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VIROJ PONGTHANAPISIT: LABORATORY INVESTIGATION OF VIRAL ETIOLOGIC AGENTS IN PEDIATRIC PATIENTS WITH ACUTE VIRAL ENCEPHALITIS. THESIS ADVISOR: PILAIPAN PUTHAVATHANA, Ph.D., URAIWAN KOSITANONT, M.Sc., SONTANA SIRITANTIKORN, Dr.rer.nat., BOONYOS RUENGSAKULRAJ, Ph.D., KULKANYA CHOKEPHAIBULKIT, M.D., PISAMAI BODHIPHALA, M.Sc. ISBN 974-663-436-4

Encephalitis is an acute inflammatory disease that effects the brain, and it almost always involves inflammation of the adjacent meninges. Thus, the term encephalitis or meningoencephalitis usually applies to the same disease. Encephalitis in hosts with intact immunity is most commonly caused by a variety of viral infections. Viral encephalitis is usually acute and occurs as a consequence of the destruction of the infected neuronal cells of the host immune system.

The common cause of viral encephalitis are herpes simplex virus (HSV), arboviruses (e.g., Japanese encephalitis virus(JEV), St.Louis encephalitis virus), enterovirus, rabies virus and mumps virus; and in a lesser extent: human herpesvirus 6 (HHV-6), cytomegalovirus (CMV) and Epstein-Barr virus (EBV).

The present study employed several laboratory methods to investigate the infection rate of viral etiologic agents in pediatric patients who were clinically diagnosed as acute viral encephalitis. The subjects were hospitalized at Siriraj Hospital during the period of February 1996 to October 1998, and included 36 cases of viral encephalitis, 23 cases of CNS infection, 61 cases of other manifestations and 43 cases of unknown diagnosis. The methods used in our study were 1) the detection of HSV and HHV-6 DNA genomes in CSF by PCR, and of JEV and enterovirus RNA genomes by RT/PCR; 2) determination for ratio of CSF: Serum HSV IgG as expressed in term of antibody specific index (ASI) by ELISA; 3) detection of IgG and IgM to JEV and Dengue Virus antigens in CSF and paired sera; 4) detection for a four-folded rise of hemagglutination inhibiting(HI) antibodies to JEV and dengue virus type 1 and 2 in paired sera; and 5) detection of specific antibodies in paired sera, i.e., HSV IgG and IgM, HHV-6 IgG and IgM, and enterovirus IgG, IgM and IgA Using various laboratory methods mentioned above. With limited amount of CSF samples and sera, we discovered the prevalence of 26.09%(6 of 23) of Japanese encephalitis,16.67% (6 of 36) of HSV encephalitis, 8.33%(3 of 36) of HHV-6 encephalitis and 3.13%(1 of 32) of enterovirus encephalitis. We also discovered four cases of JEV infection based on the criteria that the diagnosis of JEV infection should be given in cases of CSF not being available or cannot diagnosed but sera were positive by ELISA IgM or by a four-folded rise of HI antibody titer. Five cases(13.88%) of Dengue infection were diagnosed 36 patients who were at first presented with symptoms and signs suggestive of viral encephalitis but later progressed to dengue hemorrhagic fever. With information from routine laboratory two more cases of mumps, one case of varicella zoster encephalitis and one case of rabies encephalitis were also found in our subjects. We concluded that 25(69.44%) of 36 acute viral encephalitis cases were laboratory confirmed viral infections. Because of the laboratory methods, the diagnosis of viral encephalitis could not be achieved without investigation of the CSF samples, either by detection of viral genomes or of the specific antibodies. The present study suggested that PCR and RT/PCR are very useful tools in the diagnosis of CNS infections. And, since the above diseases are caused by many viral agents, multiplex PCR should be further developed in order to reduce materials and time consumed; and most of all when the specimens obtained are of very minute amount. However it should be kept in mind that PCRs are susceptible to contamination with extraneous DNA fragments that can be amplified and carried over through successive amplification rounds. Moreover, PCR may yield false positive result caused by nonspecific amplification of unrelated nucleic acid sequences. And the lack of gold standard against which to validate the PCR result makes the interpretation of positive PCR tests extremely difficult.