Case Report
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Relapsed Herpes Simplex Virus Encephalitis after Epilepsy Surgery

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Relapsed herpes simplex virus (HSV) encephalitis after neurosurgery is a very rare condition. An 11-year-old boy suffered from relapsed HSV encephalitis five days after neurosurgery to remove the epileptogenic focus six years after prior HSV encephalitis. He was diagnosed with HSV encephalitis reactivation after positive HSV polymerase chain reaction results following a lumbar puncture, and this diagnosis was supported by consistent radiologic and histopathologic findings. Moreover, focal cortical dysplasia coexisted with inflammatory changes resulting from a viral infection based upon the removed brain tissue. This case may support the hypothesis that neurosurgery may be a triggering factor of HSV reactivation. **(2013;3:28-31)**

Key words: Herpes simplex virus, Encephalitis, Neurosurgery

Introduction

Herpes simplex virus (HSV) encephalitis is the most common form of sporadic viral encephalitis. The majority of HSV patients are left with severe neurological sequelae in spite of early acyclovir treatment. Several cases of early relapse of HSV encephalitis have been reported,[1,2] though rare cases are known to relapse more than three months after the initial episode. Nonspecific symptoms of HSV encephalitis make early diagnosis difficult as it requires cerebrospinal fluid examination including serology. Polymerase chain reaction (PCR) of deoxyribonucleic acid (DNA) can accurately diagnose primary cases and relapsed HSV infections.[3] However, the pathogenesis of late relapse is not fully understood, It can possibly be explained as reactivation from a latent infection in the cranial nerve ganglia. This report reviewed a case of relapsed HSV encephalitis after cortisectomy of the left parietal lobe during epilepsy surgery to treat intractable epilepsy caused by prior HSV encephalitis. The patient was treated successfully after recognition of reactivation of HSV by PCR.

Case report

An 11-year-old boy with a past medical history of HSV encephalitis at the age of five presented to Severance Children's Hospital with a history of intractable seizures for the past six years. He had been healthy with normal neuropsychological development until the onset of the encephalitis. Magnetic resonance imaging (MRI) demonstrated focal encephalomalacia in the right temporal and left parietal lobes, suggestive of sequelae of previous insult (Fig. 1). He had suffered from daily convulsive seizures, which were sometimes provoked by auditory stimulation. His electroencephalogram (EEG) showed diffuse slowing in both hemispheres; frequent generalized slow sharp and wave discharges; frequent generalized paroxysmal fast activities; and frequent sharp waves from multifocal areas with

