Intracerebral Varicella Zoster Virus Vasculopathy in a Patient with Systemic Lupus Erythematosus and Imaging-Clinical Discordance

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Financial support: None declared
Conflict of interest: None declared

Patient: Female, 59-year-old
Final Diagnosis: Varicella zoster virus infection • vasculitis
Symptoms: Diplopia • headache
Medication: —
Clinical Procedure: —
Specialty: Infectious Diseases • General and Internal Medicine

Objective: Challenging differential diagnosis
Background: Varicella zoster virus (VZV) infection can increase the risk of cerebrovascular disease, involving small and large arteries, especially in immunosuppressed patients with ophthalmic division of the trigeminal nerve involvement. We present the case of a patient with intracerebral VZV vasculopathy without overt clinical manifestation but with abnormal imaging findings in the brain magnetic resonance (MR).

Case Report: A 59-year-old woman with systemic lupus erythematosus (SLE), without other traditional cardiovascular risk factors, presented to the hospital due to headache, vertical diplopia, decreased visual acuity of right eye, and disseminated varicella zoster virus (VZV) infection with predominant skin lesions distributed along the ophthalmic division of the right trigeminal nerve. Cerebrospinal fluid (CSF) testing revealed meningitis and positive polymerase chain reaction (PCR) for VZV, and a brain MRI scan showed a right occipital hemorrhagic lesion; thus, she was diagnosed with disseminated VZV infection with neurological involvement. She received intravenous acyclovir for 10 days. One month later, a physical examination was unremarkable and she was asymptomatic, but control brain MR angiography showed stenosis of the right internal carotid and the right middle cerebral artery, compatible with VZV vasculopathy. The PCR for VZV turned negative in CSF but the titers of anti-VZV IgG antibodies in CSF were high, and no increase of plasma autoimmune biomarkers were detected at any time in the course of the clinical evolution.

Conclusions: Discordance between imaging findings and clinical manifestations can appear in intracerebral VZV vasculopathy. A differential diagnosis is mandatory, especially if there is underlying immunosuppression.

Keywords: Vasculitis, Central Nervous System • Lupus Erythematosus, Systemic • Encephalitis, Varicella Zoster

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/936707
**Background**

Varicella zoster virus (VZV) is a neurotropic alpha-herpesvirus that can remain latent in the autonomic, dorsal root, and sensory ganglia, including the trigeminal ganglion, after primary infection. Reactivation of VZV via trigeminal or hematogenous pathway of the sympathetic nervous system can lead to virus spread to cerebral arteries [1,2]. The virus infects the arterial tissue and this can contribute to persistent inflammation, particularly if there is previous damage from pre-existing vascular risk factors, thus increasing the risk of cerebrovascular disease [3], especially stroke, with a nearly 35% higher rate than in populations without previous infection [4]. Cerebrovascular VZV involvement is mostly seen in immuno-compromised patients [1].

We present a case of a patient with systemic lupus erythematosus (SLE) that could be a previous risk factor of arterial tissue inflammation, who developed intracerebral vasculopathy secondary to disseminated VZV. Clinical management and a brief differential diagnosis approach are described.

**Case Report**

A 59-year-old woman, with SLE treated with hydroxychloroquine and methotrexate, without history of toxic habits or cardiovascular risk factors, was admitted to the hospital due to scattered vesicular skin lesions with predominance in skin innervated by ophthalmic division of the right trigeminal nerve, headache, vertical diplopia, and decreased of visual acuity of right eye. Cerebrospinal fluid (CSF) revealed meningitis and positive polymerase chain reaction (PCR) for VZV. A cerebral computed tomography (CT) scan at admission did not reveal lesions. Eleven days later, a brain MR showed a right occipital hemorrhagic lesion. Disseminated VZV infection with neurological involvement, as a complication of right-sided herpes zoster ophthalmicus, was diagnosed. HIV serology was negative. She received intravenous acyclovir for 10 days. One month later, she was asymptomatic, but control brain MR angiography to revise the previous hemorrhagic lesion showed stenosis of the right internal carotid artery with occlusion from the cavernous segment (Figure 1) and stenosis of the right middle cerebral artery with filiform flow (Figure 2). A differential diagnosis regarding intracerebral vasculopathy in this patient was performed. Since there were no clinical or laboratory parameters suggestive of SLE flare (anti-double-stranded antibodies, anti-DNA, were negative and plasma complement levels were normal) and anticardiolipin and anti-beta2-glycoprotein I antibodies were negative, SLE or antiphospholipid syndrome-related non-infectious vasculopathy were fairly ruled out. The absence of medical history of hypertension, dyslipidemia, or diabetes mellitus made any underlying atherothrombotic...
mechanism unlikely. Electrocardiogram tracing did not reveal ant atrial fibrillation that could cause a cardioembolic stroke. Therefore, antiplatelet or anticoagulant treatment would not confer a definite benefit.

A new lumbar puncture showed a CSF with paucity of cells and the PCR for VZV was negative. High titers of anti-VZV IgG intrathecal antibodies were detected. Therefore, since there were no impaired autoimmune biomarkers to suspect an SLE flare or other associated autoimmune condition, the radiology findings were compatible with VZV vasculopathy. The patient had already received acyclovir, and VZV was not identified from the CSF 1 month later. Despite the absence of inflammatory activity biomarkers, the patient received high-dose pulse intravenous steroids with 1 g of methylprednisolone daily for 5 days. The clinical evolution was uneventful.

Discussion

VZV vasculopathy can affect both small and large arteries and can be unifocal or multifocal [2]. The virus spreads through the afferent trigeminal fibers, to the cerebral arteries causing infection, inflammation, and intimal proliferation of the endothelial cells [5]. Several manifestations in the central nervous system, with involvement of intra and extracranial circulation, have been described, like subarachnoid hemorrhage, thrombosis, and aneurysms [6]. VZV vasculopathy is more common in immunosuppressed patients or with ophthalmic branch of the trigeminal nerve involvement and it is not necessarily preceded by zoster rash [1]. The diagnosis includes CSF analysis and neuroimaging. The detection of anti-VZV IgG intrathecal antibodies is the best test for diagnosis, with a sensitivity of nearly 98% [2,6]. Several radiologic features can be shown in the MRI, including vessel wall enhancement, diffuse irregularity of the wall, and stenotic with post-stenotic dilation [5,7].

Conclusions

Discordance between imaging findings and clinical manifestations can appear in intracerebral VZV vasculopathy. A differential diagnosis is mandatory, especially if an immunosuppression status is underlying.

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