

RESEARCH NOTE

ETIOLOGY OF ACUTE NON-A, B, C HEPATITIS IN THAI PATIENTS: PRELIMINARY STUDY

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Abstract. To better characterize the etiology of acute non-A, B, C hepatitis, 24 sera from 50 acute hepatitis without acute markers for hepatitis A, B, and C were examined for acute markers for the hepatitis E virus (HEV), cytomegalovirus (CMV), herpes simplex virus type 2 (HSV-2), and Epstein-Barr virus. Immunoglobulin M (IgM) specific for HEV, HSV-2, and CMV was detected using ELISA and total Ig specific to EBV was determined by standard indirect immunofluorescence. IgM to CMV was not observed in sera from any of the patients; whereas, IgM to HEV was detected in sera from 2 patients and IgM to HSV-2 was detected in 5 of 24 acute hepatitis patients. In addition, high titer of antibody was found in 2 of the patients. This results indicate that HSV-2 and HEV circulate in Thailand and are responsible for a small proportion of non-A, B, C hepatitis in Thailand.

Viral hepatitis refers to the disease caused by infection with one or more members of a small group of hepatotropic viruses including hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus and hepatitis E virus (Fields *et al.*, 1990). Furthermore, cytomegalovirus (CMV), Epstein-Barr virus (EBV), herpes simplex virus -2 (HSV-2) and some arboviruses may cause hepatitis (Regenstein and Perrillo, 1989).

In Thailand, HAV is endemic, causing self limited acute hepatitis with occasional small outbreaks. Over the last 15 years, the prevalence of anti-HAV in school children in urban areas has been decreasing, while that for rural areas remains high at 20-100%. HBV is a major cause of chronic liver disease and the prevalence in the general population is about 6-10%. HCV, infecting about 1.5% of the general population, is the second major cause of chronic hepatitis and liver disease in Thailand (Chainuvati, 1994). To date, very few seroepidemiologic studies of HEV infection have been conducted in Thailand. Dawson *et al.* (1992) using a solid phase immunoenzymatic assay, found IgG to HEV in 7 of 100 sera from a rural Thai village in Northern Thailand (Dawson *et al.*, 1992). Later, the same laboratory reported the finding of

IgG to HEV in 2.8% of serum samples from normal healthy blood donors in Bangkok (Paul *et al.*, 1994). Reports actually describing an outbreak of HEV in Thailand cannot be found; although, during the last 15 years outbreaks of HEV have been documented in nearby countries including China (Zhuang *et al.*, 1991; Cao *et al.*, 1991), India (Arankalle *et al.*, 1994), Nepal (Shrestha, 1987), Myanmar (Uchida *et al.*, 1993), Vietnam (Corwin *et al.*, 1996) and Indonesia (Corwin *et al.*, 1995).

The present study was designed to determine the presence of HEV infection in Thailand and to investigate the other possible causes of non-A,B,C and E hepatitis in Thailand including CMV, HSV-2 and EBV.

Sera were collected from 50 patients with clinically suspected acute viral hepatitis admitted to the Hospital for Tropical Medicine, Pramongkutklao Army Hospital, and Ramathibodi Hospital in first week of admission. Viral hepatitis was suspected in patients who presented with sign and symptoms that included anorexia, nausea, malaise, abdominal pain, dark urine, jaundice or sclera icterus. Exclusion criteria includes a history of exposure to hepatotoxic drugs, chemicals, or chronic alcohol use.

Sera were first screened for evidence of HAV, HBV, or HCV infection using commercially-available ELISA kits (HAV AB-EIA, CORZYME, AUSZYME MONOCLONE, and HCV-EIA 2nd Generation; all kits were manufactured by Abbot Laboratories). Evidence of acute HAV, HBV and HCV infection was found in 7 (14%), 14 (28%) and 5 (10%) patients, respectively. Therefore, the cause of hepatitis could be attributed to either HAV, HBV, or HCV in 26 of 50 patients. This study focused on the remaining 24 patients.

Sera were then examined for IgG and IgM to HEV using commercially-available ELISA kits (Genelabs Diagnostics, Singapore). IgG to HEV was detected in 6 of 24 sera, whereas IgM to HEV was detected in only two (8%) sera. IgG to HEV in the absence of IgM to HEV was considered a sign of past HEV infection rather than a diagnostic marker for acute infection. Therefore, HEV was considered to be the cause of hepatitis in only 2 patients. The remaining sera were then examined for IgG and IgM to HSV-2 using commercial-available ELISA kits (HUMAN, Germany). Both IgG and IgM to HSV-2 were detected in 5 of 24 (21%) patients; therefore, HSV-2 was considered as the cause of hepatitis in 5 patients. The remaining sera were then examined for total immunoglobulin to EBV using a standard indirect immunofluorescence technique with goat anti-human IgG to EBV (DAKO, Denmark). High titers of antibody to EBV were detected in two of the patients; therefore EBV was considered to be the cause of hepatitis in two patients. Finally, the remaining sera were examined for IgG and IgM to CMV using commercially-available ELISA kits (HUMAN, Germany). No evidence of CMV infection was found in any of the sera. In summary, of the 24 cases of hepatitis that could not be attributed to either HAV, HBV, or HCV, HEV was considered the cause of hepatitis in 2 patients, HSV-2 was considered the cause of hepatitis in 5 patients and EBV was considered the cause of hepatitis in 2 patients. The cause of hepatitis in the remaining 15 patients was not identified.

Although this study was preliminary, the results indicate that HEV, HSV-2 and EBV are responsible for a small proportion of non-A,B,C hepatitis in Thailand. In comparison to neighboring countries, HEV infection in Thailand today appears to occur at low levels. However this may not have always been true. Previous high levels of HEV infection may

have occurred prior to the identification of HEV as a cause of hepatitis. Low levels of both HEV and HAV infection today may be attributed to better education and higher standards of hygiene among Thai people (Clayson, 1996). No previous study has been reported about the role of HSV-2 and EBV in causing hepatitis in Thailand. Herpes viruses are not hepatotropic and liver is not primary target organ. Therefore hepatitis symptoms are usually only observed after generalized infection (Regenstein and Perrillo, 1989). Although we did not identify CMV as a cause of hepatitis among adults in Thailand, Poovorawan *et al* (1990) reported that CMV is a cause of neonatal hepatitis in Thailand. Our preliminary results suggest that further investigation into the causes of non-A, B, C hepatitis is warranted.

ACKNOWLEDGEMENTS

The authors thank the following for excellent technical assistance: (AFRIMS) Sumitda Narupiti, Kittinan Hussem, Surin Siriranond, Chonticha Kumthong; (Faculty of Medicine, Siriraj Hospital) Sutiruk Singnok.

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