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## Successful Intravenous Thrombolysis for Acute Stroke in a Child

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We report an 8-year-old white girl with no previous medical history who developed sudden onset right hemiplegia, left gaze preference, and global aphasia. An acute left middle cerebral artery stroke syndrome was diagnosed. She was treated with intravenous recombinant tissue plasminogen activator, 2 hours after the onset of symptoms. A magnetic resonance image demonstrated an acute left middle cerebral artery stroke, and a magnetic resonance angiography showed a patent left middle cerebral artery. At discharge, she was able to speak normally and

walk without support. She was also able to raise the right arm up to the level of the shoulder and showed increased motility of the hand and fingers. No treatment-related complications happened. To the best of our knowledge, this is, so far, the youngest child successfully treated with intravenous recombinant tissue plasminogen activator for acute ischemic stroke.

**Keywords:** pediatric stroke; intravenous thrombolysis; recombinant tissue plasminogen activator

Intravenous recombinant tissue plasminogen activator is indicated for the therapy of acute ischemic stroke in adults. Childhood stroke is rare, and there are presently no approved treatments for acute ischemic stroke in children. The benefits and risks of intravenous thrombolytic therapy in the pediatric population are not well described. We here present the successful use of intravenous recombinant tissue plasminogen activator in a pediatric patient with an acute left middle cerebral artery stroke.

## Case Report

An 8-year-old, right-handed, white girl without significant past medical history was brought to the emergency department by fire rescue after collapsing at her school. According to school staff, she was "running around," playing with classmates at the playground when she suddenly fell to the floor, unable to speak or move the right side. No complaints had been reported earlier during the school day. No

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head or neck trauma preceded the episode, and no convulsive movements were seen at the onset of symptoms. She did not have any history of headaches, seizures, recent illnesses, rashes, or recent travel. She was not taking any medicines and had no known allergies.

Upon arrival to the hospital, 90 minutes after the onset of symptoms, her blood pressure was 93/57 mm Hg. On initial examination, she was awake, alert, anxious, and tearful, showing frustration for being unable to speak, but she was able to follow some commands. A left gaze preference with right homonymous hemianopsia, right hemianesthesia, and a dense right hemiplegia affecting face, arm and leg equally, were noticed. A Babinski reflex was present on the right side. The initial National Institutes of Health Stroke Scale was 22. Her initial electrocardiogram showed a sinus rhythm, and the results of the initial laboratory studies, including complete blood count, comprehensive metabolic profile, prothrombin time, partial thromboplastin time, and toxicology screen, were normal.

Computed tomography (CT) of the head showed no significant abnormalities. A left middle cerebral artery ischemic stroke was suspected, and the treatment options were fully discussed with the child's parents at this time. We discussed the risks and benefits of intravenous recombinant tissue plasminogen activator, explicitly stating that this therapy is not approved by the United States Food and Drug Administration for children. They agreed to the treatment.

The intravenous recombinant tissue plasminogen activator was started 120 minutes after the onset of symptoms. She received 0.9 mg/kg, 10% of the dose as an initial bolus

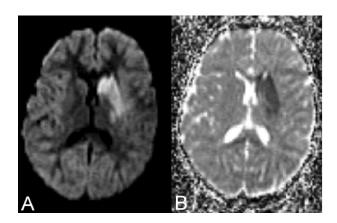


Figure 1. Magnetic resonance image of the brain. (A) Diffusion-weighted image. (B) Apparent diffusion coefficient. Images show restricted diffusion on left basal ganglia and deep white matter.

and the remaining 90% infused over 60 minutes. A transcranial Doppler ultrasound study performed immediately after the initial bolus showed a peak systolic velocity of 280 cm/s and an end diastolic velocity of 100 cm/s at the level of the distal left internal carotid artery and proximal left middle cerebral artery. On the right side, peak systolic velocity/end diastolic velocity was 145/65 cm/s at the distal internal carotid artery and 160/65 cm/s at the level of the proximal middle cerebral artery.

Upon completion of the recombinant tissue plasminogen activator infusion, her gaze preference had improved and she was now able to move the right leg horizontally (2/5), but the arm remained plegic and language did not improve. An immediate magnetic resonance imaging (MRI) scan, 30 minutes after completion of the intravenous recombinant tissue plasminogen activator treatment, showed a left middle cerebral artery striatocapsular ischemic stroke (Figures 1A and B). The magnetic resonance angiography (MRA) showed patent intracranial vessels (Figure 2).

Further endovascular treatment was not pursued, and she was transferred to the pediatric intensive care unit. Initial management in the unit included intravenous fluids and vasopressors. The next morning, 18 hours after onset, she was able to say a few words and also to lift the right leg up from the bed (3/5 strength). There was resolution of the gaze preference, but the right homonymous hemianopsia persisted. The National Institutes of Health Stroke Scale was then 14.

