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Capsular Warning Syndrome Leading to Acute Ischemic Stroke in a Pediatric Patient Secondary to Varicella Zoster Virus

Min Ye Shen, MD[1,2] and Arezou Heshmati, MD[1,2]

Abstract

We report the case of a 3-year-old boy who presented with recurrent stereotyped transient episodes of left sided weakness consistent with capsular warning syndrome (CWS) which eventually progressed to acute ischemic stroke (AIS). He received thrombolytic therapy with tissue plasminogen activator. Workup was notable for positive CSF varicella (VZV) PCR, and positive CSF and serum VZV IgG and negative IgM. On further history, he was unvaccinated and had a rash consistent with VZV 5 months prior to presentation. This case highlights the importance of recognizing CWS given the increased risk of progression to AIS. In addition, it emphasizes the importance of considering VZV vasculopathy in pediatric AIS and inquiring about infectious history and immunization status despite high rates of vaccination in the United States.

Keywords

pediatric stroke, acute ischemic stroke, capsular warning syndrome, transient ischemic attack, post-infectious, varicella zoster virus

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Introduction

Capsular warning syndrome (CWS) is a rare type of transient ischemic attack (TIA) characterized by recurrent motor or sensory symptoms and is associated with a high risk of developing a completed stroke. It is rare, and occurs in 1.5–4.5% of patients presenting with TIA.[1,2] In the pediatric population, acute ischemic stroke (AIS) is rare, with an incidence of 1 to 2 cases per 100,000 in developed countries.[3] Risk factors for pediatric AIS include infection, arteriopathies, sickle cell disease, cardiac disease, thrombophilia, and systemic inflammatory disorders. We report the case of a 3-year-old boy with stereotyped episodes consistent with CWS, leading to AIS, in the setting of varicella zoster virus (VZV).

Case

A 3-year-old healthy boy presented with 3 episodes of left sided weakness and slurred speech with spontaneous resolution. The first episode occurred 4 hours prior to presentation to the emergency room when he had acute onset left sided weakness and trouble speaking, which resolved spontaneously after 15 minutes. He then had 2 more events of the same semiology one hour later at home and in the ambulance, both with spontaneous resolution. His initial neurological exam on arrival was normal. Head CT and CT angiography of the head and neck were normal. However, his symptoms recurred after the CT and did not resolve. Examination showed left facial droop, left hemiparesis, and dysarthria. He did not have gaze deviation, neglect, or sensory changes, and his comprehension was intact. Pediatric NIHSS was 8. His blood pressure remained stable without significant changes. Other vital signs were normal for age.

Initial laboratory testing, including electrolytes and glucose, was unremarkable. Given concern for stroke, he received a brain MRI with and without contrast which showed diffusion restriction in the right putamen and caudate without FLAIR changes, corresponding to acute stroke. No enhancement was seen on the MRI. He received tissue plasminogen activator (tPA) 2.5 hours after stroke

[1]Department of Neurology, Columbia University Irving Medical Center, New York, NY, USA
[2]New York-Presbyterian Hospital, New York, NY, USA

Corresponding Author:
Min Ye Shen, MD, Department of Neurology, Columbia University Irving Medical Center, New York, NY, USA
Email: ms3493@cumc.columbia.edu

