Viral Infection of Central Nervous System in Children: One Year Prospective Study

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Viral infection of central nervous system (CNS) is a common problem worldwide, especially in children. The clinical manifestations of viral CNS infection are the most important clues for diagnosis and treatment. The 1-year prospective study to explore the prevalence, clinical manifestations, and laboratory findings of viral CNS infection in children, including human herpes virus (HHV) type 1, 2, 3, 4, 5, 6A, 6B, 7, enterovirus B, mumps virus, measles virus, Japanese encephalitis virus, JC virus, BK polyomavirus, Nipha virus and influenza virus (H1N1, H3N2) were performed. Total of 71 children suspected CNS infection, aged between 2 days to 12.9 years were enrolled from May 2009 to April 2010. Total 4 children with non CNS infection, 5 bacterial meningitis, 2 tuberculous meningitis CNS infection were excluded. The HHV2 (50.0%) was the most common viral CNS infection. Other viral CNS infection included HHV1 (11.6%), VZV (6.7%), HHV6 (3.3%), HHV7 (3.3%), enterovirus B (1.67%) and H3N2 (1.67%). Diarrhea, irritability and CSF pleocytosis may helpful for differentiation between subtype of viral CNS infection.

Keywords: *Viral infection, Central nervous system, Children*

J Med Assoc Thai 2011; 94 (Suppl. 7): S24-S31
Full text. e-Journal: *http://www.jmat.mat.or.th*

Deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) viral CNS infection, the common problem in children worldwide, has severe sequels unless proper treatment. The previous publications showed various incidences ranged between 3 to 33 per 100,000 person-year with higher incidence in children[1-5]. In the present study from the USA (New York), HHV1 (Herpes simplex virus, HSV) and HHV3 (Varicella-zoster virus)-CNS infection were found to be 15.3 and 5.8%, respectively[6]. In immunocompromised hosts, there is an increased incidence of encephalitis caused by CMV, EBV and HHV6 infection[7].

In Thailand, Ministry of Public Health reported the increasing prevalence rate of encephalitis for 5 consecutive years. In 2009, 543 viral encephalitis adult and children were reported. The estimated incidence of encephalitis was 0.86 per 100,000 person-year. Peak incidence found in aged less than 4 years old, of which, approximately 1.1 per 100,000 person-year. However, 80 percent were diagnosed by clinical manifestations without viral identification and 20 percent diagnosed by using ELISA for Japanese encephalitis. So this report may be under estimate the exactly incidence in Thailand[8].

Between 1996 to 1998, 40 Thai children with viral encephalitis was reported. The prevalence of dengue virus, Japanese encephalitis virus, HHV1, HHV6, mumps, enterovirus, VZV and rabies were 31, 23, 15, 11, 8, 4, 4 and 4 percent respectively[9]. Between 2001-2002, the incidence rate of HHV5 (Cytomegalovirus, CMV)-CNS infection in HIV adult patient was reported approximately 7 per 100 person-years in northern Thailand[10,11].

The objectives of the present study were to 1) identify the prevalence of common viral CNS infection and 2) to characterize the important clinical manifestations of each viral CNS infection and 3) to calculate the sensitivity and specificity of multiplex hybridization real time polymerase chain reaction (RT-PCR) when compare to clinical gold standard.

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Material and Method

A 1 year prospective study of children with clinically suspected viral CNS infection, who had no contraindication and able to be perform for lumbar puncture or anterior fontanel tapping and able to give informed consent by their relatives were enrolled. Children suspected severe virulent viral infection such as bird flu (H5N1), rabies and severe acute respiratory distress syndrome (SARS) were excluded. Clinical manifestations, laboratory data included complete blood count (CBC), anti HIV results, as well as CD4 counts were recorded. Cerebrospinal fluid (CSF) examination and culture, along with Sybergreen® and multiplex Hybridization® real time polymerase chain reaction (RT-PCR) for HHV 1, 2, 3, 4, 5, 6A, 6B, 7, enterovirus B, mumps virus, measles virus, Japanese encephalitis virus, JC virus, BK polyomavirus, Nipha virus and Influenza virus (H1N1, H3N2) and Mycobacterium tuberculosis were performed.

DNA and RNA extraction

The total volume of CSF obtained from the patients suspected of having viral CNS infection, was 200 µl and underwent automated DNA and RNA extraction (MagNa pure Compact Nucleic and Isolation Kit-Roche®). The DNA was eluted into 100 µl of nuclease free water and stored at -20°C for DNA and -80°C for RNA before RT-PCR analysis.

