

Case report

Unilateral occlusion of the middle cerebral artery after varicella-zoster virus infection

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Abstract

We report a 4-year-old child who developed hemiplegia 6 months after varicella-zoster virus (VZV) infection. Cerebral angiography showed complete occlusion of the right middle cerebral artery with basal moyamoya vessels. Elevation of anti-VZV antibody in the cerebrospinal fluid indicated central nervous system involvement. The association between VZV cerebral angitis and unilateral occlusion of right middle cerebral artery is discussed. © 2002 Elsevier Science B.V. All rights reserved.

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1. Introduction

Although stroke in children is uncommon, it sometimes occurs and in these cases often causes severe neurological sequelae. A variety of etiologies and risk factors have been reported [1].

Here, we report a 4-year-old child who developed unilateral occlusion of the middle cerebral artery (MCA) 6 months after varicella-zoster virus (VZV) infection. The pathogenetic mechanism between VZV infection and vascular pathology is discussed.

2. Case report

A 4-year-old boy without a remarkable past history developed varicella with slight fever and vesicular exanthema mainly on the face and head. He immediately received acyclovir therapy for 3 days. Three months later, he repeatedly showed weakness in the left leg. This persisted for 2 months. Six months after VZV infection, he suddenly showed left leg weakness, which immediately advanced to the left upper limb. Subsequently he suffered from hemiplegia with mild consciousness disturbance. Because of neurological deterioration, he was admitted to a local hospital. Computed tomography scans on the first day after onset demonstrated an edema in the right

temporo-parieto cortical area suggesting infarction. Routine laboratory investigation of his blood showed nothing remarkable. Cerebrospinal fluid (CSF) showed 17 mononuclear leukocytes and two polymorphonuclear leukocytes/mm³, a protein level of 45 mg/dl, and a glucose level of 68 mg/dl. During hospitalization, he received conventional transfusion therapy. His condition gradually improved within 1 week. For evaluating the etiology of the infarction, he was referred to our institution 2 weeks after onset. Neurological examination on admission revealed hyperactive deep tendon reflexes, and extensor planter response on left side of the body. Complete blood count and blood chemistry were normal. Erythrocyte sedimentation rate was 13 mm/h. Coagulation tests including bleeding time, prothrombin time, partial thromboplastin time, fibrinogen, protein C, protein S and anti-thrombin III were normal. The serum VZV IgG was 49.2 EIA units/ml (<0.8) and that of IgM was not detected. Autoantibodies, such as anti-nuclear and anti-cardiolipin, were negative. Lactate and pyruvate levels in the blood and CSF were normal. Electrocardiography and echocardiography showed no abnormalities. CSF showed eight mononuclear leukocytes and one polymorphonuclear leukocyte/mm³, a protein level of 10 mg/dl, and a glucose level of 55 mg/dl. The antibody index of VZV IgG in the CSF ((CSF anti-VZV IgG × serum total IgG)/(CSF total IgG × serum anti-VZV IgG)) was 12.5 (<2) [2,3]. A polymerase chain reaction (PCR) for VZV on CSF was negative. The IgGs of human herpes virus 6 and 7 were negative in the CSF. T1-

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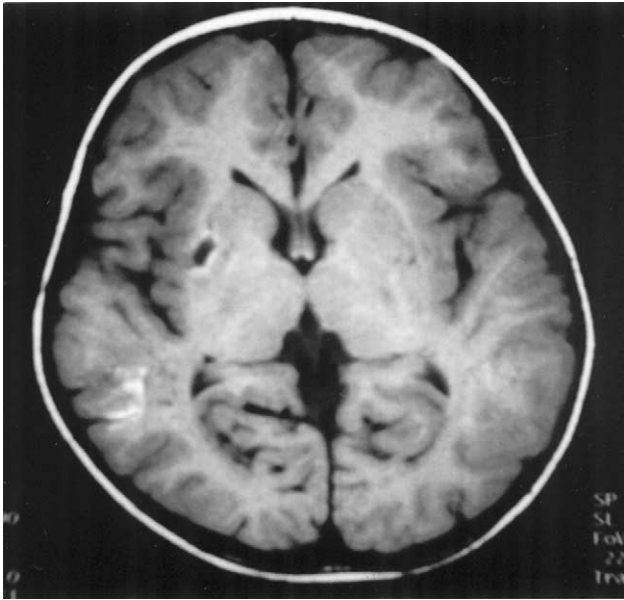