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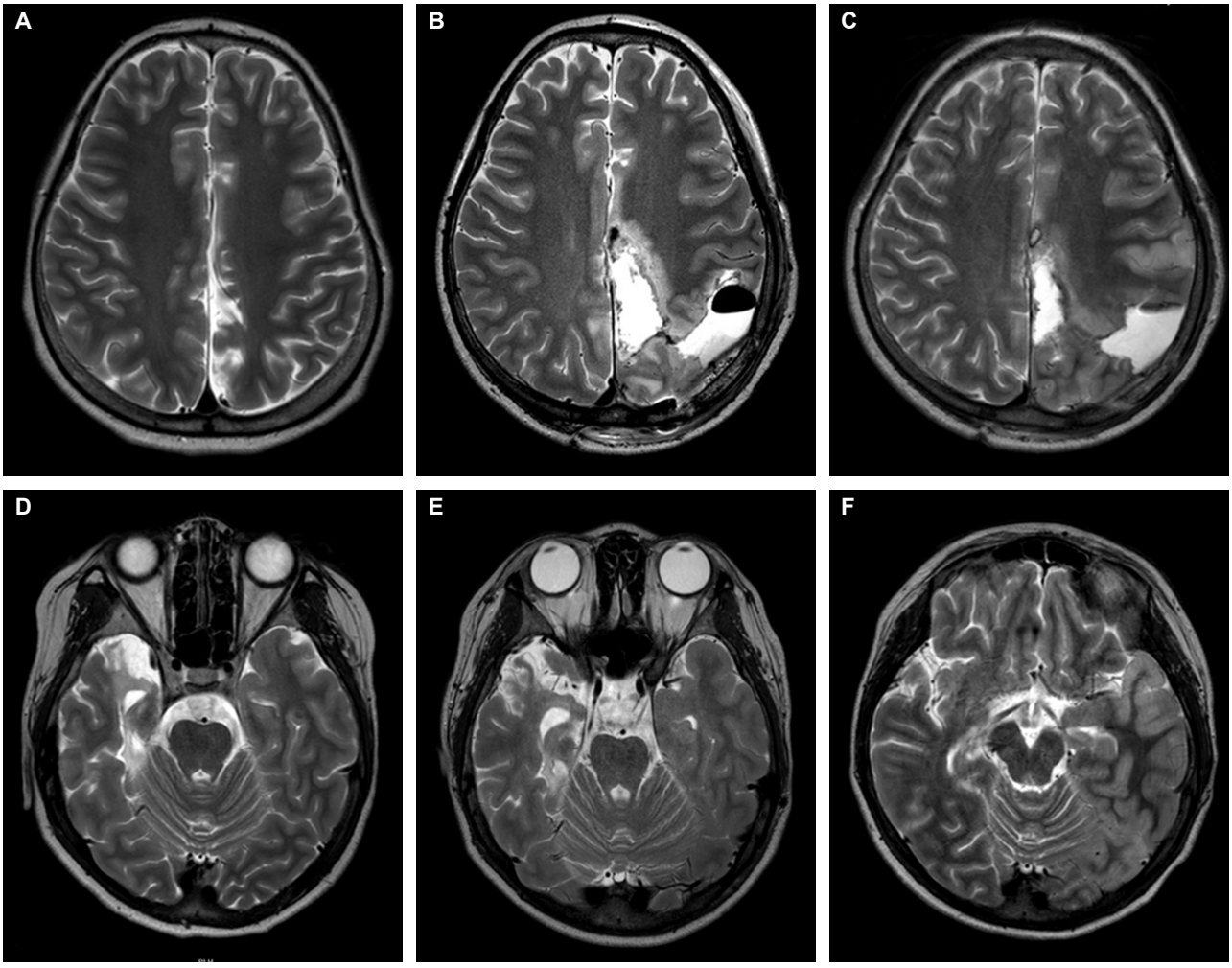

Figure 1. Axial T2-weighted MR images acquired before neurosurgery (A, B) show focal encephalomalacia in the right temporal and left parietal lobes, suggestive of sequelae of previous insult. Axial T2-weighted MR images acquired on the third postoperative day (C, D) showed swelling and increased subdural fluid collection near the resection margin. On postoperative day 10, axial T2-weighted MR images (E, F) showed hyperintensity in the left temporoparietal region not adjacent to the resection margin, suggestive of cerebral venous infarction or encephalitic change.

ictal episodes originating from the left parietal area. He underwent left parietal cortisectomy after an extensive presurgical evaluation. Five days after the operation, he presented with a high fever, lethargy and recurrent seizures. Cerebrospinal fluid (CSF) examination by lumbar puncture showed 5/mm^3 red blood cells, 105/mm^3 white blood cells (99% lymphocytes), 90.1 mg/dL protein, and 60 mg/dL glucose. CSF HSV type 1 PCR was positive, and CSF HSV culture was not available. Brain tissue pathology from cortisectomy revealed focal cortical dyslamination with giant and dysmorphic neurons, accompanied by focal microglial cell nodules (CD 68 positive) with perivascular lymphocytic infiltrations that implied an old viral infection which is consistent with focal cortical dysplasia (FCD) type IIId. Brain MRI showed swelling and hyperintensity in the left temporoparietal region on T2-weighted images that were widely distributed from the surgical resection margin, suggesting the possibility of ischemic insult or infection (Fig. 2). EEG showed excessive delta activity, generalized rhythmic sharp wave discharges, and occasional subclinical seizures from the left occipital area. Intravenous acyclovir 45 mg/kg/day was initiated after relapsed HSV encephalitis was suspected based on these results. High spiking fever and altered mental status improved during the three-week intravenous acyclovir treatment. When he visited the outpatient clinic one month later, our patient's neurological function had returned to baseline status, including cognition, mental, speech, and motor functions.

