Acute Haemiplegia after Chickenpox

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Abstract

Stroke in children, although uncommon, is increasingly recognised as an important clinical entity. The underlying cause of childhood stroke is largely different from stroke in adults. Varicella infection has been recognised as an important aetiopathological factor in childhood stroke. We report a Chinese girl who presented with acute haemiplegia with left middle cerebral artery infarct after a recent varicella infection.

Key words
Childhood stroke; Haemiplegia; Varicella infection

Case Report

A 3-year-old girl presented to the emergency department with one day history of fever and repeated vomiting. She had been well until the day of admission. Her mother reported that the child had a gradual onset of walking difficulty, that progressed and she became unable to walk on that day. The mother also noticed the child could not speak on the same day. There was no abdominal pain or diarrhoea. There was no history of trauma or head injury. On further enquiry, her medical history was unremarkable except her mother revealed the child has had a history of chickenpox infection six weeks ago. Her immunisation was up-to-date. She did not receive chickenpox immunisation. There was no family history of hypercoagulability or cardiac disease. On the physical examination, she was afebrile. Her blood pressure was 120/58 mmHg with pulse rate 80 beats per minute of regular rhythm. General examination found there were few healed skin lesions over the abdomen compatible with recent chickenpox infection. Cardiac examination revealed normal first and second heart sounds, and no murmur. Peripheral pulses were all normal. Her chest and abdominal examinations were normal. On neurological examination, she was found to have right haemiplegia. Muscle power on the right side was graded 1/5. The muscle tone of right upper and lower limbs was decreased and the jerks were brisk. Plantar reflex on the right side was extensor while it was flexor on the left side. Muscle power and reflexes on the left side were completely normal. There was also right facial palsy affecting the lower half of the face. Other cranial nerves examination was normal. She had expressive dysphasia. There were no cerebellar signs. Gait could not be examined because of the significant muscle weakness.

Preliminary blood test results of complete blood picture, liver function test and renal function test were normal. Erythrocyte sedimentation rate was 20 mm/hr. Serum varicella zoster virus antibody titre was raised to 160. An urgent computed tomography (CT) of brain showed a wedge-shaped left middle cerebral artery infarct (Figure 1). A magnetic resonance imaging (MRI) of brain and magnetic resonance angiography (MRA) subsequently showed infarct in the left middle cerebral artery territory and acute left internal carotid artery inflammation, most at skull base and left cavernous sinus portion with left middle cerebral artery occlusion (Figures 2-4). Blood was sent for the metabolic screen and prothrombotic disorders, including clotting profile, antithrombin III, protein C, protein S, anti-
Figure 1  CT Brain. Wedge shaped hypodensity involving grey and white matter was seen at left MCA territory.

Figure 2  MRI brain. T1 slightly hypointense and T2 hyperintense DW hyperintense changes without significant contrast enhancement was seen involving the left frontal lobe and parietal lobe.

Figure 3  Cranial MRA. The left internal carotid artery was narrowed starting from lower neck to its intracranial portions.

Figure 4  Cranial MRA. Left middle cerebral artery was completely occluded.
anomalies of the cerebrovascular system. In about a fifth of the children with ischaemic stroke, however, no cause can be found.

Neurological complications caused by varicella, such as encephalitis, cerebellar ataxia, aseptic meningitis, transverse myelitis are well known, the estimated risk is about 0.01% - 0.03%. The commonest one is cerebellar ataxia with an incidence of 1 in 4000 cases. In recent years, varicella infection has been recognised as a potential risk factor for arterial ischaemic stroke (AIS) in children. However studies are limited. Around 20 case series of children with varicella-associated ischaemic stroke have been published. The absolute risk of varicella-associated arterial ischaemic stroke was estimated at 1 in 15000 children. Among children between 2 and 10 years of age with AIS, up to a third of them have angiopathy occurring weeks to months after varicella infection. The mean interval from varicella infection to arterial ischaemic stroke was 2.6 months, with a range of 0.2 to 12 months. The underlying mechanism for varicella virus causing ischaemic stroke is not well understood. Varicella virus may cause vasculopathy from damage to the vessel wall media by direct viral invasion. The viral spread may occur via intraneuronal migration of nuclear antibody (ANA), anti-neutrophil cytoplasmic antibody (ANCA), anti-cardiolipin antibody, C3, C4. All were normal. Electrocardiography showed sinus rhythm. Cardiac echocardiography showed normal heart anatomy.

In view of significant infarct, low molecular weight heparin, tinzaparin 200 units/kg/day, was given, but it was stopped after three doses since she developed gross haematuria. Aspirin 4 mg/kg/day was also started. She developed one episode of seizure with eye blinking, arching of back and impaired consciousness for few seconds. She was loaded with intravenous phenytoin followed by maintenance. Repeated CT brain showed same infarct with no haemorrhagic transformation. Electroencephalography demonstrated asymmetrical background with left side slow wave, but no epileptiform discharge was captured. There was no more seizure. Anticonvulsant was stopped. MRI brain was repeated one week later which showed interval improvement of the inflammation of the intracranial portion of left internal carotid artery and revascularisation of the previous completely occluded left middle cerebral artery. Her neurological signs gradually improved. She started to have some antigravity movements of limbs and she could speak some double and combined words. She was discharged three weeks later with aspirin. When she was followed up 2 months later, she could speak with full sentences and walk with minimal aid. MRI brain and MRA was repeated again. It showed that the left internal and middle cerebral artery continued to increase in caliber although they were still slightly smaller than the counterparts on the right side (Figure 5). She continued to have aspirin as prophylaxis to prevent recurrence of stroke.

