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= Abstract =

Clinical Significance of Enterovirus in Febrile Illness of Young Children

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Purpose : Enterovirus is a common cause of aseptic meningitis and nonspecific febrile illness in young children. During the summer and fall months, enterovirus-infected young children are frequently admitted and evaluated to rule out bacterial sepsis and/or meningitis. The purpose of this study was to evaluate the relationship between nonpolio enterovirus infection and febrile illness in infants under 3 months of age during the summer, fall months by using a stool culture to identify the presence of enterovirus.

Methods : Patients included febrile infants under 3 months of age admitted to Masan Fatima Hospital for sepsis evaluation from May 1999 to September 1999. Cultures were performed from stool and Cerebrospinal fluid samples and then were tested for enterovirus infection. Viral isolation and serotype identification were performed by cell culture and immunofluorescent testing. Enteroviruses not typed by immunofluorescent testing were confirmed by reverse transcription-polymerase chain reaction.

Results : A total of 44 febrile infants were enrolled; of those, 20(45%) were positive for enterovirus. Two enterovirus culture-positive infants had concomitant urinary tract infection and one had Kawasaki disease. All infants infected with an enterovirus recovered without complications. Serotype of 20 enteroviruses were isolated from stool, 3 of echovirus type 9, 1 of echovirus type 11, 1 Coxsachievirus type B4, 15 of untyped enteroviruses. One untyped enterovirus was isolated in the CSF.

Conclusion : Nonpolio enterovirus infections are associated with nonspecific febrile illnesses in infants under 3 months of age.

Key Words : Enterovirus, Febrile illness, Young children

Primer Probe 5' noncoding region
 , 9
 100% (Gene-med Biotechnology, INC., San francisco, CA)
 가
 RNA 4 μL
 2 μL antisense primer(10 pmol/μL), 8 μL
 dNTP(10 mM/μL), avian reverse tran-
 scriptase 가 42 90 가 .
 sense primer(10 pmol/μL, 5'-CCTCCGG-
 CCCCTGAATGCGGCTAAT-3'), antisen-serprimer(10
 pmol/μL, 5'-ATTGTCACCATAAGCAGCCA-3')
 8 μL, 10 U Taq polymerase PCR
 가 denaturation(90) 1 , annealing(50)
 1 , extension(72) 1 37
 PCR
 154 bp 가 ,
 .
 1999 5 9 3
 가 1 4).
 1999 5 9
 3
 RT-PCR
 .
 -30
 5). hu-
 man embryonal rhabdomyosarcoma(RD), African
 green monkey kidney(BS-C-1), human lung diploid
 (MRC-5), human cervix epidermoid carcinoma(HeLa)
 . reverse
 transcription-polymerase chain reaction(RT-PCR)
 6).
 RT-PCR 100 μL RNasin 40 U
 가 TRI REAGENT® BD(Molecular Research
 Center, INC, Cicinnati, OH) 가 RNA

가
 RNA 4 μL
 2 μL antisense primer(10 pmol/μL), 8 μL
 dNTP(10 mM/μL), avian reverse tran-
 scriptase 가 42 90 가 .
 sense primer(10 pmol/μL, 5'-CCTCCGG-
 CCCCTGAATGCGGCTAAT-3'), antisen-serprimer(10
 pmol/μL, 5'-ATTGTCACCATAAGCAGCCA-3')
 8 μL, 10 U Taq polymerase PCR
 가 denaturation(90) 1 , annealing(50)
 1 , extension(72) 1 37
 PCR
 154 bp 가 ,
 .

3
 44
 가 20 ,
 1 . 15 , 5
 (Table 1).
 가
 6 9 가 6 가
 가 (Fig. 1).
 4 13 375/mm³

Table 1. Age & Sex Distribution of Patients

Age (Month)	Male/Virus (+) [*]	Female/Virus (-) [†]	Total/Virus (+) [*]
> 1	8/5	3/2	11/7
1 2	13/7	8/3	21/10
2 3	7/2	5/1	12/3
Total	28/14	16/6	44/20

^{*}culture positive, [†]culture negative

6 :

