Cerebral varicella-zoster vasculopathy sine herpete

Atypical Ramsay-Hunt syndrome in an immunocompetent patient

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Vasculitides constitute a heterogeneous group of diseases characterized by inflammation and necrosis of the blood vessel wall. Varicella-zoster virus (VZV) can be reactivated, causing neurologic complications including CNS vasculitis. The incidence of VZV vasculopathy in adults is unknown. It is more common in immunocompromised individuals.¹ The clinical presentation of this condition includes ischemic and hemorrhagic strokes, TIAs, aneurysms, carotid dissections, arterial ectasias, and subarachnoid hemorrhages. A history of recent zoster, varicella rash, and CSF pleocytosis is the classic presentation. However, 30% of cases present with no previous rash or without typical CSF pleocytosis.^{1,2}

Ramsay-Hunt syndrome (RHS) is traditionally defined as zoster oticus and lower motor neuron facial palsy. RHS sine herpete includes a localized radicular pain with virologic evidence of VZV infection in the absence of rash.

We report the case of an immunocompetent patient with atypical RHS sine herpete associated with acute VZV CNS vasculopathy.

Case report

A 54-year-old immunocompetent man without medical history of varicella or zoster was admitted with left hearing loss, tinnitus, and vertigo. He had minor peripheral left facial paresis and horizontal nystagmus evoked by lateral gaze bilaterally. No lesions were seen in the ear channel or on the palate. No fever, headache, or encephalopathy were present. MRI showed multiple lesions in different vascular territories consistent with acute stroke (figure, A–C). Angio-RM demonstrated narrowing of anterior cerebral arteries and left posterior cerebral artery. HIV serology was negative, and CSF had proteins of 60 mg/dL, without pleocytosis. CNS vasculitis was suspected, and the patient was started on IV methylprednisolone 1 g/d for 5 days. Brain MRI at day 3 of admission showed new asymptomatic ischemic lesions, and digital subtraction brain angiography demonstrated progression of arterial narrowing (figure, D–F). IV cyclophosphamide was initiated. PCR tested in the initial CSF (DNA genomic Wizard purification kit with an in-house PCR nested protocol using the sequences of gene 29 by Read and Kurtz³) resulted positive for VZV. Antibodies against VZV were not tested in CSF.

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Figure Brain MRI at arrival and cerebral digital angiography 3 days after arrival

(A) Diffusion-weighted imaging (DWI) shows high-intensity signal lesions at the left vermis (arrow), (B) left pons and medium cerebellar peduncle (arrow), and (C) right striatum nuclei (arrow), compatible with small ischemic strokes. (D, E) Cerebral digital angiography shows segmental irregularities in the anterior cerebral arteries (arrows) and (F) irregularities of both posterior cerebral arteries with left predominance (arrows).

IV acyclovir 800 mg 3 times daily (TID) for 14 days was started with substantial clinical and imaging improvement. Two weeks after admission, the patient was asymptomatic.

Thirty days after admission, the patient presented transient right brachio-crural paresis, without new brain lesions. Repeat CSF had cell count of 1/mL and protein level of 86 mg/dL, with persistence of positive VZV PCR. A second course of IV acyclovir 800 mg TID for 14 days was completed, followed by oral acyclovir. The patient remains asymptomatic 14 months later.

DISCUSSION

We report a case of an immunocompetent 54-year-old man with atypical RHS associated with acute VZV CNS vasculopathy. This patient did not have rash or pleocytosis. This confirms that rash or CSF pleocytosis are not required for the diagnosis of VZV vasculopathy.¹

In zoster ophthalmicus, afferent fibers from trigeminal and other ganglia to both intracranial and extracranial blood vessels provide an anatomical pathway for the transaxonal spread of the virus. Infarctions in the left pons suggests a pathway for spreading of VZV from geniculate ganglion to brainstem and posterior circulation arteries. Few report the association between zoster oticus and brainstem strokes.^{4,5}

VZV vasculopathy is caused by viral infection of arteries.⁶ Patients are typically treated with IV acyclovir. In our patient, an immunomodulatory treatment for primary CNS angiitis, before diagnosis of VZV presence, was initiated, which may have worsened vascular involvement. Some patients with VZV vasculopathy continue to have neurologic symptoms after initial IV acyclovir treatment, and additional oral antiviral treatment for some months is recommended.⁷ The reported cases were in immunocompromised patients (HIV-positive, AIDS, or diabetes). In a single case report from the literature, the VZV PCR turned undetectable at 14–50 days after the admission.⁷ In our patient, it is possible that positive VZV

PCR persistence up to 30 days after admission despite treatment with acyclovir may have been related to the immunosuppressive treatment.

VZV CNS vasculopathy may present with atypical clinical and CSF characteristics. Patients with suspected CNS vasculopathy without pathologic confirmation should be tested for this treatable condition, regardless of their immune status.

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