Real time polymerase chain reaction

Real time polymerase chain (20 µl) reaction (RT-PCR) by DNA and RNA Sybergreen®-Roche® used viral specific primer and multiplex DNA and RNA Hybridization fast start®-Roche® RT-PCR used probes viral specific sequences for HSV human herpes virus (HHV) type 1, 2, 3, 4, 5, 6A, 6B, 7, enterovirus B, mumps virus, measles virus, Japanese encephalitis virus, JC virus, BK polyomavirus, Nipha virus and influenza virus (H1N1, H3N2), each designed to a viral target on the basis of a full search of the GenBank database (www.ncbi.nlm.nih.gov) with sensitivity of 93 and specificity 100. The negative predictive value was 83% and positive predictive value 100%[12].

PCR conditions

Both DNA virus Sybergreen®-Roche® and Multiplex DNA virus Hybridization fast start®-Roche® using RT PCR as followings, preincubation (95°C for 10 minutes), 45 cycles of amplification (95°C for 2 seconds, then 52°C for 30 seconds and 62°C for 30 seconds), melting curve analysis by using range 40°C to 95°C with ramp rate 0.1°C/second. For Both RNA virus Sybergreen®-Roche® and Multiplex RNA virus Hybridization fast start®-Roche® using RT PCR as followings, reverse transcriptase 45°C for 15 minutes, denaturation (95°C for 3 minutes), 45 cycles of amplification (95°C for 10 seconds then 60°C for 10 seconds and 72°C for 20 seconds), melting curve analysis by using range 50°C to 95°C with ramp rate 0.1°C/second.

Clinical diagnosis of viral CNS infection in infant and children included 1) fever, headache, seizure, decrease sensorium, behavioral change, poor feeding, irritability, focal neurological deficit, hyperreflexia, areflexia and/or neck stiffness or bulging anterior fontanel 2) history of maternal genital herpes lesion 3) increased CSF protein and 4) Sybergreen or multiplex Hybridization RT-PCR positivity for DNA or RNA specific sequence of virus (Table 1).

The present study has approved the ethical consideration by the ethical committee, Thammasat University: Code MTU-P-1-56-51.

Statistics

Descriptive statistics were used for reporting the demographic data. Analytical statistics compared the mean and standard deviation (SD) in HIV and non HIV subgroups using a student-t test (Cytel Studio®). Mean incidences with 95% confidence intervals (Poisson variable) were calculated by STATA Version 6.0™. Nonparametric two independent binomial statistical analyses was done using Fisher's exact test (CYTEL® studio) for numerical data, such as number of patients. A significant p-value was p 0.05 (two tailed).

Results

The 71 children, 39 boys and 32 girls, aged between 2 days to 12.9 years, mean (SD) of 1.38 (2.67) were screened from May 2009-April 2010. One children was sero-positive for HIV. The dermographic data was showed in Table 2.

Total of 11 children with 4 unable to perform lumbar puncture or anterior fontanel tapping, 1 bacterial CNS infection, 3 bacteremia , 1 bacteremia and bacterial CNS infection and 2 tuberculous meningitis were excluded from study analysis (Fig. 1).

In 60 children enrolled, 46 percent were neonates. 48 percent of neonates had HHV2 CNS infection which 92% of mothers had no history of genital herpes during pregnancy. Only 1 of 27 cases had history of active genital herpes lesion for 2 weeks before delivery. Only one patient in the present study had

Table 1. Sequences of viral specific primers used and RT-PCR product size in this study

