CASE REPORT

FATAL DENGUE ENCEPHALITIS

Prasonk Witayathawornwong

Department of Pediatrics, Petchabun Hospital, Petchabun, Thailand

Abstract. Central nervous system involvement is not an uncommon manifestation of dengue virus infection, but encephalitis is a rare entity. We report the case of a 5-year-old girl with fever and convulsions. She developed coma and shock during the high fever stage without abnormal bleeding. Treatment was supportive and symptomatic. The shock was poorly controlled. High fever persisted for 7.5 days then she expired. Cerebrospinal fluid (CSF) and blood dengue-IgM antibody showed dengue infection.

INTRODUCTION

The indirect effects of dengue infection on the central nervous system may be an explanation for encephalopathy. The encephalopathy was thought to be secondary to vasculitis with resultant fluid extravasation, cerebral edema, hypoperfusion, hyponatremia, and hepatic and renal failure (Nimmannitya et al, 1987; Jimenez et al, 1988; Lum et al, 1993). However, cases of dengue encephalitis have been increasingly reported with the presence of IgM antibody to dengue in the CSF and virus isolation from brain tissue and the CSF of patients with neurological symptoms, suggesting direct virus invasion and replication in the CNS (Lum et al, 1996; Miagostostovich et al, 1997; Hommel et al, 1998; Ramos et al, 1998; Thisyakorn et al, 1999; Kankirawatana et al, 2000; Pancharoen et al, 2001; Nogueira et al, 2002).

CASE REPORT

A 5-year-old girl, who had previously been well, was admitted to Petchabun Hospital on 15 June, 1999, having had fever for 4 days and convulsions for half an hour. On admission, she was stuporous, with no meningeal or other abnormal neurological signs. The temperature was 39°C, respiratory rate 26/minute, blood pressure 110/70 mmHg, and body weight 18 kg. There was no rash, lymphadenopathy, or hepatosplenomegaly. The results of the rest of the physical examination were normal. A diagnosis of acute encephalitis was made. A complete blood count (CBC) showed hematocrit 34%, WBC 7,600/mm³, neutrophils 67%, lymphocytes 31% and atypical lymphocytes 2%, platelets 153,000/mm³. CSF analysis revealed normal pressure, clear and colorless, RBC 10/mm³, no WBC, protein 744 mg/dl, sugar 120 mg/dl, blood sugar after lumbar puncture was 153 mg/dl, Indian ink negative, and Gram stain negative. Urinalysis was normal. Initial management was supportive and symptomatic; intravenous fluid, anticonvulsants and antibiotics. Five hours after admission she developed coma but still responded to deep pain. The blood pressure was normal. She developed respiratory insufficiency, then mechanical ventilation was introduced. Shock (BP 70/40 mmHg) and deep coma developed on the second day with high fever (39.0°C), but no abnormal bleeding. Repeat CBC showed a hematocrit of 35%, WBC 5,800/mm³, neutrophils 54%, lymphocytes 42% and atypical lymphocytes 4%, and platelets 138,000/mm³. A vasopressor drug was used without improvement. Shock was poorly controlled and high fever persisted (38.5°-39.5°C) for 3.5 days, then she expired (total fever of 7.5 days). Repeat CBC on the third day showed a hematocrit of 34%, WBC 4,700/mm³, neu-
FATAL DENGUE ENCEPHALITIS

Vol 36 No. 1 January 2005

Trophils 38%, lymphocytes 52% and atypical lymphocytes 10%, and platelets 124,000/mm³. CSF culture for bacteria and hemoculture were negative. A postmortem examination was refused by her parents.

DISCUSSION

The initial diagnosis of the patient was encephalitis. Japanese encephalitis (JE) virus was suspected to be the causative agent because Petchabun Province (the lower part of northern region of Thailand) is endemic for this organism (Chokephaibulkit et al, 2001) and there was no history of JE vaccination for this patient. Consciousness deteriorated into deep coma, and shock developed later without signs of bleeding. Uncontrolled shock then death are due to the severity of the disease (Chimelli et al, 1990; Janssen et al, 1999; Nogueira et al, 2002). Blood and CSF showed only dengue IgM, not JE IgM.

IgM can not cross the blood-brain barrier. Detection of dengue IgM in the CSF of a patient with encephalitic symptoms suggests dengue encephalitis (Lum et al, 1996). The CSF was tested later for Herpes simplex virus (HSV) and mumps virus but was not found. Serology of the patient showed primary dengue infection. It is possible the patient had dengue hemorrhagic fever but the patient died before the fever defervesced. Dengue encephalitis can arise in primary or secondary dengue infection; in dengue fever or dengue hemorrhagic fever (Lum et al, 1996; Ramos et al, 1998; Janssen et al, 1999).

Although there is evidence that dengue 2 and 3 viruses have neurovirulent properties (Lum et al, 1996; Miagostovich et al, 1997), dengue encephalitis is still a rare disease. These findings imply that there may be factors associated with dengue viruses entering the brain. Direct dengue invasion may occur by disruption of the blood-brain barrier at hemorrhagic foci (Chatuverdi et al, 1991) or by mutation at a specific point in the envelope glycoprotein of the dengue virus allowing it to pass through the blood-brain barrier (Sistayanarain et al, 1996). Mutation of other viruses, such as the poliovirus type 3, where a point mutation in the non-coding region is associated with an increase in the neurovirulence of the virus (Evans et al, 1985). Infected circulating mononuclear infiltration of the brain, a Trojan horse mechanism (Peluso et al, 1985), may allow dengue to directly invade the brain. The exact mechanism by which dengue enters the brain should be further elucidated. The outcome of dengue encephalitis may be an uneventful recovery (Lum et al, 1996; Kankirawatana et al, 2000; Pancharoen et al, 2001), neurological sequelae or death (Chimelli et al, 1990; Lum et al, 1996; Hommel et al, 1998; Janssen et al, 1999; Thisyakorn et al, 1999; Nogueira et al, 2002).

ACKNOWLEDGEMENTS

The author thanks Dr Usa Thisyakorn (Department of Pediatrics, Faculty of Medicine, Chulalongkorn University), Dr Anannitya Visudhiphan (Department of Pediatrics, Ramathibodi Hospital, Mahidol University) for worthy consultation about the case presentation and Officials of the Regional Medical Science Center, Phitsanulok Province for dengue serology testing.

REFERENCES


