Pediatric ischemic stroke – an unlikely diagnosis: a report of three cases

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ABSTRACT

Pediatric ischemic stroke is a rare and devastating disease. A patient presenting with acute neurological deficit should raise suspicion of a possible stroke. However, stroke “mimics” account for a majority of suspected stroke cases in childhood. We present three cases of pediatric acute ischemic stroke, two of which are arterial, and one caused by thrombosis of venous sinuses. In the first case, we present a 16-year-old male patient who was admitted to our hospital due to a rare Artery of Percheron occlusion. The second case represents a 17-year-old female patient with thrombosis of multiple cerebral venous sinuses, venous infarctions and secondary hemorrhages. As the third case, we present 6-year-old male patient with a herpes simplex infection and a vertebrobasilar stroke. All three patients had experienced an altered mental status and other nonspecific symptoms. Etiology and risk factors for stroke in adults differ when compared to pediatric population. Given the rarity and the non-specific symptoms of ischemic stroke in pediatric population, efficient diagnosis and treatment often depends on familiarity with possible risk factors. Here we present three cases of ischemic stroke in childhood with emphasis on clinical presentation.

Keywords: Pediatric ischemic stroke, stroke, acute ischemic stroke, thrombosis

INTRODUCTION

Pediatric stroke is a rare disease with a variety of symptoms and results in high morbidity. A patient diagnosed with an acute neurological deficit always identifies the risk of a possible stroke. However, stroke “mimics” account for up to 76% of all cases of suspected stroke during childhood (1).

The annual incidence of arterial ischemic stroke (AIS) is 1-2 in 100 000 children (2), with stroke-specific mortality rate being 5%, and neurological sequelae in 67% of the cases, respectively (3). Meanwhile, the incidence of sinovenous thrombosis is 0.6 per 100 000 children up to 16 years old (4). Etiology and risk factors for stroke in adults differ when compared to pediatric population. Given the rarity and the non-specific symptoms of ischemic stroke in pediatric population, efficient diagnosis and treatment often depends on familiarity with possible risk factors. Here we present three cases of ischemic stroke in childhood with emphasis on clinical presentation.

CASE REPORT 1

A 16-year old male patient presented to the emergency department (ER) due to an altered mental status. In previous years the otherwise healthy patient had been complaining of headaches which were regarded as migraine. Upon arrival, the patient's Glasgow coma scale was at 10/15, and his vitals were stable (HR 59 bpm, BP 102/51 mmHg, RR 16 bpm, SpO2 97%, temperature 37.1°C). The patient was transferred to the pediatric intensive care unit (PICU) where he had an episode of focal seizures. Complete blood count (CBC), blood serum electrolytes, blood glucose test results were within normal ranges, tests for illicit drugs showed negative results. Brain MRI scan revealed bilateral focal lesions in the medial parts of the thalamus consistent with acute ischemia in the Percheron artery area (Figure 1). The patient was given saline infusions and acetylsalicylic acid for further stroke prophylaxis. Further evaluations for heart anomalies, rheumatologic diseases, coagulation disorders (including values of protein C and S, mutations of Leiden and prothrombin factor genes) showed no abnormalities. The patient recovered completely within two days after the onset of symptoms and was discharged home.

Figure 1: T2W/FLAIR (A) and DWI (B) lesions corresponding with ADC map (C) in medial parts of the thalamus 24 hours after the onset of symptoms depicting a characteristic pattern of ischemia caused by the occlusion of Percherons’ artery.
A 17-year-old female patient was admitted to the ER for severe headache on the left side of the head that corresponded to 8 points on the Visual Analogue Scale and has been lasting for five days. A day before, she presented to the ER with the same complaints and had her brain CT scan which showed no abnormalities; her mother then refused further evaluations, and the patient was discharged from the hospital. The patient had type 1 diabetes mellitus and poorly controlled hyperglycemia for the previous five and two years, respectively. Upon admission, her vitals were stable (HR 86 bpm, BP 133/73 mmHg, RR 16 bpm, SpO2 98%, temperature 36.7°C) and no focal neurological deficits were detected. However, due to increasing headaches and worsening of her mental status, the patient was transferred to the PICU.