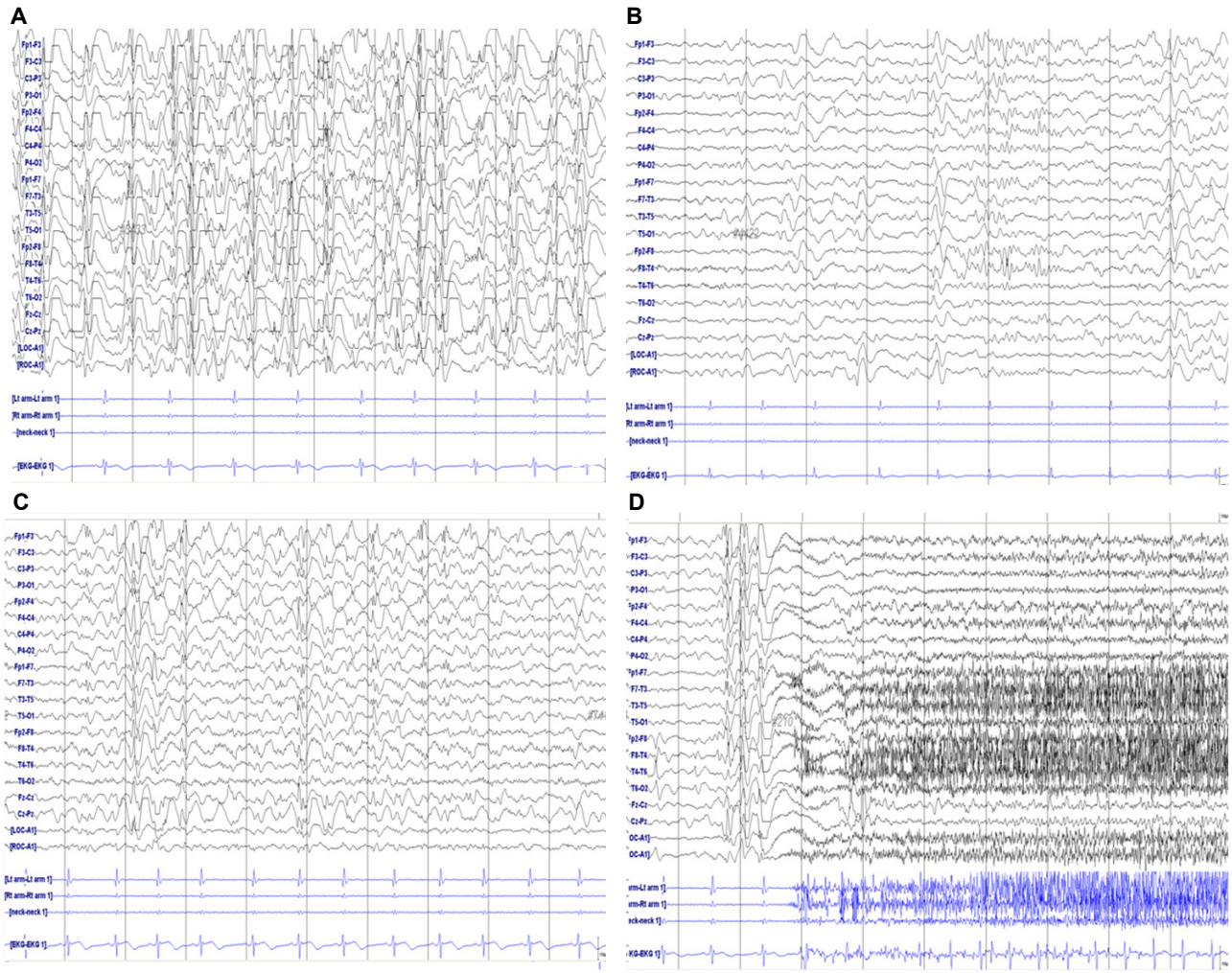

Figure 2. Preoperative EEG features. Generalized slow sharp and wave discharges are seen typical in LGS patients (A). Left side dominant rhythmic sharp and wave discharges and paroxysmal fast activities (B, C). Ictal EEG shows generalized slow wave discharges followed by electrodecrement admixed with fast activities while the patient presented tonic seizure (D).

Discussion

HSV encephalitis can relapse after brain surgery in rare incidences. HSV 1 is the most common cause of sporadic viral encephalitis, with greater than 90% of HSV encephalitis found in immunocompetent patients.[3] This condition occurs rarely as a primary infection; most cases are caused by reactivation of a previous infection during infancy that typically is located in the trigeminal sensory ganglion, with recurrence seen even after conventional acyclovir therapy.[4] Some cases have suggested that neurosurgery can trigger the reactivation of HSV, with a long inactive interval of more than several years.[4,5] It is not fully understood whether the neurosurgery itself or simply the stress of the surgical procedure causes reactivation of HSV. In this case, we recognized the characteristic histopathologic findings in removed brain tissue consistent with previous viral infection commonly found in HSV encephalitis. However, the HSV virus was not detected in the tissue. The discrimination between progressive inflammation and static encephalopathy since prior HSV infection is sometimes difficult; each can occur in clinical situations, especially such as the epileptic encephalopathic patient diagnosed with Lennox-Gastuaut syndrome due to prior HSV encephalitis. Our patient showed characteristic hyperintensity on T2-weighted MR images; these findings are commonly observed in necrotic reactivations rather than in an inflammatory reactivation of HSV that makes diagnosis easier if accompanied by CSF examination.

