

Ataxia and Headache in a Child

A Case of Acute Cerebellar Infarction

Kathryn M. Hewett, MD, Brett Lorenzetti, MD, and Benjamin F. Jackson, MD

Abstract: A 4-year-old female patient presents to the pediatric emergency department with acute onset of ataxia and occipital headache. Initial investigation, including computed tomography imaging, failed to demonstrate any focal neurologic lesion. Subsequent studies, however, reveal an acute thrombosis of the superior cerebellar artery. Further work up identified the likely causative factor to be a heterozygous mutation at the methylene tetrahydrofolate reductase gene. In this case report, we will discuss the work-up of pediatric ataxia, the evaluation and management of cerebrovascular accidents in children, and the association between stroke and mutation of the methylene tetrahydrofolate reductase gene.

Key Words: ataxia, stroke, methylene tetrahydrofolate reductase gene

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CASE

A 4-year-old female was carried into the pediatric emergency department of a tertiary care hospital by her father after the acute onset of an inability to ambulate steadily on her own. Approximately an hour and a half earlier, the patient had been in her normal state of health and was swimming in a pool when she developed a headache and a feeling of “dizziness.” The headache quickly subsided; however, the dizziness was incapacitating. There was no history of trauma or injury. She denied chest pain, shortness of breath, nausea, vomiting, and abdominal pain. She had no recent fever, respiratory tract infection, or other illness. Parents insisted that the child did not have access to any medications or toxic ingestions. Past medical history was significant only for occasional otitis media. Family history was negative for any neurologic condition, blood clotting disorder, or cerebrovascular disease. She lived at home with her mother and father.

Physical examination revealed an alert, nontoxic, well-developed, well-hydrated, well-perfused child who appeared somewhat reserved but interactive. She was afebrile without respiratory irregularity, tachycardia, or blood pressure abnormality. The patient was alert and oriented in an age-appropriate manner. She had no rash or any external evidence of trauma. Her ocular exam revealed symmetrically reactive pupils, extraocular muscles intact, and no nystagmus. Her tympanic membranes were clear and without effusion. The patient's neck was supple with full range of motion. Her cardiac exam was normal without rhythm irregularity or murmur. Lung exam demonstrated clear breath sounds, and her abdomen was soft with normoactive bowel sounds.

Cranial nerves II to XII were intact. The patient demonstrated no truncal ataxia and sat upright without support. Sensation was intact in all extremities. Deep-tendon reflexes were brisk and symmetric. Extremity strength was 5/5 in all extremities. Upon

ambulation, she was notably ataxic. Her finger-nose-finger test demonstrated dysmetria.

Initial differential diagnostic considerations included acute cerebellar ataxia, unrecognized toxic ingestion, and basilar artery migraine. However, because of the acuity of her presentation and the profundity of her cerebellar exam, noncontrast head computed tomography (CT) scan was obtained and pediatric neurology was consulted. The CT scan showed no evidence of hemorrhage, visible mass lesion, edema, or any other gross abnormality. The pediatric neurology consultant agreed with differential diagnosis and recommended admission to the general pediatrics services for observation and magnetic resonance imaging (MRI) with angiography of the brain due to the acute onset of ataxia in association with headache and the persistence of ataxia after resolution of headache. Brain MRI with and without contrast demonstrated an acute infarct within the territory supplied by the left superior cerebellar artery (LSCA). Imaging confirmed absence of signal in the LSCA consistent with occlusion or severely diminished flow in the region supplied by the LSCA (Fig. 1). All other vessels in the head and neck appeared normal; there was specifically no dissection of either vertebral artery.

