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Letter to the Editor

Gadolinium enhancement in perforating arteries in a patient with varicella zoster virus vasculopathy: A case report

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Dear Editor,

A 35-year-old man was admitted to our hospital because of right hemiparesis. His initial National Institutes of Health Stroke Scale score was 8. He had a 1-week history of fever and headache that had occurred approximately 1 month prior to admission. Diffusion-weighted imaging on admission showed hyperintensities in the left putamen and corona radiata (Supplementary Fig. 1). There were no atherosclerotic changes or findings suggesting intracranial arterial dissection or carotid artery disease on magnetic resonance (MR) angiography. The patient was diagnosed with ischemic stroke and treated with intravenous alteplase and edaravone followed by intravenous argatroban and oral clopidogrel. MR images on day 4 showed gadolinium enhancement of the right lenticulostriate artery on three-dimensional T1-weighted fast spin-echo imaging (volumetric isotropic turbo spin-echo acquisition [VISTA]), which is a high-resolution MR vessel wall imaging modality, suggesting inflammation in the vessel wall of the perforating arteries (Fig. 1). Carotid ultrasonography, transthoracic and transesophageal echocardiography, and 7-day Holter electrocardiography showed no evidence of embolism. Serum antibodies for varicella zoster virus (VZV) by enzyme immunoassay were elevated (immunoglobulin M [IgM], 1.28; IgG, ≥128). The VZV IgG level in the cerebrospinal fluid (CSF) by enzyme immunoassay was also elevated at 5.70. The antibody index for VZV IgG (calculated by the CSF IgG, serum IgG, CSF albumin, and serum albumin levels) was elevated at 5.23 (reference, < 1.5), demonstrating increased VZV antibody in the CSF [1]. Accordingly, the patient was diagnosed with ischemic stroke secondary to VZV vasculopathy. He was treated with intravenous acyclovir and high-dose methylprednisolone. His symptoms fully resolved after rehabilitation (modified Rankin Scale score of 0), and follow-up MR imaging on day 179 showed no gadolinium enhancement of the right lenticulostriate artery on VISTA (Supplementary Fig. 2).

VZV is a herpes virus that may lead to a variety of neurological complications such as encephalitis, meningitis, retinal necrosis, or myelitis after its reactivation. In addition, VZV can spread transaxonally from branches of the trigeminal nerve to cerebral arteries and cause ischemic or hemorrhagic ischemic stroke secondary to inflammatory vasculopathy. Several cohort studies have shown an increased risk of stroke after herpes zoster infection [2–4]. The risk of stroke after herpes zoster is especially notable among patients aged ≤40 years [4,5].

The diagnostic criteria for VZV vasculopathy are not well-established or internationally recognized. The diagnosis of VZV vasculopathy is based on a recent medical history of herpes zoster infection, neurological symptoms, neuroimaging findings associated with ischemic or hemorrhagic stroke, angiographic studies showing vasculopathy, demonstration of VZV infection by VZV-polymerase chain reaction or the presence of specific IgM or IgG antibodies in the CSF, or the presence of VZV antigen from biopsy of the brain tissue or cerebral arteries [6,7]. Diagnostic criteria using a combination of these clinical features have recently been proposed [6], and using these criteria, the definitive diagnosis in our patient was VZV vasculopathy. In a study of 30 patients with virologically confirmed VZV vasculopathy [7], 11 (37%) patients had no rash. Suspicion of VZV vasculopathy relies on the presence of a typical herpes zoster rash; the diagnosis of VZV vasculopathy in patients without a rash, as in our patient, can be challenging [6].

Abnormalities in brain imaging are common in patients with VZV vasculopathy. A study of 30 patients with virologically confirmed VZV vasculopathy [7] revealed abnormalities in 29 (97%) patients, typically lesions at gray–white matter junctions, while the remaining patient demonstrated exclusively posterior ciliary arterial involvement. Of 23 patients evaluated by conventional angiography or MR angiography, 15 (50%) patients showed abnormalities in large and small vessels, 11 (37%) showed abnormalities in small arteries, and 4 (13%) showed abnormalities in large vessels [7]. High-resolution MR imaging was recently suggested as being useful for evaluating various patterns of blood vessel wall abnormalities in VZV vasculopathy, such as stenosis, vessel wall thickening, and abnormal enhancement [8–10]. Abnormalities in the cerebral arteries in VZV vasculopathy evaluated using high-resolution MR imaging were seen predominantly in the terminal internal carotid artery and the M1 segment of the middle cerebral arteries [8–10]. Moreover, the abnormalities improved following treatment. To our knowledge, abnormal enhancement of the perforating