3

97

10%

90%

^{16, 19)}

6.7 11%

7

10

^{15, 20)}

1993

103 65%, Respiratory syncytial virus(

RSV) 1

4

81

40%,

5,090

1%

48

A

1

2

49

, Guillian-Barre

22%

가

. 3

가

⁷⁾

6

RSV

가

¹²⁾

가

가

가

¹¹⁾

3

²¹⁾

가

가

¹³⁾

1996 , 1997

48

3

20.1%, 13.8%

3 4

^{10, 11)}

^{1, 2, 4, 12, 22, 23)}

3

가

²⁴⁾

3

96

¹⁰⁾ 97

23

9.7%

¹¹⁾

가

^{2, 25)}

13%

21%

가

^{14, 15)}

RT-PCR

가

가

가

가

2

^{24, 26 28)}

- echovirus type 9 3 , echovirus type 11 1 ,
Coxsackievirus type B4가 1 , 15
1
가 가
RT-PCR
- 2
1 Kawasaki
- 1) Cherry JD : Enterovirus : Polioviruses, Coxsackievirus, Echoviruses, and Enteroviruses. Pediatric Infectious Disease. 3rd ed. Philadelphia : WB Saunders Co., 1992:1705-53.
- 2) Dagan R, Jenista JA, Prather SL, Powell KR, Menegus MA. Viremia in hospitalized children with enterovirus infection. J Pediatr 1985;96:397-40.
- 3) Dagan R, Jenista JA, Marilyn A, Menegus. Association of clinical presentation, laboratory findings, and virus serotypes with the presence of meningitis in hospitalized infants with enterovirus infection. J Pediatr 1988;113:975-8.
- 4) Dagan R, Jenista JA, Menegus. Clinical epidemiological and laboratory aspects of enterovirus infections in young infants. In L. de la Maza, E.M. Peterson ed. Medical Virology Lawrence Erlbaum Associates Inc., 1985:123-51.
- 5) , , . 1993
9
1994;14:185-92.
- 6) , , , .
RNA
1996;3:163-7.
- 7) , , , , , . 1993
- 8) , , . 1993
9
1994;14:185-92.
- 9) , , , , . 1993
1995;38:
901-6.
- 10) , , , , , .
. 96
1997;4:97-105.
- 11) , , , , , . 1997
1998;5:
104-14.
- 12) Dagan R, Hall CB, Powell KR, Menegus MA. Epidemiology and laboratory diagnosis of infection with viral and bacterial pathogens in infants hospitalized for suspected sepsis. J Pediatr 1989;115:351-6.
- 13) Dagan R, Powell KR, Hall CB, Menegus. Identification of infants unlikely to have serious bacterial infection although hospitalized for suspected sepsis. J Pediatr 1985;107:855-60.
- 14) Jenista JA, Powell KR, Menegus MA. Epidemiology of neonatal enterovirus infection. J Pediatr 1984;104:685-90.
- 15) Alan ML, Brian AI, Julia CC, Richard LW, Kenneth M. Enterovirus infection in neonate. J Pediatr 1976;89:787-91.
- 16) Mark JA, Myron JL, Harley AR. Profile of enterovirus disease in the first two weeks of life. Pediatr Infect Dis J 1993;12:820-824.
- 17) Modlin J. Perinatal echovirus infection : insight from a literature review of 61 cases of serious infection and 16 outbreaks in nurseries. Rev Infect Dis 1986;9:18-26.
- 18) Modlin J. Fatal echovirus 11 disease in premature neonates. Pediatrics 1980;66:775-80.
- 19) Modlin JF, Polk BF, Horton P, Etikind P, Crane E, Spiliotes A. Perinatal echovirus infection : Risk of transmission during a community outbreak. N Eng J Med 1981;305:368-71.

- 20) Ira B, Michael JP, Michael JP, Ellen RW, Darleen C, Audrey LH, H Gerry T. Outcome in children with enteroviral meningitis during the first year of life. *J Pediatr* 1987;10:705-9.
- 21) Yodaft Y, Nishmi M. Epidemiologic and clinical observations in six outbreaks of viral disease in a kibbutz 1968-1971. *Am J Epidemiol* 1973;97:415-23.
- 22) Sanders DY, Cramblett HG. Viral infections in hospitalized neonates. *Am J Dis Child* 1968;116:251-6.
- 23) Linnemann CC, Steichen J, Sherman WG, Schiff WG. Febrile illness in early infancy associated with ECHO virus infection. *J Pediatr* 1974;84:49-54.
- 24) Dagan R. Nonpolio enterovirus and the febrile young infant: epidemiologic, clinical and diagnostic aspects. *Pediatr Infect Dis J* 1996;15:67-71.
- 25) Wilfert CM, Nusinoff-Lehrman S, Katz SL. Enteroviruses and meningitis. *Pediatr Infect Dis J* 1983;2:333-41.
- 26) Hamilton MS, Jackson MA, Abel D. Clinical utility of polymerase chain reaction testing for enteroviral meningitis. 1999;18:533-7.
- 27) Byington CL, Taggart EW, Carroll KC, Hilliard DR. A polymerase chain reaction-based epidemiologic investigation of the incidence of nonpolio enteroviral infections in febrile and afebrile infants 90 days and younger. *Pediatrics* 103:E27.
- 28) Rotbart HA, Mccracken GH, Whitley RJ, Molin JF, Cascino M, Shan S, et al. Clinical significance of enteroviruses in serious summer febrile illnesses of children. *Pediatr Infect Dis J* 1999;18:869-74.
- 29) Richard B. Specimen collection and transport. In Storch GA editor. *Essential of diagnostic virology*. 1st ed. London :Churchil Livingstone, 2000:26-36.