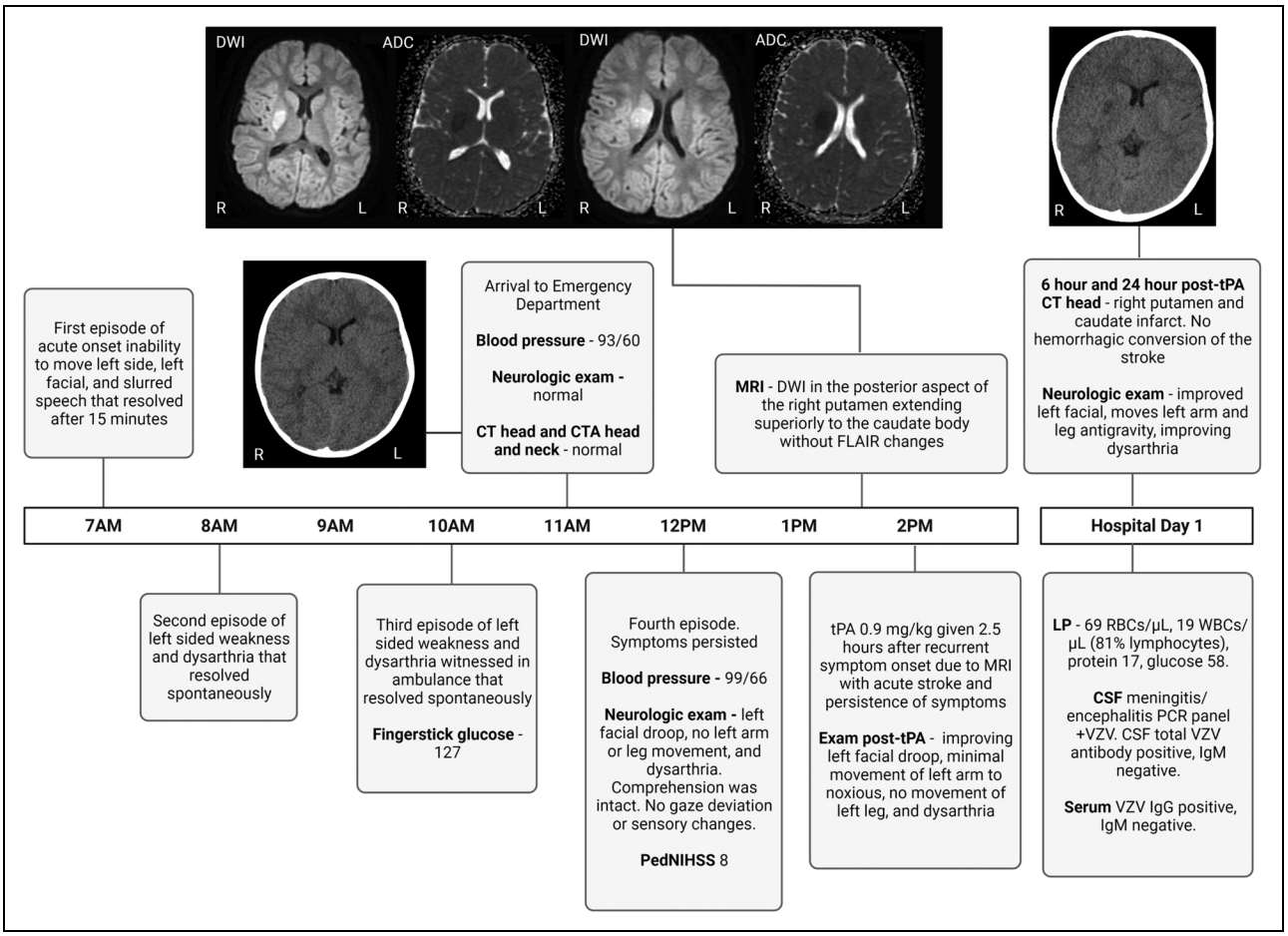

Figure 1. Timeline of patient's clinical course.

onset. Workup for etiology of stroke was notable for a lumbar puncture with elevated WBC with a lymphocytic predominance. CSF meningitis/encephalitis PCR panel was positive for VZV. CSF VZV total antibodies and serum VZV IgG were positive. CSF and serum VZV IgM were negative. CSF culture was negative. Inflammatory, autoimmune, metabolic, hypercoagulable workup, and echocardiogram were unremarkable. Figure 1 depicts the patient's course.