Further deterioration of the patient’s condition was observed: lateral gaze paralysis of her left eye and positive Babinski signs on the right. Repeated brain CT scan revealed 1.7 x 1.5 centimeter size intracerebral hematoma on the left temporal lobe (Figure 2 A). Initial CBC, electrolytes were within normal ranges, she had elevated levels of blood glucose up to 16.02 mmol/l, D-dimer up to 33.76 mg/l (reference ranges 0-0.5 mg/l), free thyroxin up to 31.09 pmol/l (ref. ranges 10-19 pmol/l), and low levels of TSH – 0.03 mU/l (ref. ranges 0-0.5 mg/l). Brain MRI scan showed thrombosis of the left transverse, straight and left sigmoid sinuses, with venous infarctions in left thalamus, and secondary hemorrhages in the left temporal lobe (Figure 2 B-K). The patient was given fraxiparin which was later replaced by warfarin. Throughout the course of the illness she developed Klebsiella pneumoniae sepsis and was treated with antibiotics. No heart anomalies, malignancies or rheumatologic disorders were detected in the search of additional risk factors regarding the thrombosis. Low values of protein C were attributed to sepsis. She was discharged home after her condition has improved without any remaining neurological deficits.

A 6-year-old male patient was admitted to ER due to an altered mental status and an episode of generalized seizure. He had recurrent diplopia for the last two weeks and herpes labialis infection lasting for one week, as well as subfebrile fever which occurred two days prior to hospitalization. Neurological examination revealed intermittent outward deviation of the right eye and horizontal nystagmus. His vitals were stable (HR 114 bpm, BP 103/68 mmHg, RR 18 bpm, SpO2 98%, temperature 36.5°C). Initial CBC, blood urea nitrogen, creatinine, glucose, serum electrolytes, liver enzyme, ammonia, and blood coagulation tests were within normal ranges. An urgent brain CT scan showed hypodense lesions in both cerebellar hemispheres and the right thalamus (Figure 3 A, B). The patient was transferred to PICU for further treatment. A subsequent MRI scan showed ischemic lesions that had occurred at different times in the vertebrobasilar region, and the findings consistent with basilar artery arteritis (Figure 3 C - L). Further thorough laboratory investigations excluded possible hematologic and autoimmune risk factors of stroke. Elevated IgG antibodies to HSV were detected (>119 U/ml). Cerebrospinal fluid PCR for herpes virus was negative. Secondary stroke prevention with acetylsalicylic acid was initiated. The patient received intravenous Acyclovir for 3 weeks and showed clinical improvement, however, speech impairment and slightly unstable gait has remained.

**DISCUSSION**

Clinical presentation of ischemic stroke may vary depending on the corresponding blood vessel. The most common symptoms of pediatric arterial ischemic stroke are acute neurological deficits, seizures and headache (5). Meanwhile, the common symptoms for sinovenous thrombosis are headaches, altered consciousness and focal neurological deficits (6). These are non-specific symptoms that may be present in disorders of other etiologies. Current Stroke in Childhood guidelines (5) offer recommendations for the diagnosis and treatment of acute pediatric stroke. It is suggested to use FAST (face, arms, speech, time) criteria to determine stroke in children. However, the absence of motor deficits, cranial nerve damage, and speech impairment does not necessarily rule out stroke. One could suspect stroke based solely on the clinical symptoms in all three cases but, on the other hand, that might not be the likely predominant diagnosis among stroke mimics, thus prolonging the diagnostic process.

A rare variant of posterior cerebral circulation was present in case one. Artery of Percheron (AoP) is a single arterial trunk that bilaterally supplies paramedian parts of the thalami and the rostral midbrain.
instead of the standard variant where the thalami and the midbrain receive blood supply from proximal parts of both posterior cerebral arteries. In our case of arterial occlusion, radiological findings were characteristic to 38% of all AoP occlusions (7).

Very few cases of AoP stroke in pediatric population have been described in literature. Given that no risk factors of ischemic stroke were present in our patient, posterior circulation stroke was among the least probable causes of the symptoms.

A sinovenous thrombosis risk factor – Graves’s disease – was present in case two. Overt hyperthyroidism is linked to elevated levels of von Willebrand and other coagulation factors, thus decreasing fibrinolysis (8), while type I diabetes is related to the worse outcomes of sinovenous thrombosis (9).

Herpesvirus infections could be a trigger of arterial ischemic stroke in childhood (10). Other risk factors of stroke were excluded in our patient; therefore, we can assume the association of Herpes simplex virus and stroke in this case. However, more studies are needed in order to confirm this relationship.

Treatment of ischemic stroke should be considered on a case-by-case basis. Despite the lack of high-quality studies, thrombolysis with tissue plasminogen activator in cases of arterial ischemic stroke could be considered if the patient meets the criteria provided in the guidelines mentioned above, including the time window of 4.5 hours during which the treatment could be beneficial. In our two cases of arterial ischemic stroke, such treatment was not possible due to insidious clinical presentation that caused diagnostic delay.

**CONCLUSION**

Due to its rarity, stroke in childhood may be a diagnostic challenge, leading to time loss in making the therapeutic decisions. On the other hand, the outcomes are likely to be more favorable compared with adults.

**REFERENCES**