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Abstract:

Stroke, also known as cerebrovascular accident (CVA), is a neurological injury caused by inadequate brain perfusion due to either ischemia or hemorrhage. There is an abundance of literature on the management of ischemic strokes in adults and this has led to well defined diagnostic and treatment guidelines. However, the management of pediatric ischemic strokes is currently based on clinical experience of experts, recommendations of consensus guidelines, case studies and extrapolation from adult clinical trials. In this case report a pediatric patient suffering from an ischemic stroke is successfully treated with IV alteplase (tPA).

Introduction:

Stoke or cerebrovascular accident (CVA) is a neurological injury to the brain caused by either ischemic or hemorrhagic insult. When a CVA is caused by ischemia and the patient has debilitating neurological deficits, thrombolytics such as tPA is recommended as long as the patient does not have any absolute contraindications. However, one of the primary indications to administer tPA is age > 18 years old. If a child is suffering an ischemic stroke, tPA use would be off-label and treatment should be coordinated with pediatric sub-specialists. Management is based on clinical experience of experts, recommendations of consensus guidelines, case studies and extrapolation from adult clinical trials.

Case Presentation:

A 15-year-old male was brought to the ED for difficulty speaking, left sided facial droop and left sided weakness. Last known normal was approximately 30 minutes prior to arrival. The patient had a past medical history of hypoplastic left heart syndrome (HLHS) surgically palliated via "fontan surgery on day 3, 6 months and 18 months of life". The patient's medications included 81 milligrams aspirin every other day. Vital signs on arrival were a blood pressure of 119/62, heart rate of 84 beats per minute, respiratory rate of 20 breaths per minute, oxygen saturation of 93% on room air and oral temperature of 98.1F. The patient weighed 59.8 kilograms.

On exam the patient was resting comfortably and in no acute distress. He was able to talk but had moderate dysarthria. He was awake, alert and oriented to person, place and time. He had a left upper and lower facial droop. He was unable to move his entire left upper extremity, 0/5 in strength. His left lower extremity was weak, 3/5 in strength. The patient's NIH Stroke Scale was 10 for left sided facial palsy, left upper extremity paralysis, left lower extremity weakness, and dysarthria. Remainder of his exam was unremarkable.

Our patient underwent prompt neuro-imaging after establishing vascular access and documenting a blood glucose of 68. CAT scan of his head without contrast showed concern for hyperdense thrombus in the M1 segment of the right middle cerebral artery (MCA) [Figure 1] and the CT angiogram of the head and neck confirmed complete occlusion of mid to distal M1 segment of right MCA with an intraluminal thrombus, which spanned approximately 8mm [Figure 2, 3].

These results were discussed with the on-call neurologist and neurosurgeon at a local tertiary pediatric center who recommended administration of tPA and immediate transfer to their hospital. tPA was administered (.9 mg/kg/dose, 10% bolus over one minute as bolus and remainder over one hour as an infusion). When he arrived at the receiving hospital, a repeat neurological exam showed the patient regained 3/5 strength in his left upper extremity but still had a facial droop, dysarthria and left lower extremity weakness. The patient underwent a mechanical thrombectomy where the clot was successfully removed from the right MCA with a penumbra suction catheter. Post-suction angiography showed satisfactory flow in the right MCA. The patient was admitted to the ICU where his neurological exam significantly improved during his hospital stay. He regained 5/5 strength in all extremities and his dysarthria resolved but a mild left lower facial droop was still slightly visible when he smiled. The patient had a negative hypercoagulable workup. Bilateral upper and lower extremity venous ultrasounds were negative for deep vein thromboses. Transthoracic echocardiogram and cardiac MRI showed normal post-fontan anatomy and physiology without signs of intracardiac thrombi or vegetations. The patient was started on anticoagulation (Lovenox). The patient had no incidence of bleeding or symptomatic intracranial hemorrhage (sICH). The patient remained stable and by hospital day six was discharged.

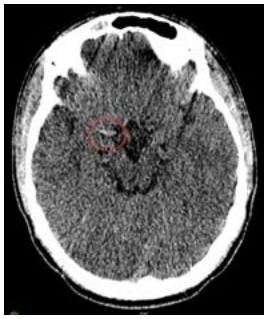

Figure 1: CT Head without IV contrast showing the focal hyperdensity circled in red is known as the "hyperdense MCA sign".