VIRUS	Sequence 5'-3' Forward primer	Sequence 5'-3' Reverse primer	Hybridization Probe -FL	Hybridization Probe-PH	PCR product (size basepair)
HSV-1	tccttcttgtcgtctcctttcc	accataggatgaacaaaccacc	gttcgattggccaatgttgtc-FL	LC610-ccggttgatttttgggtgg-PH	361
HHV2	tgtcgatccgtaattgtttctg	tctataccctctttctgagccgc	gagtacgagtccaacttggc-FL	LC640-ggatcagcagcataaagtacc-PH	442
VZV (HHV3)	gacggccatttagtatcaagc	gaggagtgccaatgttacatga	tcaaccctctgtttgcatgt-FL	LC705-ggaacatttggcatcattgc-PH	708
EBV(HHV4)	tgtgaacctatggagatgtgc	tattgaccaagcatttccagtg	ggcctgagtctctttaagct-FL	LC610-acaaggagctgaagcg-PH	444
CMV(HHV5)	acgatgagtttctccgttt	caataggcttggttttcaaagg	tgtttgttgtttggatgcttga-FL	LC670-atatcctgttctatgggtaga-PH	526
HHV 6A	gtctagaactccaccacgatcc	aggggagacgaaacatagtcaa	tgagacccagatgcgttcaa-FL	LC705-ctgcggtgagtaaacgtacg-PH	299
HHV 6B	tgctaatgacataacagtccc	ctctaaccccgaacagatgtc	agcaaatgaaacaaactgctg-FL	LC640-aacgacaaaaaacacatcctc-PH	744
HHV 7	tgtagaattggcaatgttttcg	tttctccactaaaacagcccat	gagaatcaagtcctgtggac-FL	LC670-aagtcctgtatatcggacaaatgta-PH	732
JE	tatactcatgtgggaggctg	tttcacgctctttctacagtcgatg	acccaaaatgtaagaatggagactggga-FL	LC610-ttgtcattaccaccgacatctctgaaatg-PH	172
Mumps	atttcttgtctgtgcctggaatcaga	tgatggtcaatctggttagcacagg	gtgaaaatgtgtgcccaactgctt-FL	LC705-gtgtcagggggtttatcttgatccct-PH	671
BK	actgggaagagcattgtgatt	caggcttggttacaatgaatga	tcagctacaggcctaaacca-FL	LC670-ttagcagtagcaacaaggtca-PH	396
Measles	actggaaatcatttgctggagtgaga	catgccctcatttttgtaagtcatttagcg	gtcacggaggcttgtagatgtttccttaa-FL	LC670-attcgagctttgacccacccatatgataaatg-PH	351
JC	tatactcatgtgggaggctg	tacttgagcatccatgccatac	agtaccagatggaacaatttt-FL	LC640-ccaaagaatgccacagtg-PH	666
Entero B	tcctccggcccctgaatgc	caccggatggccaatccaa	gggcagtgtgtcgtaacg-FL	LC640-caactctgcagcggaaccg-PH	198
NIPHA	ctgctgcagttcaggaaacatcag	accggatgtgctcacagaactg	tggaggcagtgatcaagatatcgatgaa-FL	LC640-ggaagaacctatagaacagagtggcag-PH	227

Table 2. Demographic data of children patients

Total number	n = 60
Age mean (day) + SD, range (day)	506 + 976 (2-4,738)
Gender (Female:Male)	29:31
Non-HIV:HIV	59:1
Non-viral CNS infection	14
Viral CNS infection	46

Fig. 1 Diagnosis of patients with clinically suspected CNS infection in children

acquired-immunodeficiency disease. Forty-six patients (76.67%) were diagnosed viral CNS infection.

The prevalence of HHV1, HHV2, VZV, HHV6, HHV7 and enterovirus B CNS infections were 11.67, 50, 6.67, 3.33, 3.33 and 1.67 percent, respectively. There were no EBV, CMV, mumps, measles, JE and dengue viral CNS infections diagnosed in the enrolled group. One patient had co-incidence of VZV CNS infection and seasonal flu (H3N2).

For clinical manifestations, diarrhea, irritability, and CSF pleocytosis may helpful for differentiation between subtype of viral CNS infection. No statistical significant difference of other clinical clues included fever, headache, seizures, decrease sensorium, behavioral change, poor feeding, maternal genital herpes lesion, focal neurological deficit, alteration of consciousness, neck stiffness, bulging anterior fontanel, hyperreflexia, areflexia, abnormal head circumference, cerebellar sign, ataxia and skin lesion between non-viral and viral CNS infection. Amongst clinical manifestations and laboratory data, diarrhea

were only important clinical clue in children with, enterovirus CNS, VZV and HHV6 CNS infection ($p < 0.01$), where as, irritability may be dominant clues for HHV1 CNS infection ($p = 0.05$) (Table 3).

Interestingly, CSF pleocytosis (mean $\pm$ SD = 468 cell per mm^3 $\pm$ 1,230) may be common in HHV1 CNS infection ($p = 0.09$). CSF red blood cell was predominately observed in HHV2 infected neonatal group (mean $\pm$ SD = 1,524 cell per mm^3 $\pm$ 714) more than HHV1. There were no other laboratory datas or CSF characteristics that had statistical significant between viral and non-viral CNS infection (Table 4).

