

## Clinical Notes

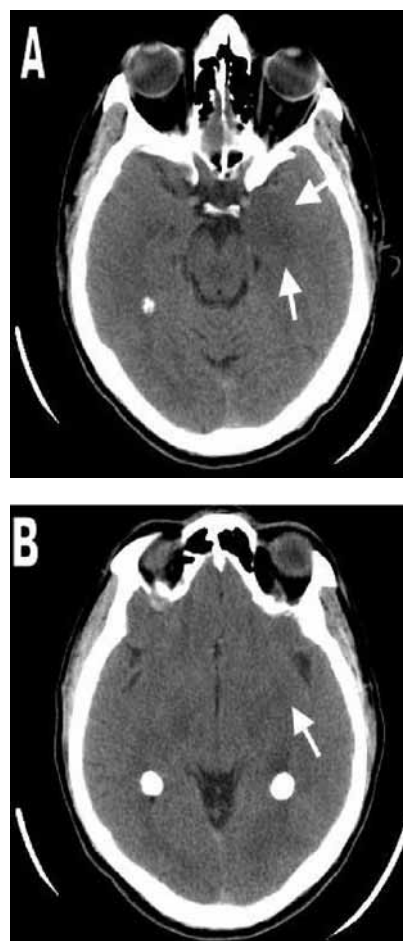
### Steroid pulse therapy in herpes simplex encephalitis

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The term “acute viral encephalitis” (from Greek enkephalos + -itis, meaning brain inflammation) is used to describe restricted CNS involvement (namely, involvement of the brain, sparing the meninges). Epidemiologic studies estimate the incidence of viral encephalitis at 3.5 to 7.4 per 100,000 persons per year. Overall, viruses are the most common cause of encephalitis. The Centers for Disease Control and Prevention (CDC) estimates an annual incidence of approximately 20,000 new cases of encephalitis in the United States; most are mild in nature. The mortality depends largely on the etiologic agent of the encephalitis. Mortality in untreated patient with herpes simplex encephalitis (HSE) reaches 70%. Patients with encephalitis have an altered mental status ranging from subtle deficits to complete unresponsiveness. Meningeal irritation is not a usual sign of encephalitis unless there is involvement of meninges. Since it is an inflammation of brain parenchyma seizure will be common; also focal neurological deficit can occur. Even with prompt initiation of acyclovir therapy, herpes simplex virus (HSV) encephalitis is associated with significant morbidity and mortality. One study in Sweden<sup>1</sup> involving 236 patients with confirmed HSV-1 encephalitis demonstrated a one-year mortality of 14%, with epilepsy occurring in 24%, and neuropsychiatric sequelae in 22% of surviving patients. The aim of this report is to highlight the effectiveness of steroid pulse therapy in HSE.

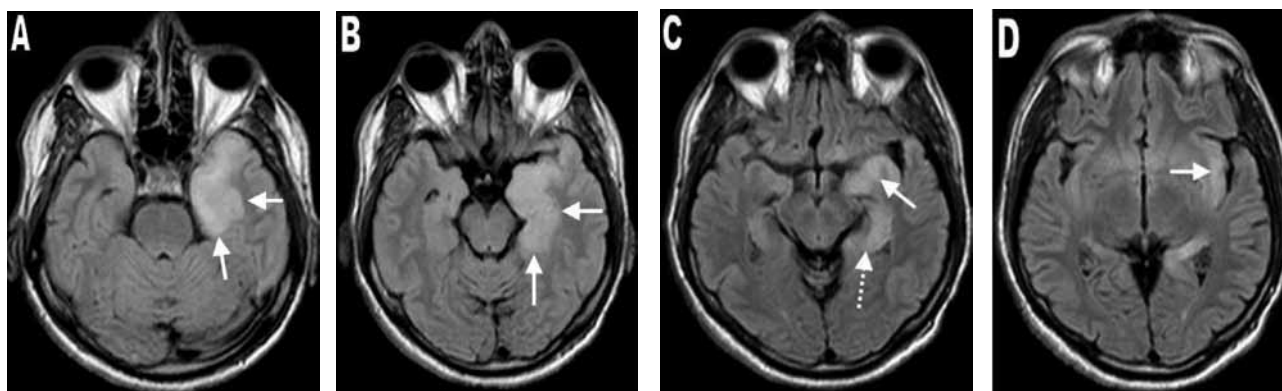
A 47-year-old Asian male without any previous medical problems presented with a history of confusion. This was associated with severe headache and nausea. He denied any history of fever, seizure, or photophobia. On examination, he was conscious but disoriented to time, place, and person. His vital signs showed a temperature of 38.9°C with stable blood pressure and oxygen saturation. Lumbar puncture showed increased white blood cell (WBC) count (13 cell/m<sup>3</sup>). The differential shows a predominance of lymphocytes (80%). The CSF protein was 0.5 g/l, with a glucose of 3.9 mmol/l. Polymerase chain reaction (PCR) for HSV

type 1 was positive. A brain CT scan (Figure 1) and MRI were obtained (Figure 2), showing multiple abnormal T2 hyperintensity involving the cortical and subcortical white matter structures, notably the anterior and mesial left temporal lobe with restricted water diffusion. He was admitted as a case of herpes encephalitis and started on acyclovir. The next day, he developed focal seizure with secondary generalization. The EEG showed left fronto-temporal periodic lateralized epileptiform discharges (PLEDs) and focal slowing. He was loaded with phenytoin and started on levetiracetam. His level of conscious did not improve despite no status epilepticus on EEG. He was shifted to the intensive care unit for observation and started on steroid pulse therapy with methylprednisolone (Depo-Medrol® IV, Pharmacia & Upjohn, Purr, Belgium) (500mg daily) for 5 days. The next day his level of conscious improved, and he became oriented to time, person, and place. The



**Figure 1** - Brain CT without contrast showing A) faint hypodensity involving the left mesial temporal lobe region, B) extension of hypodensity to the subsinsular region.

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**Figure 2** - Fluid attenuated inversion recovery (FLAIR) MRI of brain showed hyperintensity involving predominantly the cortical and subcortical white matter structure notably A) the anterior left temporal lobe, B) uncus, C) amygdale (arrow) and hippocampus (dashed arrow), and D) left insular cortex.

PLEDs disappeared. He was transferred to the ward in good condition.

Herpes simplex virus encephalitis is a neurological emergency because it carries high mortality (70%) if not treated.<sup>2</sup> The HSV encephalitis can cause hemorrhage, edema, and necrosis in the frontal and temporal lobes, with cell death caused by viral invasion and acute inflammatory infiltration.<sup>3</sup> The use of steroids to treat HSV encephalitis was initially tested on animal models. Brain abnormalities on MRI were significantly reduced in a mouse with HSV-1 infection when methylprednisolone and acyclovir were administered compared with acyclovir alone. Another study<sup>4</sup> on a mouse with HSV encephalitis showed that dexamethasone when given immediately can lead to neuro protection of neuronal cells from death. One study of 45 patients has provided additional support for the use of steroids in HSV encephalitis.<sup>5</sup> Corticosteroid treatment in the acute illness was the only independent predictor of good outcome. To date there is no clinical recommendation for the use of steroids in HSV encephalitis. There is a randomized clinical trial in progress looking for the use of dexamethasone to treat HSV encephalitis (GACHE trial).<sup>6</sup>

In conclusion, our HSE patient had good improvement in his level of conscious and seizure control after steroid pulse therapy. The dose used was 500 mg methylprednisolone for 5 days.

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