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## VARICELLA-ZOSTER VIRUS ENCEPHALITIS LOCALIZED TO THE BILATERAL MEDIAL TEMPORAL LOBES

### OPEN

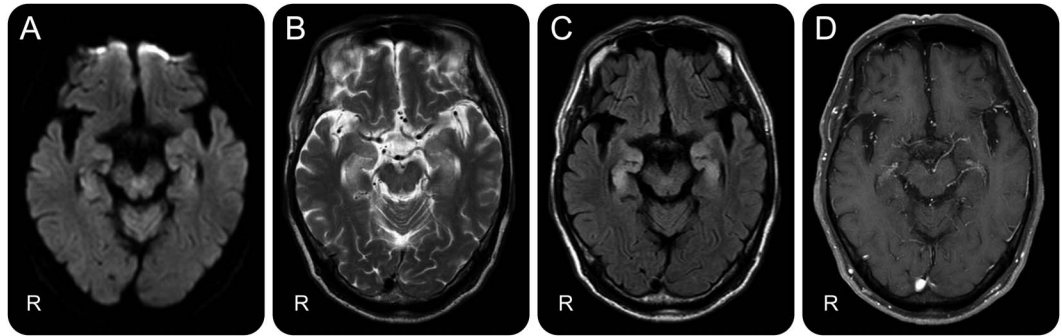
**Case report.** An immunocompetent 66-year-old man was admitted to a local hospital with fever and severe amnesia without a rash. T2-weighted MRI revealed symmetric hyperintense lesions in the bilateral medial temporal lobes. Magnetic resonance angiography showed no abnormalities. CSF analysis revealed 14 leukocytes/mm<sup>3</sup> and protein and glucose concentrations of 34 mg/dL and 79 mg/dL, respectively. He was administered IV acyclovir (1,500 mg/day) for suspected herpes simplex virus (HSV) encephalitis. He did not recover and was transferred to our university hospital on day 11. On admission, his temperature was 37°C and he had no rash. A neurologic examination showed no focal signs except severe anterograde amnesia. He remembered nothing of the past few days. His Mini-Mental State Examination score was 21/30. His delayed recall was most impaired. Laboratory results showed increased antinuclear antibody (ANA, 104.4 index) and anti-SSA/Ro antibody (108.4 index). All antibodies to known neuronal antigens were negative, including NMDA receptor, leucine-rich glioma-inactivated 1, and glutamic acid decarboxylase. Anti-varicella-zoster virus (VZV) IgG (40.9 enzyme immunoassay [EIA] units/mL) was elevated, but IgM (0.30 EIA units/mL) was not. CSF analysis revealed pleocytosis; normal glucose, protein, and myelin basic protein levels; and the absence of oligoclonal bands. The IgG index was 0.71. The antibody index to VZV (the ratio of CSF/serum-specific IgG antibodies to VZV compared with CSF/serum total IgG) was elevated at 2.8 (normal <2.0). PCR for CSF was positive for VZV (13,000 copies/mL) and negative for HSV, human herpesvirus 6, Epstein-Barr virus, and cytomegalovirus. Diffusion-weighted (figure, A), T2-weighted (figure, B), and fluid-attenuated inversion recovery (figure, C) images from a brain MRI showed lesions more clearly than the images from the previous hospital. The lesions were not enhanced on gadolinium-enhanced T1-weighted images (figure, D). Contrast-enhanced CT of the chest, abdomen, and pelvis was normal.

Based on PCR for VZV DNA in CSF and the elevated VZV antibody index reflecting intrathecal

production of anti-VZV antibodies,<sup>1,2</sup> the patient was diagnosed with limbic encephalitis (LE) caused by VZV without a rash. He was treated with IV acyclovir (1,500 mg/day for 19 days) and methylprednisolone pulse therapy followed by oral prednisolone (50 mg/day for 21 days and thereafter gradually decreased). A follow-up MRI showed improvements in abnormal signal intensity and atrophy in the same areas. PCR for VZV DNA became negative, and the VZV antibody index normalized. His amnesia slightly improved.

**Discussion.** Reactivation of VZV is associated with various CNS complications, particularly in immunocompromised patients.<sup>3</sup> Among these, VZV encephalitis is important, as its prognosis is poorer than VZV meningitis.<sup>2</sup> In contrast to more common lesions such as gray-white matter junction lesions,<sup>2</sup> localized focal symmetric medial temporal lesions are extremely rare. To our knowledge, only one such case has been reported, in an immunocompromised patient who had undergone prolonged immunosuppressive therapy.<sup>4</sup> He showed limbic lesions extending to the basal ganglia and died. In comparison, our patient had the following features: (1) the absence of major risk factors for VZV encephalitis, (2) localized bilateral medial temporal lobe lesions, and (3) survival with mild cognitive recovery. LE due to HSV infection or paraneoplastic neurologic syndromes could be excluded based on the results of various examinations. We believe the ANA and anti-SSA/Ro antibody elevation reflects an autoimmune mechanism for this condition; however, the patient did not show any findings suggesting a connective tissue disorder such as systemic lupus erythematosus or Sjögren syndrome. Although acute disseminated encephalomyelitis associated with VZV infection is common, it is unlikely because the lesions are symmetric and confined to the bilateral medial temporal lobes. With the exception of old age, the patient had no risk factors for VZV encephalitis.

Three mechanisms have been proposed for the pathophysiology of VZV encephalitis: demyelinating disease, vasculopathy, and acute infectious encephalitis of undetermined pathophysiology.<sup>5</sup> However, the most likely pathophysiology in this case is an autoimmune mechanism, based on the symmetric lesions and changes in MRI signal intensity and anatomic structure with time. HSV occurs primarily in the limbic system.



The diffusion-weighted image (A), T2-weighted image (B), and fluid-attenuated inversion recovery image (C) revealed areas of hyperintensity with mild edema in the bilateral medial area of the temporal lobes. The gadolinium-enhanced T1-weighted image (D) showed no apparent enhancement.

HSV infection can be a trigger of autoimmune-mediated anti-NMDA receptor encephalitis.<sup>6</sup> Whether this mechanism is specific to HSV is unclear. VZV reactivation might also cause autoimmune encephalitis through an unidentified antibody because VZV is highly neurotropic like HSV.

Although the administration of acyclovir is recommended,<sup>1</sup> combined acyclovir/steroid treatment might be effective, as this treatment would prevent deterioration in immunocompetent patients with an autoimmune mechanism.<sup>7</sup>

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