Discussion

In children , By using both Sybergreen® and multiplex Hybridization® RT-PCR, the authors found the higher prevalence (76.6%) of viral encephalitis when compare to previous Thai encephalitis study[9]. HHV 2 was the most common cause of viral CNS infection (48.0%), especially in neonate, where as, prevalence of maternal genital lesions were not different from other studies[13-16]. In neonates, 75% of the mothers had no history and clinically suggestive of active herpes genital lesions during pregnancy[16,17]. Other common viral CNS infection in children were HHV1, VZV, HHV6, HHV7 and enterovirus which not different from developed countries[18-23]. However, previous Thai encephalitis study reported dengue virus and JE virus as the most common than herpes viruses between 1996 to 1998, of which may be due to epidemic changed, inadequate immunization, and the present study design enrolled only children without neonate[9].

In children, fever, headache, seizure and alteration of consciousness were not difference between non-viral and viral CNS infected children when compare to previous study worldwide. Interestingly, diarrhea, irritability and CSF pleocytosis may be important clinical clues for differentiate the viral subtype. The children with symptoms of viral CNS infection and diarrhea should be aware of enterovirus, VZV and HHV6 CNS infection ($p = 0.01$). If children presented with symptoms of viral CNS infection and irritability, CSF showed pleocytosis, this should be aware of HHV1 CNS infection ($p = 0.05$ and $p = 0.09$).

There were no different between non-viral and viral CNS infected group in CBC and neuroimaging study, CSF protein and CSF/blood glucose ratio. In resource limited setting, these major clues may help physician to identify HHV1 CNS infection and prompt treatment with acyclovir may be played important role for empirical treatment. Different from other study, the authors found only one child with AIDS (CD4 count 1.61%) who presented with viral CNS infection. This may be due to national HAART program for pregnant mother with HIV seroconversion, decreased prevalence of AIDS children was observed. This improvement of CD4 of children with HIV may be adequate for protection of viral CNS infection.

Conclusion

Human herpes virus, especially HSV-CNS infection was found to be common in children. Diarrhea ($p < 0.01$) may be clinical clue for diagnosis of enterovirus, VZV and HHV6 CNS infection, where as irritability ($p = 0.05$) and CSF pleocytosis ($p = 0.09$) may be clinical clue for HHV1 CNS infection in children. Unlike the CSF/blood sugar ratio and CSF pleocytosis, clinical manifestations may not be helpful for differentiation between HSV encephalitis and non-HSV/HHV-CNS infection in children. RT-PCR with high sensitivity and specificity remained important methods for diagnosis of viral CNS infection.

Acknowledgement

The authors wish to thank Dr. Piyathida Harnsomboonrana for provision of laboratory resources and Dusit Sujirarat for the statistical analysis. Finally, the authors wish to acknowledge and thank all the patients who participated in the present study.

Potential conflicts of interest

The authors are grateful to the Rajavithi Biomolecular Research Center at Rajavithi Hospital in Bangkok and Thammasat University in Pathumtani, Thailand, for the unlimited grant support.

References

1. Johnson RT. Acute encephalitis. Clin Infect Dis 1996; 23: 219-24.
2. Nicolosi A, Hauser WA, Beghi E, Kurland LT. Epidemiology of central nervous system infections in Olmsted County, Minnesota, 1950-1981. J Infect Dis 1986; 154: 399-408.
3. Koskiniemi M, Rantalaiho T, Piiparinen H, von Bonsdorff CH, Farkkila M, Jarvinen A, et al. Infections of the central nervous system of suspected viral origin: a collaborative study from Finland. J Neurovirol 2001; 7: 400-8.
4. Koskiniemi M, Rautonen J, Lehtokoski-Lehtiniemi E, Vaheri A. Epidemiology of encephalitis in children: a 20-year survey. Ann Neurol 1991; 29: 492-7.
5. Henrich TJ, Hutchaleelaha S, Jiwariyavej V,

Table 3. Clinical characteristics of patient with nonviral and viral CNS infection