Fig. 1. Axial T1-weighted MRI (TR = 670 ms; TE = 14 ms) 3 weeks after onset shows low intensity in the right putamen with a high intensity marginal lesion caused by involvement of small penetrating arteries. In the right hemisphere, cortical atrophy and high signal intensity were also noted, consistent with laminar cortical necrosis in the territory of the right MCA.

weighted magnetic resonance imaging (MRI) 3 weeks after onset revealed a low-intensity lesion in the right putamen and a high-intensity lesion in the temporal cortical area as well as a focal cortical atrophy change in the area of the right MCA (Fig. 1). The high-intensity lesions in the putamen and the temporal cortical area were hyper-intensive on T2-weighted MRI, indicating cortical laminar necrosis [4]. Cerebral angiography 1 month after onset demonstrated

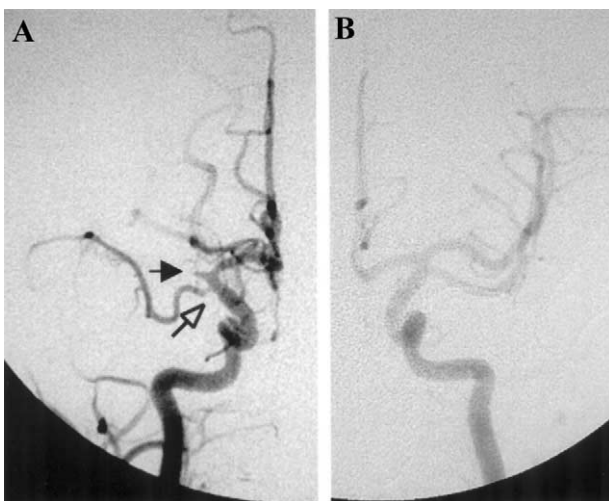


Fig. 2. (A,B) Right internal carotid angiogram 1 month after onset, anteroposterior view (A). There is mild stenosis at the C1 portion of the right ICA (open arrow) and complete occlusion of MCA (solid arrow). Left internal carotid angiogram, anteroposterior view (B). There are no abnormal findings.

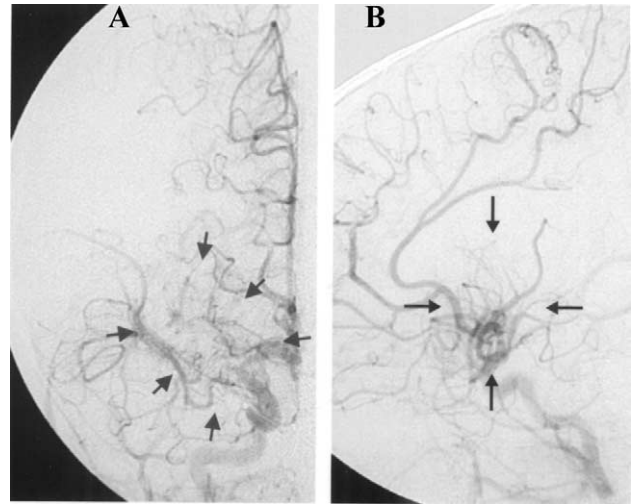


Fig. 3. (A,B) Right internal carotid angiogram, anteroposterior view (A) and lateral view (B). There are basal moyamoya vessels in the area indicated by arrows.