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Postoperative infection is a common complication of neurosurgical procedures, and infections usually originate from bacteria, although several cases have been reported to stem from herpes simplex virus.[6,7] Nonspecific symptoms make it difficult to differentiate HSV encephalitis from other common postoperative complications, including infarction, bacterial infection and abscess. As a result, early suspicion and decisions by the clinician are essential to diagnose and treat this serious infection. PCR using HSV DNA has been shown to be the most sensitive method to diagnose HSV encephalitis in both the primary episode and in any reactivation that can produce a positive result in culture-negative HSV encephalitic brain tissue.[3,8] However, a brain biopsy is needed if PCR is normal in highly suspicious patients to rule out the possibility of herpetic encephalopathy of the inflammatory form.

We incidentally detected focal cortical dysplasia type IIId according to the new classification.[9] in the removed tissue, and this dysplasia was accompanied by the typical features of a previous viral infection. However, the causal relationship is not clear in this case, for definite FCD is sometimes found in brain tissues from pharmacoresistant epileptic patients but might not be caused by HSV infection. Moreover, no reports have found that HSV can cause focal cortical dysplasia; only one recent case from Japan reported non-herpetic acute limbic encephalitis–related FCD type IIb in a hippocampal sclerotic operative patient.[10]

Intravenous acyclovir is still the gold standard of treatment for reactivated and primary HSV encephalitis.[11] The time interval between symptom onset and acyclovir administration is highly associated with postinfection prognosis. Our patient developed a fever five days after the surgery and remained untreated for five days until we obtained the result of HSV PCR from CSF and began administering acyclovir. Fortunately, the patient recovered to baseline before HSV reactivation and was free from seizures throughout the surgery. He remained on antiepileptic medications for six months and suffered from rare unprovoked seizures.

Prophylactic acyclovir treatment has to be considered if a patient has a history of HSV encephalitis and an unexplained fever after neurosurgery.

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