Sign and symptom	Number of patient (%) Viral CNS infection							
	Non viral infection	HHV1	HHV2	VZV	HHV6	HHV7	Enterovirus	p-value
Fever > 38°C	11 (78.57)	5 (71.43)	23 (76.67)	2 (50.00)	2 (100.00)	1 (50.00)	1 (100.00)	0.68
Headache	1 (16.67)	1 (33.33)	2 (20.00)	0	0	1 (100.00)	1 (100.00)	0.68
Seizures	5 (35.71)	3 (50.00)	11 (36.67)	1 (25.00)	0	0	1 (100.00)	0.31
Decrease sensorium	10 (71.43)	3 (42.86)	11 (36.67)	2 (50.00)	1 (50.00)	1 (50.00)	1 (100.00)	0.25
Behavioral change	3 (21.43)	1 (14.29)	5 (16.67)	0	0	0	0	0.25
Poor feeding	5 (35.71)	4 (57.14)	16 (53.33)	3 (75.00)	1 (50.00)	1 (50.00)	1 (100.00)	0.18
Irritability	4 (28.57)	5 (71.43)	8 (26.67)	0	0	0	0	0.05
Diarrhea	1 (7.14)	0	5 (16.67)	3 (75.00)	2 (100.00)	0	1 (100.00)	< 0.01
Maternal genital herpes lesion	0	0	1 (3.33)	0	0	0	0	0.71
Focal neurological deficit	0	1 (14.29)	2 (6.67)	0	0	0	0	0.94
Alteration of consciousness	7 (53.85)	3 (42.86)	10 (33.33)	1 (25.00)	2 (100.00)	0	0	0.23
Neck stiffness	2 (14.29)	1 (14.29)	4 (13.33)	1 (25.00)	1 (50.00)	1 (50.00)	0	0.36
Bulging anterior fontanel	0	1 (14.29)	0	0	0	0	0	0.43
Hyperreflexia	1 (7.14)	2 (28.57)	2 (6.67)	0	0	0	0	0.23
Areflexia	1 (7.14)	0	0	1 (25.00)	0	0	0	0.99
Abnormal head circumference	0	0	1 (3.33)	0	0	0	0	0.71
Cerebellar sign	1 (7.14)	0	0	2 (50.00)	0	0	0	0.41
Ataxia	1 (50.00)	0	1 (11.11)	2 (66.67)	0	0	0	0.53
Skin Lesion	3 (21.43)	1 (14.29)	6 (20.00)	0	0	1 (50.00)	0	0.72

p-value were estimated by Kruskal-Wallis Test method
Significant p-value is $p < 0.05$, borderline significant p-value $p = 0.05$
p-value were calculated by using StatXact® Cytel® studioversion 6.0 license number 2060107

Table 4. Laboratory of patients with nonviral and viral CNS infection in children

Laboratory	Mean (standard deviation) Viral CNS infection							
	Non viral infection	HHV1	HHV2	VZV	HHV6	HHV7	Enterovirus	p-value
Age (day)	604 (1173)	352 (557)	503 (1066)	381 (323)	46 (33)	976 (1,342)	254 (-)	0.96
Hemoglobin	12.5 (2.6)	11.4 (2.5)	13.1 (1.0)	1 (25.00)	9.7 (4.0)	12.2 (0.2)	107 (-)	0.53
Hematocrit	38.4 (8.4)	35.5 (8.4)	37.4 (9.1)	39.8 (3.2)	30.4 (13.5)	37.3 (0.28)	33.5 (-)	0.85
PMN	7,624 (4,360)	10,308 (6094)	6,084 (3,573)	10,290 (6,191)	6,087 (2,498)	8,668 (6,047)	8,342 (-)	0.25
Lymphocyte	10,430 (15,272)	5981 (2746)	5,444 (3,557)	5,407 (1706)	9,605 (3,217)	1,418 (743)	5,400 (-)	0.53
Platelet	376,928	426,285	341,400	354,500	403,000	363,500	212,000	0.60
	130,375	119,170	131,037	90,717	36,769	122,329	(-)	
Blood sugar	97.9 (20.1)	96.0 (24.3)	94.4 (33.5)	119.2 (29.0)	94.0 (14.1)	110.0 (22.6)	146.0 (-)	0.45
CSF Open pressure	15.0 (11.3)	13.0 (-)	16.3 (11.1)	15.0 (5.5)	Not Done	26.0 (-)	Not Done	0.84
CSF protein (neonate)	84.8 (25.9)	121.4 (49.0)	114.9 (61.3)	94.0 (-)	59.3 (-)	90.1 (-)	35.4 (-)	0.69
CSF protein (non neonate)	35.4 (12.0)	28.0 (7.4)	78.3 (105.5)	84.7 (116.2)	31.9 (-)	28.0 (-)	22.7 (-)	0.85
CSF/Blood sugar ratio	0.63 (0.26)	0.64 (0.15)	0.59 (0.18)	0.59 (0.11)	0.73 (0.14)	0.54 (0.04)	0.53 (-)	0.94
CSF pleocytosis	5.07 (13.1)	468.2 (1,230.1)	62.1 (264.4)	5.0 (6.7)	2.5 (3.5)	17.5 (24.7)	2.0 (-)	0.45/0.09
CSF% PMN	9.2 (26.7)	11.4 (30.2)	1.5 (8.2)	25.0 (50.0)	Not Done	10.0 (14.1)	0	0.47
CSF% Lym	33.5 (47.0)	17.1 (37.2)	55.1 (49.7)	50.0 (57.7)	50.0 (70.7)	40.0 (56.5)	100 (-)	0.45
CSF RBC	2,547.0	509.5	1,524.0	177.5	0	26.0	0	0.92
	6,088.7	1,327.4	714	(-)	(-)	26.8	(-)	

