RESIDENT & FELLOW SECTION

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Child Neurology: Childhood basilar artery occlusion and stroke

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Stroke is one of the major causes of childhood mortality. Pediatric arterial ischemic stroke (PAIS) has an annual estimated rate as high as 3.3 cases per 100,000 children (with the vertebrobasilar territory involved in up to 36% of cases); however, the incidence of isolated childhood basilar artery occlusion (BAO) and stroke (BAS) is unknown.[1] Adult BAO carries up to a 90% mortality rate, while death or severe neurologic deficits may be seen in 50% of children with BAO/BAS.[1,2] The following case report describes a 12-year-old boy with BAO leading to BAS. Clinical symptoms, differential diagnoses, associated comorbidities, and current trends in acute treatment of pediatric BAO/BAS are also discussed.

CASE REPORT A 12-year-old right-handed boy was transferred from an outside hospital with right-sided weakness for 9 hours. He had a medical history of congenital cytomegalovirus infection, hearing loss, cochlear implantation, and behavioral issues. The patient was only able to communicate via sign language. Seven days earlier, the patient had visited an emergency room for left-sided weakness lasting for 30 minutes. However, those symptoms occurred in the context of an emotional outburst and were thought to represent conversion disorder; urgent investigations for other etiologies were therefore not pursued. Family history was pertinent for antiphospholipid syndrome in his mother with multiple TIAs. The patient's initial pediatric NIH Stroke Scale (NIHSS) was scored at a minimum of 10 (best language and dysarthria could not be accurately scored due to his preexisting condition): 2 for the right lower facial weakness and 8 for complete right hemiplegia (4 for each limb). The gag reflex was symmetrically reduced. His initial cranial CT scan at the transferring hospital suggested remote infarcts within the right thalamus (figure, A) and left cerebellum (figure, B). An urgent CT angiogram of the head and neck revealed absence of flow in the basilar artery at the level of the pons (figure, C). An intra-arterial mechanical recanalization was performed 13 hours after the onset of symptoms, which successfully achieved complete filling of the expected vascular territory (thrombolysis in cerebral infarction grade 2b/3 as demonstrated in the figure, D and E). A repeat cranial CT scan 12 hours after the procedure showed a new area of hypoattenuation in the left pons in addition to the previously mentioned infarcts (figure, B). Secondary stroke prevention with acetylsalicylic acid (81 mg daily) was initiated. At 48–72 hours, the NIHSS assessment was repeated and improved to 6: 1 for minor facial weakness, 3 for right arm movement without antigravity effort, and 2 for right leg movement against gravity. After initial monitoring in the pediatric intensive care unit, the patient was eventually transferred for inpatient rehabilitation. Due to dysphagia, he was fed through a nasogastric tube for 6 weeks. At 8-week follow-up, the patient showed further clinical improvement. He demonstrated effort against gravity in both the right arm and leg along with resolution of facial weakness (NIHSS 4: 2 for each limb). Initial routine and suggested PAIS-specific investigations (C-reactive protein, erythrocyte sedimentation rate, antiphospholipid antibodies [lupus anticoagulant, anticardiolipin, and anti-β2-glycoprotein], protein C and S testing, antithrombin III activity, activated protein C resistance assay, homocysteine levels, and transthoracic echocardiography) were within normal limits.[3] Other tests included in our institutional stroke workup (HIV screen, rapid plasma reagin, varicella titers, prothrombin and methylenetetrahydrofolate reductase genetic testing, antineutrophil cytoplasmic antibodies, and antibodies against SSA, SSB, Smith, SCL-70, and RNP antigens) also were unremarkable. Lipoprotein (a), factor VIII, and von Willebrand factor antigen testing will be added to this workup.[3]

DISCUSSION **Clinical features of BAO/BAS.** BAO can present with a variety of neurologic deficits, which may have an abrupt, progressive, or stuttering presentation.[4] Most children present with motor deficits, altered sensorium, and lower cranial nerve palsies.[1] Some children may also present with headaches.[5] Prodromal TIAs are reported in >50% of