After consultation with pediatric hematology, the patient was immediately started on aspirin anticoagulation. The day following presentation, the patient was clinically improved with steadier ambulation. Hypercoagulability evaluation demonstrated mutation of the methylene tetrahydrofolate reductase (MTHFR) gene, a mutation known to be associated with hypercoagulable states. After pediatric hematology consulted with the family about the risks and benefits of anticoagulation in an active 4-year-old, she was switched to subcutaneous low molecular weight heparin (LMWH). On hospital day number 4, our patient was symptom-free and was discharged in stable condition on LMWH for 6 months. During that 6-month period she experienced no adverse bleeding as a side effect of her anticoagulation therapy and was then changed to low-dose aspirin for 4 more months. Subsequent MRI at 3 months from presentation demonstrated complete resolution of the vascular occlusion. One year after discontinuation of anticoagulation therapy, our patient remained healthy with a normal neurological examination.

DISCUSSION

This case of ataxia as the presenting sign of acute stroke represents a rare clinical entity, especially in the pediatric population. Although acute ataxia is a more common pediatric complaint than stroke, most pediatric practitioners do not and should not prioritize ischemic stroke as the diagnosis in children presenting with ataxia.¹ As this case illustrates, however, there are certain symptoms, signs, and clinical contexts that warrant a heightened degree of suspicion and more advanced testing. A child who presents with acute ataxia associated with focal neurologic deficits, recent head trauma, or signs of increased intracranial pressure should undergo urgent head CT to evaluate for mass, hemorrhage, and hydrocephalus.² If accompanied by fever, nuchal rigidity, or toxic appearance, a lumbar puncture should be obtained if the scan is normal.

From the Department of Pediatric Emergency Medicine, Medical University of South Carolina, SC.

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Reprints: Kathryn M Hewett, MD, Department of Pediatric Emergency Medicine, Summerville Medical Center, Summerville, SC 29485 (e-mail: katehewett@gmail.com).

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FIGURE 1. Brain MRI demonstrating acute infarct within the territory supplied by the left superior cerebellar artery.

Although CT does not reliably identify acute ischemic stroke (AIS) within the first 24 hours, it is useful in the emergency setting to exclude hemorrhage, venous sinus thrombosis, mass, or, in the case of the febrile child, abscess. If the concern for stroke is high based on clinical findings, contrasted MRI with arteriography and venography is warranted to evaluate the brain as well as the vasculature in greater detail.³

Stroke, or cerebrovascular accident (CVA), is defined as the rapid loss of brain function due to disturbance in its blood supply. Ischemic stroke has an incidence of 1.6 per 100,000 children per year and mostly affects children with chronic medical conditions.⁴ Pediatric patients at increased risk for stroke include those with sickle cell disease, vasculopathies, and certain types of cardiac disease. Trauma, tumors, hematological abnormalities, and certain chemotherapeutic regimens further predispose children to CVA. Specific risk factors for cerebellar infarction include very low birth weight prematurity, cardiac emboli, previous stroke, marijuana use, and more common adult diseases such as hypertension, type II diabetes, and hypercholesterolemia.^{3,5,6} Stroke in children has a wide variety of presentations, with hemiparesis being the most commonly observed. Other symptoms vary on the location of the artery involved. Lower extremity weakness suggests involvement of the anterior cerebral artery, whereas upper extremity hemiplegia and visual changes suggest involvement of the middle cerebral artery circulation. Acute ataxia can be an early presenting symptom of ischemic stroke, hemorrhagic stroke, and cerebral venous sinus thrombosis, and the presence of ataxia aids in localization of the lesion to the cerebellum or posterior circulation.^{7,8}

Cerebellar infarction, as in our patient, accounts for less than 5% of all incidents of AIS, regardless of age. Ataxia, vertigo, hemiparesis, visual changes, and nystagmus are the most common

manifestations of stroke in the posterior circulation.⁹ Vertebral artery dissection with resultant effects on the posterior circulation is a well-described cause for cerebellar stroke.¹⁰⁻¹² Pediatric posterior circulation stroke is a rare, but significant cause of ataxia, requiring an emergency physician to maintain a high level of suspicion when other less worrisome etiologies are not readily identified.