**Discussion**

Stroke in childhood is uncommon but its recognition has been increased in recent years. Ischaemic stroke affects approximately 1.2 per 100,000 children per year. It can cause mortality and significant long term morbidity such as neurological deficit or epilepsy. The causes are diverse and are largely different from adults. The commonest cause is congenital or acquired heart disease. Any cardiac lesion can sometimes lead to stroke but cyanotic heart disease with polycythemia probably has the highest risk. Arteriopathy has also been increasingly recognised as an important cause of paediatric ischaemic stroke. Other common causes of childhood stroke include trauma, migraine, infection, haematologic disorders and coagulopathies, and structural

![Cranial MRA](image.png)

Figure 5 Cranial MRA. Previously noted complete occlusion of the left middle cerebral artery had resolved. The artery could now be seen but was still relatively narrow.
the virus from the trigeminal nerve ganglion to the ophthalmic division of the trigeminal nerve. This theory is supported by the arteries innervated by this nerve correspond to the typical distribution of vascular involvement in varicella-associated ischaemic stroke.\(^9\,10\) The viral spread may also occur via the bloodstream or cerebrospinal fluid. Since viral antigen has not been demonstrated in all cases, a possible immune-mediated vascular reaction has also been advocated.\(^10\) The role of thrombosis in stroke after chickenpox has also received attention. There is evidence to suggest transient deficiency of both protein S and protein C.\(^8,11,12\) The virus mediated endothelial injury also promotes local thrombosis and vascular occlusion.\(^13\)

There are distinctive clinical and radiographic features of varicella-associated AIS. Clinical presentation with haemiparesis is more likely in varicella-related strokes while seizures are less likely to occur.\(^9\) Patients may also present with transient ischaemic attacks with protracted neurological symptoms and signs. Concerning the radiographic features, children with preceding chickenpox are more likely to have large vessel involvement, resulting in ischaemia of the deep structures of the affected hemisphere.\(^5\) But in contrast to the old notion, recent studies show that involvement of both large and small arteries in the same patient is the commonest pattern.\(^14\) Only half of the EEGs reveal focal findings.\(^5\) We believe that our case is a varicella-associated AIS because of the temporal relationship of the chickenpox infection and the onset of stroke. Also the MRI finding is typical in varicella associated vasculitis.

Although there are no randomised controlled trials, there are three published paediatric stroke guidelines in the past five years, which combined the best available evidence with expert consensus to guide the therapy in different subtypes of paediatric stroke. In all types of paediatric stroke, neuroprotective measures are important and these include control of fever and seizure, maintain adequate blood pressure and blood glucose level. In varicella-associated AIS, the role of antiviral therapy, steroid, and immunosuppressants are all unclear. Antiviral agents and steroid may not be indicated because of various reasons. First, the temporal relationship between the varicella infection and the onset of neurological symptoms is variable. Second, there is a risk of reactivation of the virus causing resurgent infection by immunosuppressant and steroid. In addition, the observed survival rate in varicella-associated AIS is excellent, most patients recovered nearly completely regardless of therapy.\(^15\)

Thrombolytic agents like tissue plasminogen activator (tPA) are believed to be effective but the safety profile is uncertain in children because of lack of relevant clinical trials. They are currently not recommended.\(^16\) The International Pediatric Stroke Study has reported tPA treatment in 15 children. In these 15 children, 2 children died from progressive infarction. In the remaining 13 survivors, neurological deficits were found in 12 of them. The main treatment for paediatric AIS is antithrombotic therapy includes antiplatelet and anticoagulant treatment. The use of anticoagulant in the initial phase may be useful in preventing local extension of the thrombus and embolisation. It is increasingly used in childhood stroke with reasonable safety, but controlled trials are required to establish their proper dosage and efficacy. Given the persistence of vascular abnormalities in some cases, long term therapy with aspirin is suggested for all children with varicella-associated AIS for secondary prevention.\(^6\) A commonly used dose is 3 to 5 mg/kg/day, it is recommended for at least 3 to 5 years. In order to reduce the risk of Reye's syndrome, it is recommended to have annual influenza vaccine for those taking aspirin. Warfarin or low molecular weight heparin is more effective but potentially less safe, they should be reserved for children with recurrent stroke while on aspirin. Treatments to aid rehabilitation, such as intrathecal baclofen and inhibitory repetitive transcranial magnetic stimulation are also studied in clinical trials.\(^17\)

In term of prognosis, between 50% and 80% of surviving children have neurological sequelae,\(^7\) include haemiparesis, neuropsychological deficits, poor attention, and behavioural problems. Most of the recovery takes place in the first 3 months following the stroke.\(^17\) The neurological deficits and their functional consequences may evolve with time due to ongoing growth and development in children. In varicella-related stroke, neurologic outcome is usually good and does not seem to relate to the therapeutic approach. It is believed that the risk of recurrent stroke after varicella is low and the vascular lesions usually improve with time.

**Conclusion**

Chickenpox is a common infection and it is believed to be a benign condition in children. However, the association between varicella and acute ischaemic stroke in childhood appears to be significant. Both cerebrovascular disease and thrombotic abnormalities are believed to be implicated. There are studies concerning the role of immunisation to lower the risk of varicella-related stroke, but the impact
would likely be modest and a recommendation cannot be made at this moment. We report this case aiming to alert paediatricians of this serious complication. We should always pay attention to any neurological symptoms and signs in children with a preceding history of chickenpox. There are ongoing clinical trials and study groups for childhood stroke and more experience is required to decide the best therapeutic approach.

References