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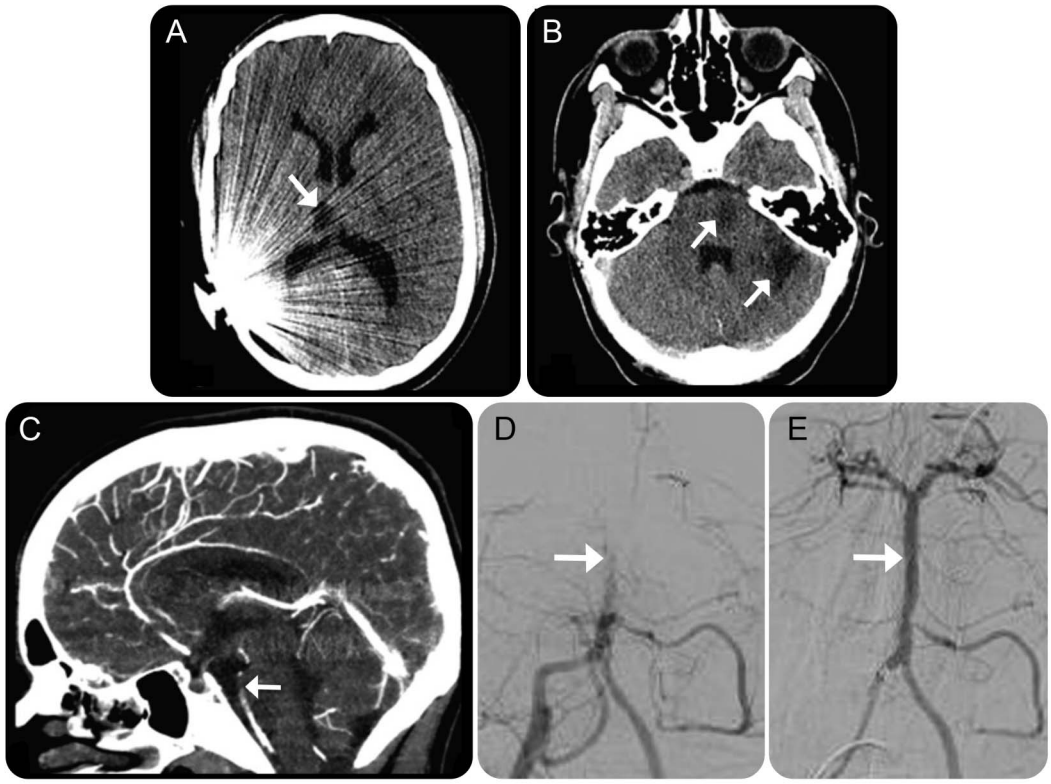
Figure Preintervention and postintervention neuroimaging studies



(A) A preintervention axial CT scan of the brain shows a remote infarct in the right thalamus (arrow). The image also shows artifact from the cochlear device on the right side. (B) A postintervention axial CT scan of the brain shows a remote infarct in the left cerebellum (lower arrow) and a new area of hypoattenuation in the left pons (upper arrow). (C) A preintervention sagittal CT angiogram shows absence of flow in the basilar artery at the level of the pons (arrow). (D) A prerecanalization angiogram shows absence of flow in the basilar artery (arrow). (E) A postrecanalization angiogram shows reestablishment of flow in the basilar artery (arrow) with complete filling of the distal vascular territory.

adults with BAO.[4] Clinical symptoms of BAO vary with the anatomical level of the vascular obstruction. A proximal or middle segment BAO can result in pontine strokes, which may present with hemiplegia or quadriplegia, dysarthria, dysphagia, cranial nerve palsies, or reduced consciousness.[4] BAO presenting with subtle brainstem signs and uncrossed hemiplegia (ipsilateral lower face, arm, and leg weakness) may eventually progress to the locked-in state (quadriplegia and mutism with preserved sensorium). In such scenarios, the initial hemiparesis represents early stages of stroke-in-evolution, and is known as herald hemiparesis.[6] Distal segment BAO may cause bilateral strokes in mesencephalic and thalamic areas (decreased sensorium, quadriparesis, and eye movement abnormalities).[4]