p-value were estimated by ANOVA Test method
Significant p-value is $p < 0.05$, at Hoc approach calculated the significant p-value $p = 0.09$
p-value were calculated by using StatXact® Cytel® studio license number 2060107

Barbazan P, Nitatpattana N, Yoksan S, et al. Geographic dynamics of viral encephalitis in Thailand. Microbes Infect 2003; 5: 603-11.
6. Huang C, Chatterjee NK, Grady LJ. Diagnosis of viral infections of the central nervous system. N Engl J Med 1999; 340: 483-4.
7. Ziai WC, Lewin JJ 3rd. Update in the diagnosis and management of central nervous system infections. Neurol Clin 2008; 26: 427-68.
8. Sanoreseang S, Vagus U, Yingyong T. Situation of Encephalitis and Japanese B encephalitis, Thailand, 2009 [database on the Internet]. Nonthaburi: Division of Infectious Disease Epidemiology, Department of Disease Control Ministry of Public Health, Thailand. 2010 [cited 2011 Jan 27]. Available from: http://www.boe.moph.go.th/files/report/20101111_17978120.pdf
9. Chokephaibulkit K, Kankirawatana P, Apintanapong S, Pongthapisit V, Yoksan S, Kositanont U, et al. Viral etiologies of encephalitis in Thai children. Pediatr Infect Dis J 2001; 20: 216-8.
10. Subsai K, Kanoksri S, Siwaporn C, Helen L. Neurological complications in AIDS patients: the 1-year retrospective study in Chiang Mai University, Thailand. Eur J Neurol 2004; 11: 755-9.
11. Subsai K, Kanoksri S, Siwaporn C, Helen L, Kanokporn O, Wantana P. Neurological complications in AIDS patients receiving HAART: a 2-year retrospective study. Eur J Neurol 2006; 13: 233-9.
12. Boriskin YS, Rice PS, Stabler RA, Hinds J, Al Ghusein H, Vass K, et al. DNA microarrays for virus detection in cases of central nervous system infection. J Clin Microbiol 2004; 42: 5811-8.
13. Volpe JJ. Viral, protozoan, and related intracranial infections. In: Volpe JJ, editor. Neurology of the ewborn. 5th ed. Philadelphia: Saunders Elsevier; 2008: 874-84.
14. Kropp RY, Wong T, Cormier L, Ringrose A, Burton S, Embree JE, et al. Neonatal herpes simplex virus infections in Canada: results of a 3-year national prospective study. Pediatrics 2006; 117: 1955-62.
15. Brown ZA, Benedetti J, Ashley R, Burchett S, Selke S, Berry S, et al. Neonatal herpes simplex virus infection in relation to asymptomatic maternal infection at the time of labor. N Engl J Med 1991; 324: 1247-52.
16. American Academy of Pediatrics. Herpes simplex. In: Pickering LK, editor. 2000 Red book: report of the committee on infectious diseases. 25th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2000: 309-18.
17. Berger JR, Houff S. Neurological complications of herpes simplex virus type 2 infection. Arch Neurol 2008; 65: 596-600.
18. Gleaves CA, Hodkinka RL, Johnston SL, Swierkosz EM. Laboratory diagnosis of viral infections: Cumitech 15A, s.1. American Society for Microbiology; 1994.
19. Mitchell PS, Espy MJ, Smith TF, Toal DR, Rys PN, Berbari EF, et al. Laboratory diagnosis of central nervous system infections with herpes simplex virus by PCR performed with cerebrospinal fluid specimens. J Clin Microbiol 1997; 35: 2873-7.
20. Whitley RJ, Gnann JW. Viral encephalitis: familiar infections and emerging pathogens. Lancet 2002; 359: 507-13.
21. Kimberlin D. Herpes simplex virus, meningitis and encephalitis in neonates. Herpes 2004; 11 (Suppl 2): 65A-76A.
22. Read SJ, Jeffery KJ, Bangham CR. Aseptic meningitis and encephalitis: the role of PCR in the diagnostic laboratory. J Clin Microbiol 1997; 35: 691-6.
23. Souza IE, Bale JF Jr. The diagnosis of congenital infections: contemporary strategies. J Child Neurol 1995; 10: 271-82.