Treatment begins with stabilization and supportive care. Early pediatric neurosurgery involvement is important to determine need for possible evacuation of hematomas or embolization. Children with sickle cell disease and evidence of AIS should have blood transfusions to decrease hemoglobin S to less than 30%.¹³ Consultation with a pediatric hematologist is recommended before the administration of anticoagulants or thrombolytics. In 2012, the American College of Chest Physicians published the 9th edition of their Antithrombotic Therapy in Neonates and Children evidence-based medicine clinical practice guidelines. These guidelines recommend against the use of thrombolysis in children outside of specific research protocols (Grade 1C recommendation). In addition, tissue plasminogen activator (tPA) is not currently approved by the Food and Drug Administration for use in children.¹⁴ Ischemic stroke in children is rare and generally presents atypically, and thus, confirming the diagnosis within the 4.5-hour time frame of tPA administration recommended for adult AIS patients is very challenging. As such, the safety and efficacy data for tPA use in pediatric AIS are understandably lacking. Evidence-based medicine guidelines in stroke in 2008 found no consensus about the use of tPA in the older adolescent who otherwise meets standard adult tPA eligibility criteria.¹⁵

Approximately 90% of children with AIS have at least 1 identifiable predisposing risk factor. Etiologic investigation is therefore warranted. Laboratory studies should include complete blood count with differential, erythrocyte sedimentation rate, c-reactive protein, prothrombin time with international normalized ratio, partial thromboplastin time, toxicology screen, and urine human chorionic gonadotropin (in the postmenarchal or sexually active female). If concern remains high for a prothrombotic state, laboratory analysis should include testing for deficiency of protein C, protein S, antithrombin III, factor V Leiden mutation, antiphospholipid antibody syndrome, homocysteinuria, and MTHFR mutation.¹⁶

An article in *The Journal of Pediatrics* in 2005 confirmed an association between MTHFR mutation and risk for stroke.¹⁷ In 2010, *Circulation* published a meta-analysis of observational studies involving thrombophilia and first childhood stroke demonstrated a statistically significant association between primary ischemic event and MTHFR T677T. Most recently, in 2013, a meta-analysis from China of 19 case-control studies consisting of 2223 cases of ischemic stroke found these patients to have a significant risk increase with the MTHFR C667T polymorphism.¹⁸

In the case presented, the patient remained on LMWH therapy for 6 months followed by aspirin for 4 months. During that time, she did not experience any adverse side effects of her anticoagulation therapy, and 1 year after discontinuing anticoagulation therapy, she remained asymptomatic. However, research has demonstrated the bleeding risk LMWH to be up to 4.8%.¹⁹ Current recommendations for use of LMWH for long-term anticoagulation therapy remain based on the risk versus benefit profile for each patient. Aspirin functions as an effective antithrombotic agent by acetylating platelet cyclo-oxygenase and irreversibly inhibiting platelet thromboxane.²⁰ Because aspirin rarely causes significant bleeding side effects, it is frequently the pediatric anticoagulant of choice for other medical conditions such as in Kawasaki disease in which coronary artery abnormalities and

aneurysms may develop, as well as in congenital heart lesions significant enough to warrant procedural intervention in which thrombosis risk is significant. Studies in adults have found a low risk of hemorrhage in AIS patients who receive aspirin therapy either acutely or as a long-term anticoagulant.¹⁹

CONCLUSIONS

The evaluation of a child with ataxia most often results in benign or treatable diagnoses. However, as our case demonstrates, life-threatening etiologies warrant consideration. It is imperative that the pediatric emergency provider maintains a high index of suspicion and an acute attention to detail when confronted with any ataxic child.

Cases such as this one highlight the importance of consultant involvement and cooperation. In an ataxia scenario in which history, physical exam, or standard ED diagnostic evaluation studies yield either a concerning etiology or no etiology at all, consultation with a neurologist is indicated. When thrombosis and CVA are identified, pediatric hematology should be additionally consulted to guide investigation of a possible hypercoagulable state and to recommend anticoagulation therapy. Many studies have linked first time stroke in children to mutations of the MTHFR gene, making this association an important one to be consider.