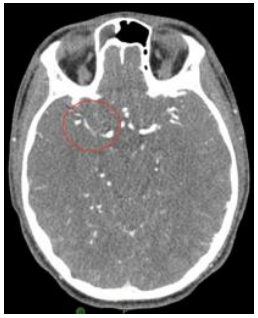

Figure 2: CT Head with IV contrast showing complete occlusion of mid to distal M1 segment of right MCA.

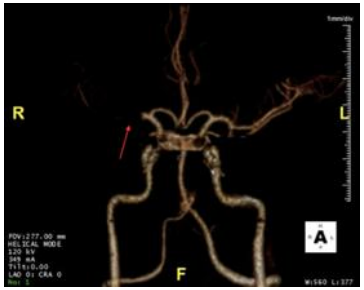

Figure 3: 3D reconstruction of the patients Circle of Willis which shows complete occlusion of the R MCA.

Discussion:

Pediatric strokes are a relatively rare (1 to 2.5 per 100,000 children in the United States per year) compared to adult strokes (up to 970 per 100,000 adults between ages 65 and 74 in the Unities States per year) (1). While strokes in adults are commonly linked to risk factors such as hypertension, hyperlipidemia, and diabetes, pediatric stroke risk factors include congenital heart disease, sickle cell disease and leukemia (2). The patient in this case study had a history of HLHS, a ductal dependent malformation that is universally fatal if not surgically palliated shortly after birth. Our patient had a three-stage procedure that included the Norwood, Glen, and Fontan surgeries, which have been shown to increase survival to 90% at 18 years of age. Unfortunately, despite improved mortality post-fontan, almost all patients experience complications including thromboembolic events.

As the medical community continues to create and provide innovative treatment modalities to patients with illnesses that have historically had poor prognostic outcomes, such as complex congenital heart anomalies, the Emergency Department is faced with new and rare pathologies that can require rapid diagnosis and treatment, including ischemic strokes in children. This changing landscape presents challenges. One study showed clinicians diagnosing stroke in a pediatric patient as late as 3 months later (3) and another study showed delay in brain imaging from symptom onset as late as 7.2 hours (4). The patient discussed in this case study presented to a community hospital with adult comprehensive stroke services but without pediatric subspecialty coverage. The clinicians in this case-study utilized their knowledge of stroke care in adults and applied it to this pediatric patient. In less than 10 minutes an emergency physician evaluated the patient, in less than 25 minutes the patient had CT scan of his head, in less than 45 minutes the CT scan results was interpreted and in one hour and thirteen minutes of arrival to the hospital (approximately one hour and 43 minutes from symptoms onset) the patient received tPA. By the time the patient arrived to the receiving children's hospital, he was able to move his left upper extremity and had near complete neurological recovery after mechanical thrombectomy.

The current FDA approval of tPA in adult patients with strokes is supported by the NINDS rt-PA trial and ECASS III trials. Although it is reasonable to consider tPA in children based on these studies, such treatment is off-label extrapolation. The fibrinolytic system is a dynamic process that continues to develop following birth and there are qualitative and quantitative differences in plasminogen and plasminogen activator inhibitors in infants, children, and adults (4). These differences could affect optimal tPA dosing in children. A major complication of administering tPA is bleeding, including symptomatic intracranial hemorrhage (sICH) which increases morbidity and mortality. The rate of symptomatic intracranial hemorrhage was 6.4% in the NINDS trial and 2.4% ECASS III trial (5) (6). Of note, patients with ischemic stroke are at increased risk of spontaneous intracranial hemorrhage even without use of thrombolytics (6). Therefore, administering tPA in acute strokes is a balance between maximizing clot breakdown to enhance neurological recovery while minimizing risk of bleeding. The patient in this case study received an adult dose of tPA, did not suffer any adverse outcome and had improved neurological function, illustrating that there is a role of tPA in pediatric strokes, but optimal dosing is still unknown.

Conclusions:

Pediatric strokes are relatively rare but result in death and lifelong disability if not appropriately identified and treated. Emergency physicians are faced with the challenge to rapidly identify and care for patients of any age presenting with strokes. Current treatment for pediatric strokes is based on clinical expertise, case studies, and extrapolation from adult trials. The problem with using adult trials to guide treatment in children is the fibrinolytic system in infants and children are different than that in adults Without evidence-based dosing guidance, children remain at risk of unintended consequences such as symptomatic intracranial hemorrhage and inadequate thrombolysis. The TIPS trial was the first multicenter, dose-adaptive, prospective treatment trial in acute pediatric strokes but it unfortunately lost funding due to lack of patient recruitment and other logistical issues (6). While another treatment trial is needed to test tPA's efficacy and risk, this case study adds the growing literature of thrombolysis in pediatrics strokes.

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