1%
 3 가 (40.7%)
 , (8.4%)가
^{21, 22)} 3, 15.2%
 4, 8 5 가
 1,989 mg/dL, 84 mg/dL, LDH 2,451 1 U/L,
 가 hexon 1,312 μ L 12.8%,
²³⁾ 25% , LDH 가
 1~7,
 11 가 .
 Ruuskanen ²⁴⁾ 105 2 가 3
 , (>39.4°C)
 (5.4) ,

. Type 7a
 type 7a 가가 가 27), ribavirin (5.0%) . , (100%), 가 (73.5%), (54.2%), (59.3%), (34%), (35%), (15.8%) . 13.5% , 28), 46 15 (32.6%)
 ganciclovir ,
 ribavirin 가 : 29)
 , 6 5 가 3 7 , 가 , 가
 :
 : 1998 6 2000 7
 . HEp-2 , 1, 2, 3, 4, 5, 6, 7, 11 .
 : 1,305 118 (9.0 %), , 3 46 (39%), 7 20 (16.9%), 1 13 (11.0%), 2 9 (7.6 %), 4 9 (7.6%), 6 7 (5.9%), 11 3 (2.5%), 5 1 (0.8%), 10 (8.5%)가 . 3 1998 10 1999 12 7 1998 6 11 . 1.0 : 0.9 1.95 . 49 (83%),

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