During her inpatient stay, multiple laboratory and imaging and studies were performed attempting to characterize the stroke etiology. Family history revealed the presence of a protein C deficiency in a maternal aunt, who had developed deep vein thrombosis during the third trimester of pregnancy. A hypercoagulability profile was

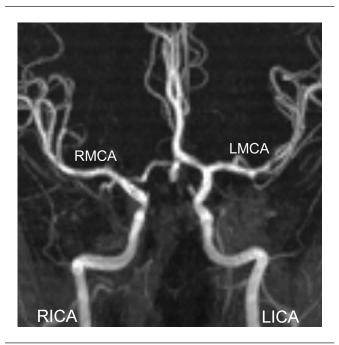


Figure 2. Magnetic resonance angiography of the brain, immediately after finishing recombinant tissue plasminogen activator shows that the left internal carotid artery (LICA), right internal carotid artery (RICA), left middle cerebral artery (LMCA), and right middle cerebral artery (RMCA) are all patent.

ordered, including anticardiolipin antibodies, factor V Leiden, factor VII, factor VIII, factor XII activity, antithrombin activity, prothrombin 20210 mutation, methylene tetrahydrofolate reductase gene assay, phosphatidylserine antibodies, lupus anticoagulant, sickle cell prep, human immunodeficiency virus, rapid plasma reagin, thyroid stimulating hormone, antinuclear antibody, protein C and S (free and total), fibrinogen, lipoprotein A, anti-B2 glycoprotein, homocysteine, lipid profile, serum protein electrophoresis, and hemoglobin electrophoresis. Of these, the only abnormal results were for antithrombin activity at 85% (range, 88%-124%), protein C activity at 60% (range, 88%-156%), and homocysteine levels at 13.80 mmol/L (range, 4.45-12.42 mmol/L).

Results of carotid ultrasound imaging, transthoracic echocardiogram with bubble study, transesophageal echocardiogram, MRA of the neck, and MRI of the neck with fat saturation were unremarkable. A cerebral angiogram 10 days after the stroke showed only a focal irregularity of the distal left internal carotid artery, but no signs of arterial dissection or intracranial vasculitis (Figure 3).

One week after admission, speech had recovered almost back to normal, she was able to walk (leg strength 4/5), and improved proximal movement of the right arm was evident (2/5 strength). On day 14, she was transferred to inpatient rehabilitation, where she received physical, occupational, and speech therapies. She was



Figure 3. Cerebral angiography (oblique projection) shows the left internal carotid artery and terminal branches, with focal irregularity in the lumen of the terminal internal carotid artery (arrow).

discharged to home 3 weeks later with aspirin therapy. At discharge, she was able to speak normally and walk without support (mildly spastic gait). She was also able to raise the right arm up to the level of the shoulder and showed increased motility of the hand and fingers, then being able to grab objects (a ball, a pen) without help.

## Discussion

Stroke among children is increasingly being recognized and reported. Childhood stroke is defined as a cerebrovascular event that occurs between 30 days and 18 years of age. The incidence of childhood stroke from population-based studies is estimated between 2 and 6/100 000 children per year.<sup>2-4</sup> Stroke risk factors in children are different than in adults, more frequently including congenital heart disease, sickle cell anemia, meningitis, postvaricella angiopathy, hypercoagulability, and craniocervical arterial dissections.<sup>5-7</sup> Genetic and metabolic causes are also important, but in many instances, stroke remains of cryptogenic etiology.<sup>5-7</sup> Adverse outcomes include death in 10%, stroke recurrence in 20%, and neurologic deficits in 66% of stroke survivors.4

Intravenous recombinant tissue plasminogen activator is the current standard of treatment for adult patients with acute ischemic strokes presenting within 3 hours of symptom onset and meeting established clinical criteria.1 Its use has been reported in a few pediatric patients,8-12 but safety, effectiveness, and outcomes of such treatment have not been established yet.

The National Institutes of Health Stroke Scale has not been validated in children, and its value as a tool for assessment and follow-up in pediatric population is still to be established.

No history of migraines or seizures was reported in this patient; therefore, we interpreted her symptoms as most likely secondary to ischemia of the complete left middle cerebral artery territory. Given the severity of the stroke, we decided to offer treatment with intravenous thrombolytics, which was started promptly after obtaining consent.

The transcranial Doppler flow signals at the beginning of the administration of intravenous recombinant tissue plasminogen activator were indicative of a high-degree of stenosis of left distal internal carotid artery and proximal middle cerebral artery. Immediately after completion of treatment, an MRA disclosed patency of all intracranial circulation.

We did not proceed with additional vascular imaging before the administration of intravenous recombinant tissue plasminogen activator because of time constraints; therefore, we are not able to prove with absolute certainty that the treatment was effective in recanalizing the artery.

No complications of treatment occurred with intravenous recombinant tissue plasminogen activator after the acute ischemic stroke in this 8-year-old girl, and she eventually showed a striking clinical recovery. Only a relative small stroke compared with the initial clinical deficit was eventually seen in follow-up imaging studies. To the best of our knowledge this is, so far, the youngest reported case of acute ischemic stroke successfully treated with intravenous recombinant tissue plasminogen activator.

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