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CASE STUDY

The effectiveness of MRA in recovery phase for pediatric cerebral infarction caused by post-varicella angiopathy

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Abstract: Post-varicella angiopathy (PVA) is the leading cause of pediatric arterial ischemic cerebral infarction. However, PVA is considered to be underdiagnosed because of the lack of both sensitive diagnostic procedures and criteria. We, herein, report a case of PVA-associated arterial ischemic stroke diagnosed by MRA. A previously healthy 5-year-old Japanese boy was admitted to our hospital with right facial nerve palsy and right hemiparesis, a transient symptom of ischemic stroke, one month after recovery from chickenpox. The neurological symptoms recovered completely by conservative therapy. In addition to clinical history, cerebral artery stenosis detected by magnetic resonance angiography (MRA) in the recovery phase enabled us to diagnose him with PVA-induced stroke despite no detection of varicella-zoster virus DNA in the cerebrospinal fluid. Thus, MRA findings in the convalescent period are useful in the clinical diagnosis of pediatric PVA-induced stroke.

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Key words: cerebral infarction; childhood; post-varicella angiopathy.

Introduction

Post-varicella angiopathy (PVA) is the leading cause of pediatric arterial ischemic cerebral infarction, the manifestation of which can cause irreversible neurological deficits.[1-10)] Several criteria exist for the diagnosis of PVA, including a clinical history of varicella zoster infection in the last one year, subsequent neurological symptoms of hemiparesis, infarction, viral study, and radiological findings.[1-3)] The detection of varicella zoster virus (VZV)-DNA in cerebrospinal fluid (CSF) by polymerase chain reaction (PCR) and increased VZV-IgG index is widely used for the diagnosis of PVA.[1-8)] However, PVA is considered to be underdiagnosed because of the lack of both sensitive diagnostic procedures and criteria.[1-3)] We, herein, report a case of arterial ischemic stroke caused by PVA that was diagnosed by both magnetic resonance angiography (MRA) findings and clinical history, despite no detection of VZV-DNA in cerebrospinal fluid.

Case presentation

A previously healthy 5-year-old Japanese boy visited a hospital with the chief complaint of skin rash. He was diagnosed with chicken pox and received oral acyclovir administration for five days. Although the patient recovered without complications, he visited our hospital after one

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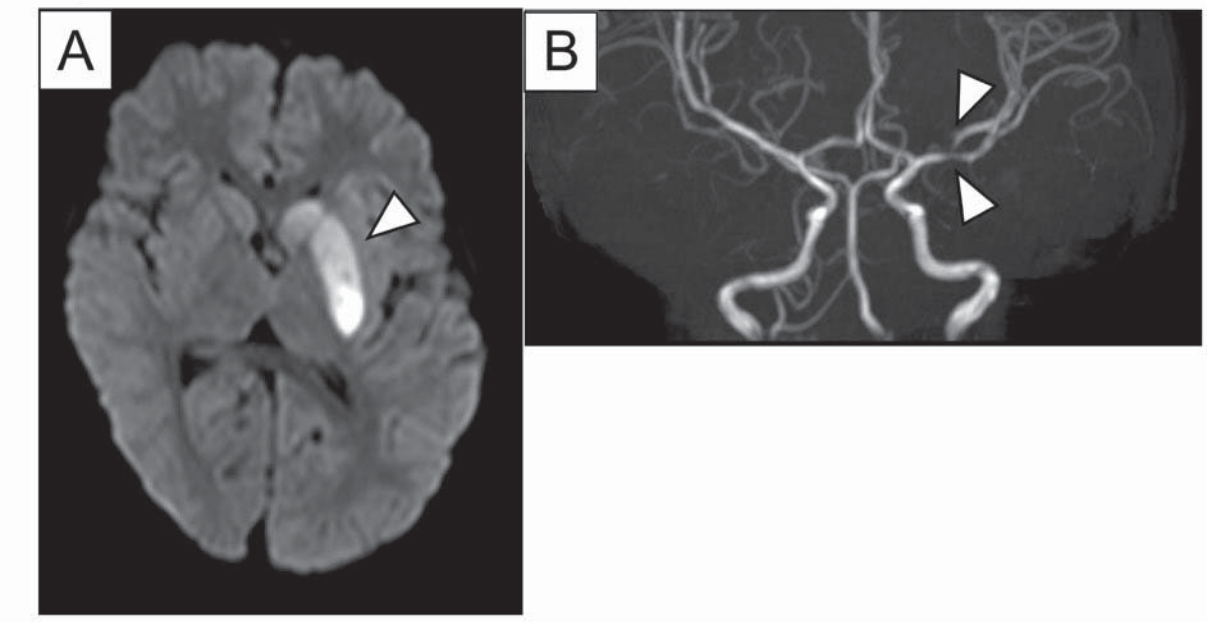