REFERENCES

- Musselman KE, Stoyanov CT, Marasigan R, et al. Prevalence of ataxia in children: a systematic review. *Neurology*. 2014;82:80–89.
- Whelan HT, Verma S, Guo Y, et al. Evaluation of the child with acute ataxia: a systematic review. *Pediatr Neurol*. 2013;49:15–24.
- Tohgi H, Takahashi S, Chiba K, et al. Cerebellar infarction. Clinical and neuroimaging analysis in 293 patients. The Tohoku Cerebellar Infarction Study Group. *Stroke*. 1993;24:1697–1701.
- Mittal SO, ThatiGanganna S, Kuhns B, et al. Acute ischemic stroke in pediatric patients. *Stroke*. 2015;46:e32–e34.
- Johnsen SD, Tarby TJ, Lewis KS, et al. Cerebellar infarction: an unrecognized complication of very low birthweight. *J Child Neurol*. 2002;17:320–324.
- Geller T, Loftis L, Brink DS. Cerebellar infarction in adolescent males associated with acute marijuana use. *Pediatrics*. 2004;113:e365–e370.
- Datar S, Rabinstein AA. Cerebellar hemorrhage. *Neurol Clin*. 2014;32:993–1007.
- Kulkarni GB, Mustare V, Abbas MM. Profile of patients with cerebral venous sinus thrombosis with cerebellar involvement. *J Stroke Cerebrovasc Dis*. 2014;23:1106–1111.
- Kirkham F. Investigation and Management of childhood stroke. *Paediatr Child Health (Oxford)*. 2010;20:428–438.
- Feudale F, Liebelt E. Recognizing vertebral artery dissection in children: a case report. *Pediatr Emerg Care*. 2000;16:184–188.
- Hutchinson PJ, Pickard JD, Higgins JN. Neurological picture. Vertebral artery dissection presenting as cerebellar infarction. *J Neurol Neurosurg Psychiatry*. 2000;68:98–99.
- Cheon JE, Kim IO, Kim WS, et al. MR diagnosis of cerebellar infarction due to vertebral artery dissection in children. *Pediatr Radiol*. 2001;31:163–166.
- Kenet G, Lütkehoff LK, Albiseti M, et al. Impact of thrombophilia on risk of arterial ischemic stroke or cerebral sinovenous thrombosis in neonates and children: a systematic review and meta-analysis of observational studies. *Circulation*. 2010;121:1838–1847.
- Monagle P, Chan AK, Goldenberg NA, et al. Antithrombotic therapy in neonates and children: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141:e737S–e801S.
- Roach ES, Golomb MR, Adams R, et al. Management of stroke in infants and children: a scientific statement from a Special Writing Group of the American Heart Association Stroke Council and the Council on Cardiovascular Disease in the Young. *Stroke*. 2008;39:2644–2691.
- Amlie-Lefond C, Gill JC. Approach to acute ischemic stroke in childhood. *Curr Treat Options Cardiovasc Med*. 2014;16:276.
- Lynch JK, Han CJ, Nee LE, et al. Prothrombotic factors in children with stroke or porencephaly. *Pediatrics*. 2005;116:447–453.
- Li P, Qin C. Methylene tetrahydrofolate reductase (MTHFR) gene polymorphisms and susceptibility to ischemic stroke: a meta-analysis. *Gene*. 2014;535:359–364.
- Long E, Pitfield AF, Kissoon N. Anticoagulation therapy: indications, monitoring, and complications. *Pediatr Emerg Care*. 2011;27:55–61.
- Schrör K. Aspirin and platelets: the antiplatelet action of aspirin and its role in thrombosis treatment and prophylaxis. *Semin Thromb Hemost*. 1997;23:349–356.