mild stenosis at the C1 segment of the right internal carotid artery and complete occlusion at the proximal portion of the right MCA (Fig. 2A) and no stenotic or occlusive lesions of the MCA on the opposite side (Fig. 2B). There was collateral circulation consistent with basal moyamoya vessels (Fig. 3). The right posterior cerebral artery (PCA) was well developed. Single photon emission computed tomography (SPECT) 5 weeks after onset showed regional reduction of blood flow in the right hemisphere. Because of the well-developed collateral circulation, neurosurgical treatment was not performed. On serial studies, the high-intensity areas gradually faded in the right temporal cortical area, while the putamen low-intensity lesion persisted. One year later, neurological deficits had disappeared completely. Results of MRI and magnetic resonance angiography 2 years after onset showed no further change in the right hemisphere, as well as an absence of vascular change on the opposite side. SPECT showed recovery of blood flow in the right hemisphere.

3. Discussion

Unilateral MCA occlusion or stenosis are rare conditions and have been reported in several diseases, such as fibromuscular dysplasia, Down's syndrome, von Recklinghausen's disease, systemic lupus erythematosus, radiation therapy and Apert's syndrome [5]. In some childhood cases with Moyamoya disease, long-term follow-up studies revealed unilateral MCA occlusion may represent the early stage of disease and develop the involvement of the opposite side later [6]. Since moyamoya disease is a chronic progressive disorder and many cases with moyamoya disease require neurosurgical therapy, differential diagnosis from self-limiting diseases appears to be important.

However, the etiology of many cases of unilateral MCA occlusion remains controversial and unclear [7,8].

In VZV infection, central nervous system (CNS) complications include encephalitis, meningitis, cerebellar ataxia, transverse myelitis and acute hemiplegia [9]. Acute hemiplegia associated with VZV infection is characterized by angiographical findings and latent intervals. Previous reports showed that the latent interval between varicella and acute hemiplegia is 10 days to 4 months [10]. Previous carotid angiographic studies demonstrated unilateral stenosis of predominantly MCA, but PCA or anterior carotid were also involved. Some cases showed multiple arterial stenoses [11,12]. The pathogenesis of VZV associated with cerebral angitis has been thought to be an inflammatory process and causes subsequent arterial wall destruction [2,12]. Histopathological study revealed that the virus causes the focal narrowing and thrombosis of the basilar arteries and subendothelial fibromuscular proliferation [12]. Since the trigeminal nerves are known to provide sensory innervation to the proximal middle artery [13], it is postulated that in the pathogenesis of VZV cerebral vasculitis trigeminovascular connections are the probable pathways of virus transmission from the trigeminal nerve to the circles of Willis.

Our patient repeatedly showed weakness in the left leg 3 months after VZV infection, and subsequently developed hemiparesis in the left limbs 2 months later. Both mild pleocytosis and elevation of the antibody index of VZV in the CSF suggested persistent inflammation due to VZV, possibly cerebral angitis. Previous studies also lacked evidence of VZV infection in the CNS. Compared with previous cases, the antibody index in our patient was markedly elevated. In addition, his angiography showed basal moyamoya vessels on the affected side and MRI showed focal atrophy in the right temporal lesion resulting from chronic ischemia. These observations lead to the conclusion that direct invasion of VZV may cause chronic progressive stenotic changes in cerebral arteries with chronic ischemic change in cerebral cortical lesions and the development of collateral circulation like moyamoya vessels, followed by complete occlusive change of MCA. So, these changes in the cerebral arteries may have been responsible for transient ischemia attack phenomenon consisting of repeated leg weakness and subsequent hemiparesis in our patient.

Despite the unilateral occlusion of MCA, our patient recovered completely 1 year later and SPECT showed recovery of blood flow in the right hemisphere. Previous

reports also showed a good outcome after VZV-associated hemiparesis [11,12]. No further progression of stenosis in association with development of collateral circulation appeared to be related to the recovery.

In the previously reported cases, the interval between VZV and delayed hemiparesis ranged from a few weeks to 4 months. Our case had a longer interval. Therefore, the possibility of VZV-angitis in CNS should be carefully evaluated in cerebrovascular disease in childhood.

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