Figure 1 Neuroimaging studies of the patient
A: Magnetic resonance imaging of diffusion-weighted image (DWI) on day 2 shows high signal intensity on the left side of the lens nucleus and caudate nucleus (arrowhead).
B: Magnetic resonance angiography performed on day 54 shows stenosis of the middle cerebral artery (arrowhead).

month, presenting with the loss of his right grip. Physical examination revealed right hemiparesis, right facial nerve palsy, and left conjugate deviation of the eyes. T2-weighted and diffusion-weighted magnetic resonance imaging (MRI) of the head demonstrated high signal intensity on the left side of the lens nucleus and caudate nucleus (Figure 1A). We diagnosed him with cerebral infarction and started treatment with edaravone (1 mg/kg/day) for neuroprotection, heparin (480 U/kg/day) for anticoagulation, and aspirin (5 mg/kg/day) for antiplatelet therapy. Blood examination indicated that both VZV-IgG (enzyme immunoassay [EIA]) and VZV-IgM (EIA) were elevated (VZV-IgG, 22 [normal range, <2.0]; VZV-IgM, 3.1 [normal range, <0.80]). Blood examination revealed no anti-cardiolipin, β2GPI antibodies, lupus anticoagulant, or clotting disorder. Moreover, the levels of metabolic parameters were normal at diagnosis, and the patient did not have any heart disease. Examination of CSF at diagnosis showed mononuclear pleocytosis; the total cell number and protein levels were 22 cells/μL and 18 mg/dL, respectively, with no detection of VZV-DNA by PCR. CSF was negative for viral isolates. The antibody index of VZV-IgG in the CSF was 1.2 and 1.0 on days 2 and 21, respectively (normal range, <2.0).[1)]

As we suspected the cause of cerebral infarction to be PVA based on clinical history, we added intravenous administration of 30 mg/kg/day of acyclovir and 1 mg/kg/day of prednisolone on day 3 to the ongoing treatment, although the MRA performed on day 2 detected no stenosis. We replaced prednisolone with dexamethasone (0.17 mg/kg/day) on day 4 because the neurological symptoms persisted. Although the patient repeatedly presented with right facial nerve palsy and dysarthria on days 5, 9, and 10, neurological deficits improved gradually, and the administration of dexamethasone and acyclovir were terminated on days 8 and 17, respectively. Subsequent MRA of the head,

performed on day 54, indicated stenosis of the left middle cerebral artery (Figure 1B). We confirmed the diagnosis of cerebral infarction induced by PVA based on the manifestation of both cerebral artery stenosis and his clinical history of varicella zoster infection. He has been well since discharge, with no neurological deficits and five months of aspirin administration.

Discussion

Herein, we report a case of PVA that was successfully treated with acyclovir and steroids within a few days from the onset of neurological symptoms, with no sequelae.

The criteria of PVA has a limitation in the capacity of detection of both VZV-DNA by PCR and vascular change by MRA, which needs to be improved. First, the diagnostic range of detection of VZV-DNA in CSF has been reported to be low especially in the pediatric population, and CSF was found to be positive for VZV-DNA in about 30-50% of the cases.[1, 2, 4-6] In VZV infection, the VZV-IgG production by VZV reactivation in CSF is known to be late.[1, 2, 7] We did not find VZV-DNA or increased IgG index, although CSF examination was performed on day 2 and repeated on day 21.

Further, diagnostic neuroimaging is not sensitive enough for the evaluation of PVA. MRA can detect stenosis in only 60–80% of patients with PVA, because MRA can only detect stenosis of the major arteries.[1-4] Previous reports have mentioned that detection of vascular change in the acute phase of PVA could be missed.[2-4, 7] We repeatedly performed MRA evaluations on days 2, 8, 54, and 185; intracranial arterial stenosis was detected only after two months from onset, suggesting that the vascular change was detectable transiently. Helmuth et al. proposed that individuals with arterial ischemic stroke with varicella infection less than 12 months before without detection of VZV-DNA in CSF were regarded as possible cases of post-varicella arterial ischemic stroke.[4] The present case is considered to be involved in the provisional category. In possible cases, the detection ratio of stenosis by MRA was only 50% even in the recovery phase—lower than those in the confirmed cases with detectable VZV-DNA.[4]

There is still uncertainty about the factors affecting the interval duration from varicella infection to stroke, detectable timing of vascular change by MRA and permanent complications. Further prospective studies to resolve these questions are needed.

In conclusion, we suggest that MRA findings in the convalescent period could be useful for the clinical diagnosis of PVA-induced stroke. It is clinically pertinent to start treatment for pediatric arterial ischemic stroke after varicella zoster infection. The determination of the optimal timing for CSF assessment by more sensitive assay and MRA evaluation is warranted.

Conflict of interest

The authors have no conflicts of interest directly relevant to the content of this article.

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Author contributions

T.I., K.K., E.I. wrote the manuscript. T.I., T.Y. and I.H. evaluated the patients and collected and interpreted the data. All authors read and approved the final manuscript.

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