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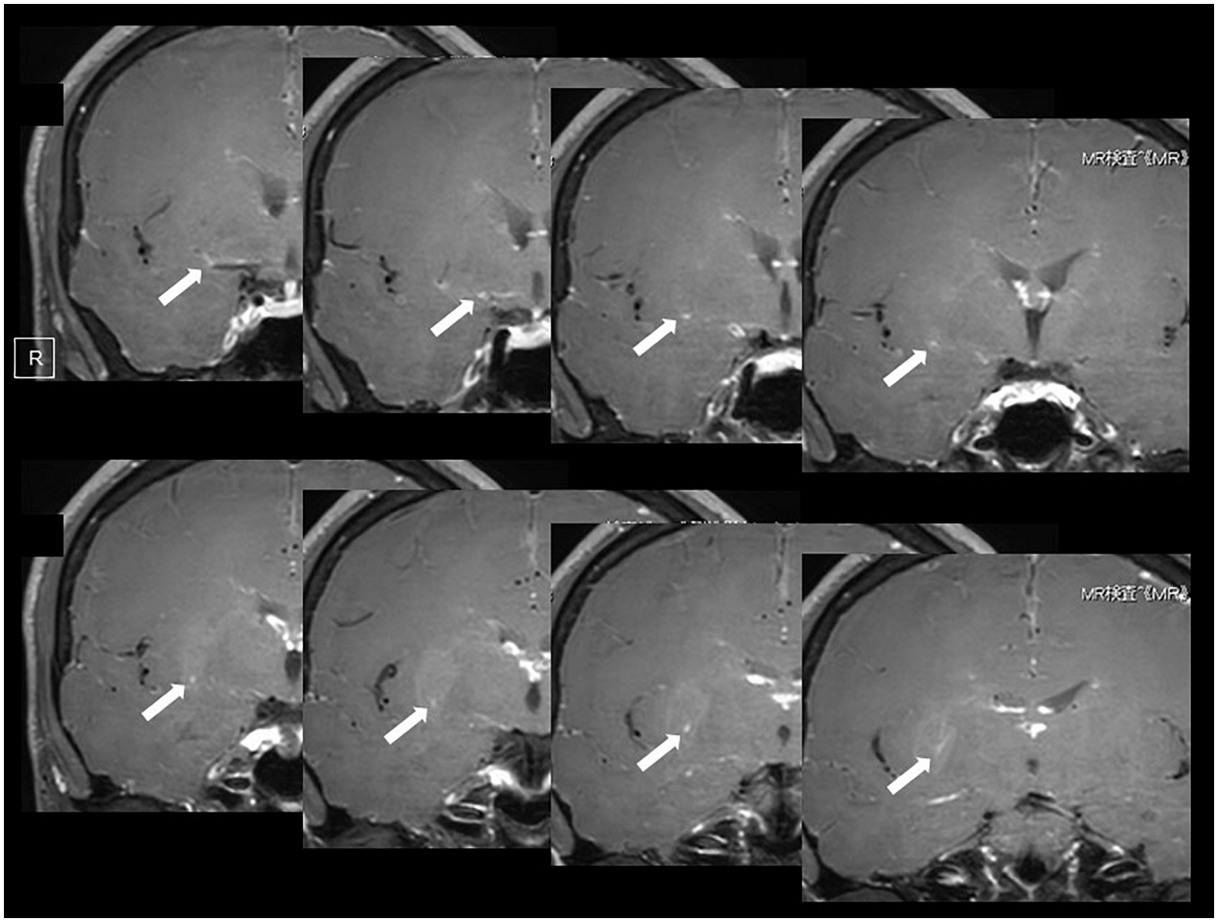

Fig. 1. Coronal sections of three-dimensional T1-weighted fast spin-echo (volumetric isotropic turbo spin-echo acquisition [VISTA]) magnetic resonance images on day 4. Gadolinium enhancement is seen along the right lenticulostriate artery (arrow). VISTA was performed with the following parameters: repetition time/echo time, 400/5 ms; turbo spin-echo factor, 20 echoes; field of view, 200 mm; acquired resolution, 0.89 × 0.90 × 0.90 mm; and reconstructed resolution, 0.45 × 0.45 × 0.45 mm. A variable flip angle refocusing scheme was used with a minimum flip angle of 90°. Spectral pre-saturation with inversion recovery was used for fat suppression.

arteries evaluated using high-resolution MR imaging, as in our patient, has not been reported in patients with ischemic stroke, including VZV vasculopathy. Our case suggests that inflammation in cerebral arterial walls caused by VZV infection can be detected using high-resolution MR vessel wall imaging in both the large vessels and the perforating arteries.

Whether the gadolinium enhancement of the perforating arteries in our case was caused by inflammation of the vessel wall is controversial. The distinctive features in this patient were that the enhancement of the right lenticulostriate artery arose from just the branching point at the right middle cerebral artery (upper left in Fig. 1) and that the enhancement was relatively uniform but tapered in the distal portion (lower right in Fig. 1). We assume that the gadolinium enhancement was caused by inflammation of the vessel wall because enhancement caused by leakage of contrast due to blood–brain barrier loss seems more difficult to explain.

If we had not performed VISTA with gadolinium enhancement, our patient might have been diagnosed with embolic stroke of undetermined source (ESUS) according to the recently proposed criteria [11]. The diagnostic criteria for ESUS do not include MR vessel wall imaging. Our case suggests that high-resolution MR vessel wall imaging in the large vessels and perforating arteries has the potential to differentiate patients with ischemic stroke associated with inflammatory disease from patients with ESUS.

In conclusion, we have presented a case of ischemic stroke secondary to VZV vasculopathy with abnormal contrast enhancement in the perforating arteries. Our case suggests that contrast enhancement of perforating arteries on high-resolution MR imaging may assist in making a prompt diagnosis of VZV vasculopathy and initiate virus-specific treatment, especially among atypical patients without a rash.

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Declaration of Competing Interest

None.

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