On further history, he was unvaccinated against VZV and had a rash consistent with VZV five months prior. He was treated with IV acyclovir for a 14 day course followed by oral valacyclovir for 7 days. He was started on aspirin 40.5mg daily for secondary stroke prevention, with plan to continue for one year after the stroke pending repeat imaging. By discharge, he had mild left facial asymmetry, clumsiness with fine motor movements with his left hand, and could run without gait abnormalities. He had complete resolution of symptoms by 2 month follow-up. 3 month follow-up MRI post antiviral treatment showed encephalomalacia at the site of his prior stroke. 3 month follow-up MRA was normal.

Discussion

CWS is rare with an incidence of 1.5–4.5% of patients with TIA.[1,2] It is defined by having at least three stereotyped episodes of a motor or sensorimotor lacunar syndrome, with complete resolution between episodes, within the span of 24–48 hours.[1,2] These episodes involve two or more body parts, and do not involve cortical symptoms. CWS is associated with a high risk of developing a completed stroke. Common stroke locations include the internal capsule, thalamus, and pons. The mechanism is unclear, but studies postulate an association with atherosclerosis or ischemia of small penetrating vessels, or with intermittent hemodynamic changes in intracranial vessels.[2]

Infection is a known cause of AIS. Herpesviruses, such as VZV, are neurotropic viruses that have been associated with cerebral vasculopathies, leading to TIAs, AIS, or hemorrhage in the setting of aneurysms. Pediatric AIS in the setting of VZV is a post-infectious phenomenon that affects unvaccinated children and occurs between 1 to 12 months, with a mean interval of 5 months after acute infection.[5,6] Post-varicella arteriopathy of childhood (PVA) causes stenosis of the internal carotid artery and the proximal segments of the anterior cerebral and middle cerebral artery, leading to infarcts in the basal ganglia and internal capsule.[4–6] The stenosis can progress in the first 6 months after AIS and is followed by spontaneous resolution.[6] Initial cerebral vascular imaging can be normal; however, patients are at risk of developing stenosis on follow-up imaging and recurrent AIS.

The proposed mechanism of VZV vasculopathy is the reactivation of VZV after it becomes dormant in the trigeminal ganglion and nerve. When the virus is reactivated, it migrates from the ganglia to the cerebral arteries. Autopsy of patients with VZV vasculopathy shows evidence of the virus within the vessel wall, suggesting direct invasion of the virus in the cerebral vessel walls.[6] Diagnosis of VZV vasculopathy is confirmed by the presence of CSF VZV IgG or DNA. As VZV vasculopathy results from the reactivation of VZV, treatment with IV acyclovir should begin as soon as VZV is suspected and is continued for a course of at least 2 weeks. The concurrent use of steroids with antivirals is controversial as steroids may worsen VZV reactivation and infection.[4] Aspirin can be used for secondary stroke prevention. However, sequelae of VZV have decreased since the introduction of the universal vaccination program in the United States.

Our unvaccinated patient presented with recurrent episodes consistent with CWS, leading to AIS. We theorize that the mechanism of CWS in our patient is intermittent stenosis and ischemia of small vessels, not visualized on imaging, from post-infectious VZV vasculopathy. CWS is rare in the pediatric population. This case emphasizes the importance of recognizing CWS in patients who present with stereotyped episodes of recurrent TIAs given the high risk of developing an infarct. In addition, this case highlights the value of considering VZV as a cause of AIS and initiating rapid treatment with antivirals. The optimal treatment of VZV vasculopathy remains unclear—in this case, our patient had rapid resolution of symptoms with antiviral treatment and remains on aspirin for secondary stroke prevention. While there are high rates of vaccination against VZV in the United States, this case demonstrates the need for inquiring about immunization status and recent history of VZV infection in pediatric AIS.

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Ethical Approval

The authors have received written consent from the patient's family to publish this case report.

ORCID iD

Min Ye Shen https://orcid.org/0000-0003-3584-402X

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