A 28-year-old woman presented with a one day history of high fever and partial seizures with secondary generalization. This was preceded by a three week history of headache, ataxia, and fatigue. An initial computed tomogram head scan showed a low density mass lesion in the right frontal operculum without enhancement. On the next day, a repeat scan showed a new frontopolar, expansile, low density cortical lesion (Figure 1A) suggestive of encephalitis. Cerebrospinal fluid showed a pleocytosis of 311 mononuclear white blood cell count per µL and an elevated protein of 1.57 g/L. She received intravenous acyclovir and antibiotics. She remained febrile and became mute. A magnetic resonance (MR) scan under general anesthesia on her fourth hospital day showed frontal and perisylvian lesions with restricted diffusion (Figure 1B - D and Figure 2). A right frontal brain biopsy showed meningoencephalitis and immunohistochemical staining was positive for herpes simplex virus (HSV) antigen (Figure 3). Subsequently, HSV-1 DNA was demonstrated in both cerebrospinal fluid and brain tissue with polymerase chain amplification. She improved after a course of intravenous therapy with acyclovir with residual frontal lobe signs, including marked executive dysfunction, and her speech became normal.

Herpes simplex encephalitis (HSE) is a serious disease due to HSV infection, with an untreated mortality of about 70% and substantial morbidity despite therapy with acyclovir.1 Herpes simplex encephalitis is an acute necrotizing encephalitis in adults, with characteristic localization of lesions that typically

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**Figure 1:** (A) Contrast enhanced CT head showing low density mass expansion of cortex and white matter of the right frontal operculum and frontopolar low density cortical lesion with elevation and effacement of the anterior horn of lateral ventricle due to mass effect. There is no enhancement of either cortical lesion. (B) T2 weighted axial image showing perisylvian and frontal cortical distribution of high signal lesions with mass effect effacing the right lateral ventricle. (C) Diffusion weighted image demonstrating curvilinear 'bright' restricted diffusion of the right operculum and frontopolar cortex, which is confirmed by corresponding dark lines (arrowheads) on apparent diffusion coefficient (ADC) mapping (D). Adjacent to the restricted diffusion is the high signal 'T2 shine through' from edema (D).
Fluid-attenuated inversion recovery coronal images

Photomicrograph showing dense enhancement may be demonstrated following administration of gadolinium. Fluid-attenuated inversion recovery sequences demonstrate superior definition of temporal lobe abnormalities compared to standard T1- and T2-weighted images. Diffusion MR studies may also be useful for early detection of lesions. Rarely, patients may have lesions in unusual locations, including the parietal and occipital lobes and cerebellum. Unusual clinical presentations, including the opercular syndrome, may be difficult to recognize as HSE. The present patient lacked the typical medial temporal lobe involvement often seen in HSE and exhibited prominent frontal lobe lesions.

The frontotemporal localization of HSV in adults is thought to relate to the route of viral entry of HSV into the brain. In 1979, Davis and Johnson hypothesized that reactivated HSV, which is often latent in trigeminal ganglia, may spread along the trigeminal nerve fibers in tentorial nerves that innervate the basal meninges of the anterior and middle fossae. It has also been postulated that HSV may enter the brain along an olfactory pathway and spread along the base of the brain, particularly during primary HSV infection. The precise factors responsible for maintaining the frontotemporal localization of the infection are uncertain, although the immune response likely plays an important role. Atypical features may occur in immunodeficient patients, while neonates and young children often have a diffuse encephalitis or multifocal lesions.

Unfortunately, the morbidity of HSE remains high despite antiviral therapy. Early initiation of therapy is important. Hopefully, the future will bring new and more effective therapies, including antiviral and neuroprotective agents, for the management of patients with HSE.

REFERENCES