โรคติดเชื้อไวรัสของระบบประสาทส่วนกลางในเด็ก: การศึกษาแบบไปข้างหน้าเป็นระยะเวลา 1 ปี

สุดาทิพย์ ผาติชีพ, สีบสาย คงแสงดาว

โรคติดเชื้อไวรัสของระบบประสาทส่วนกลางเป็นปัญหาที่พบบ่อยทั่วโลกโดยเฉพาะในเด็ก อาการแสดงทางคลินิกของโรคติดเชื้อไวรัสของระบบประสาทส่วนกลางเป็นสิ่งที่สำคัญที่สุดที่ใช้ในการวินิจฉัยโรคและการรักษา การศึกษาแบบไปข้างหน้าเป็นระยะเวลา 1 ปี เพื่อหาความชุก อาการแสดงทางคลินิก และผลตรวจทางห้องปฏิบัติการของโรคติดเชื้อไวรัสของระบบประสาทในเด็ก โดยเฉพาะการติดเชื้อจากเชื้อชนิด human herpes virus (HHV) type 1, 2, 3, 4, 5, 6A, 6B, 7, enterovirus B, mumps virus, measles virus, Japanese encephalitis virus, JC virus, BK polyomavirus, Nipha virus, and influenza virus (H1N1, H3N2) ได้ถูกดำเนินการ พบว่าเด็ก 71 ราย ที่แพทย์คาดว่าจะมีภาวะโรคติดเชื้อไวรัสของระบบประสาทส่วนกลางอายุประมาณ 2 วัน ถึง 12.9 ปี ได้ถูกรวบรวมตั้งแต่เดือนพฤษภาคม พ.ศ. 2552 ถึงเดือนเมษายน พ.ศ. 2553 มีเด็กจำนวน 4 ราย ได้รับการวินิจฉัยว่าไม่มีภาวะติดเชื้อไวรัสของระบบประสาทส่วนกลาง มีเด็กจำนวน 5 ราย ได้รับการวินิจฉัยว่าเป็นโรคเยื่อหุ้มสมองอักเสบจากเชื้อแบคทีเรีย และ 2 ราย ได้รับการวินิจฉัยว่าเป็นโรคเยื่อหุ้มสมองอักเสบจากเชื้อวัณโรค นอกจากนี้พบว่า HHV2 เป็นโรคติดเชื้อไวรัสของระบบประสาทส่วนกลางที่พบบ่อยที่สุดร้อยละ 50 โรคติดเชื้อไวรัสของระบบประสาทส่วนกลางอื่นๆ ได้แก่ HHV1 ร้อยละ 11.6, VZV ร้อยละ 6.7, HHV6 ร้อยละ 3.3, HHV7 ร้อยละ 3.3, enterovirus B ร้อยละ 1.6 และ ไวรัสไข้หวัดใหญ่สายพันธุ์ H3N2 ร้อยละ 1.6 อาการท้องเสีย กระสับกระส่าย และการตรวจพบเซลล์เม็ดเลือดขาวในน้ำไขสันหลัง (CSF pleocytosis) อาจเป็นอาการแสดงทางคลินิกที่สำคัญในการวินิจฉัยแยกโรคชนิดของเชื้อไวรัสที่ทำให้เกิดโรคติดเชื้อไวรัสของระบบประสาทส่วนกลาง