Differential diagnosis and risk factors. Brainstem hemorrhage, space-occupying lesions with transtentorial herniation, metabolic or toxic encephalopathies, and disorders presenting with rapidly progressive cranial nerve dysfunction (Miller Fisher syndrome, botulism, or myasthenic crisis) may all mimic BAO/BAS.[4] Osmotic demyelination syndromes, demyelinating disorders, and certain encephalitides can also involve the brainstem. Acute subarachnoid hemorrhage or basilar-type migraines should be considered in patients with symptoms of headaches and brainstem dysfunction.[4,5] BAS-related myoclonic jerks, decerebrate posturing, and unresponsiveness may raise concerns for seizures.[4] In a patient presenting with altered sensorium, cranial nerve dysfunction, and motor tract involvement, the index of suspicion for BAO should be high.[4] In such scenarios, urgent neuroimaging is of paramount importance to establish the diagnosis and direct management of BAO/BAS.

Most patients with PAIS have identifiable predisposing risk factors for stroke.[3] Arteriopathies (including structural anomalies and cerebral arteriopathies), vascular diseases (including vasculitides), cardiac diseases (congenital or acquired), hematologic disorders (sickle cell disease along with coagulopathies), trauma, genetic syndromes, and metabolic disorders are common risk factors for PAIS.[7] Migraines with aura, the use of estrogen-containing oral

contraceptives, and pregnancy are among the acquired predisposing factors.[3] Young patients with cryptogenic vertebrobasilar strokes and proteinuria should be investigated further for Fabry disease.[8]

Current trends in acute treatment of childhood BAO/BAS. The first randomized controlled trial studying IV tissue plasminogen activator in children was launched in 2012 as the Thrombolysis in Pediatric Stroke trial. It was terminated early, however, due to insufficient enrollment.[9] Delay in the diagnosis of PAIS is another universal problem. Studies from developed countries have revealed that the mean time from the onset of symptoms to initial neuroimaging for pediatric stroke ranges from 8.8 to 16 hours.[10] Accurate assessment of treatment effectiveness is impossible without appropriate randomized studies. Reporting bias (better outcomes are more likely to be reported) further limits the usefulness of published literature.[2] Therefore, management of PAIS is not standardized and is mostly derived from adult stroke guidelines, pediatric case reports/series, and expert opinions.

In regards to endovascular interventions, a retrospective study focusing on pediatric BAS (from 1992 to 2009) concluded that aggressive endovascular interventions were unjustified in most of the children.[1] However, a more recent literature review has suggested that endovascular interventions may be safe and effective with the introduction of modern devices and when intervening in children with higher NIHSS and proximal large vessel occlusions.[2] In this study of PAIS, 14 out of 29 children had BAO. Ten out of these 14 patients had a documented pediatric NIHSS of $\geq$15 with a mean time to treatment of 8.8 hours.[2] The most recent 2015 American Heart Association guidelines state that endovascular treatment of patients $<$18 years with large vessel occlusions may be reasonable if groin puncture can be initiated within 6 hours of symptoms onset (Class IIb; Level C).[10] Therefore, current research supports consideration of endovascular treatment options in pediatric BAO/BAS.

Evidence of remote strokes in the posterior circulation territory, new-onset uncrossed hemiplegia (possibly herald hemiparesis), and angiographic confirmation of BAO prompted an endovascular recanalization beyond the suggested 6-hour window in our patient. Complete recanalization of the basilar artery was achieved using a Solitaire device without any complications.

BAO/BAS can be devastating. Our case emphasizes the importance of early recognition of BAO, which can present with prodromal TIAs. The management of childhood BAO/BAS is still evolving. Emergent endovascular interventions are being employed more often with better outcome reports. Although the current literature is promising, stronger evidence is required to fully establish the safety and efficacy of such interventions in children.[2] The Basilar Artery International Cooperation Study is a major prospective observational registry for BAO in adults, but there is no similar study for children. Systematic enrollment of BAO/BAS in ongoing PAIS registries will thus be indispensable to identify the best treatment options.

AUTHOR CONTRIBUTIONS

Mina Lobbous: drafting and revising the manuscript, study concept and design. Sara Williams: revising the manuscript, analysis and interpretation of data. Salman Rashid: revising the manuscript, analysis and interpretation of data.

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DISCLOSURE

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