

## Idiopathic ischemic infarction of the brain stem in children

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**Abstract.** Three cases of idiopathic brain-stem infarction are added to the literature on 12 children. There is no age predilection, and the youngest case is 3 years old. However, there is a striking male preponderance of 13:2. The residual neurological deficit covers the range of normal to quadriplegia. Laboratory studies investigating hypercoagulopathy, platelet dysfunction and atrial septal defect may provide an etiology for some cases in the future.

**Key words:** Brain-stem infarction – Occlusion – Computed tomography – Magnetic resonance imaging – Angiography

The incidence of brain-stem infarctions in children is relatively low compared to that in adults. However, brain-stem lesions with or without cerebellar involvement represent a small percentage in both age groups [10]. Radiological developments in the past 15 years have provided more accurate anatomical information and additional theories of pathogenesis. Recent experience in our center with two school-age cases prompted this review. A third case is added from the pre-computed tomography (CT) era. Although no etiology could be identified in any of the patients, the diagnostic studies requested reflect changing thoughts regarding possible mechanisms.

### Case reports

#### *Cases 1–12*

The data are summarized in Table 1.

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#### *Case 13*

A 12.5-year-old black female was in good health until 10 h before admission on 5 June 1978 when she awakened, attempted to reach the bathroom, and was found on the floor, conscious but unable to walk. Two brief generalized clonic seizures developed in the 1st h.

Past medical history revealed normal growth and development and good school performance. There were no prior seizures, head injuries, or periods of hospitalization. Her menarche began 2 days prior to admission. The family history was devoid of neurological problems including childhood or young adult strokes or seizures.

Neurological examination demonstrated a flaccid quadriplegia with symmetrically active deep tendon reflexes and bilateral extensor plantar responses. Facial diplegia was present, and she refused or was unable to speak. Speech evaluation several days later suggested an unwillingness to speak because of severe dysarthria. Her blood pressure was 115/75, and her respiratory pattern was normal. She did not have a marfanoid habitus. Ocular examination was normal.

CT scan with and without contrast was normal, but the posterior fossa views were of low resolution when compared with current CT technology. Spinal fluid analysis revealed no white blood cells or red blood cells, a protein of 16 mg/dl and glucose of 77 mg/dl. Stains and cultures of the cerebrospinal fluid were normal. Cerebral angiography obtained 3 days after admission demonstrated complete occlusion of the basilar artery just beyond the anterior inferior cerebellar arteries. The posterior cerebral arteries filled from the ipsilateral carotid vessels. No mass effect was present.

Laboratory studies included urine negative for homocystine and sickle cell preparation. Clotting studies revealed a normal partial thromboplastin time (PTT) and platelet count. All cardiac studies were normal including auscultation, electrocardiography (ECG), echocardiography and a gated-flow study.

On follow-up examination 3 years later she was ambulatory with a right hemiparesis and mild dysarthria. The left facial weakness and left Babinski sign were no longer present. No new neurological problems had developed.

#### *Case 14*

A 7-year-old male was brought to the hospital on 28 May 1986 with a history of collapsing to the floor and inability to arise without aid. At that time he was awake and talking. He complained of double vision and became increasingly lethargic. There was no history of prior significant medical problems. The family history revealed no neurological problems in children or young adults.

**Table 1.** Idiopathic brain-stem infarction in childhood. CT, Computer tomography; MRI, magnetic resonance imaging

Author	Case no.	Age/sex (years)	Neurological symptoms/signs	Diagnostic studies	Outcome
Fowler [8]	1	7/M	Coma, miosis, left VII, bilateral CS tract signs	Normal carotid angiogram; midbrain infarct on PM examination	Died of pneumonia 10 weeks after stroke
Dooly and Smith [4]	2	6/M	Two brain-stem TIAs: weeks later hemiparesis, trunk and gait ataxia	Angiogram: basilar art. occlusion	99% recovery at 3 months
Ouvrier and Hopkins [22]	3	9/M	3 months of brain-stem TIAs; III nerve, hemiparesis and ataxia	Angiogram: bilateral vertebral occlusion (complete on right)	Moderate dysarthria and ataxia at 3 months
	4	7/M	Left hemiparesis, anisocoria	Angiogram: left vertebral occlusion	Marked incoordination of left arm at 12 months;
De Vivo and Farrell [3]	5	10/M	8 months of brain-stem TIAs; right hemiparesis and dysmetria	Angiogram: bilateral vertebral occlusion, left > right	Left arm ataxia at 12 months
Latchaw et al. [18]	6	7/M	Right hemiparesis, dysarthria and diplopia; much worse 48 h after admission	Angiogram: left basilar artery occlusion	Spastic quadriplegia, aphonic; mentally alert 4 years later
	7	11/M	Left hemiparesis; left XII; semicomatose. Mild head injury; 24 h PTA	Angiogram: basilar occlusion	Left hemiparesis and psychosocial delay at 2 years
Klein et al. [16]	8	8/M	Vertigo, horizontal nystagmus, hemiparesis	Angiogram: partial vertebral occlusion	Mild nystagmus and occasional vertigo at 4 months
Pascual-Castroviejo et al. [24]	9	3/M	Bilateral VII; unable to stand; bilateral dysmetria	Angiogram: bilateral vertebral occlusion	Normal examination at 1 month and 3 years
Ackerman et al. [1]	10	10/M	Diplopia, vertigo, unable to stand. Recovered in 5 days; 10 days later: mute, quadriplegic and facial diplegia	CT: pontine infarct Angiogram: basilar occlusion	Mild quadriplegia at 1 month
Mori et al. [21]	11	13/M	Right hemiparesis; aphonic	CT: left pontine infarct Angiogram: basilar occlusion	Marked improvement at 1 month
Jain et al. [14]	12	16/F	Brain-stem TIAs for 2 months; dysarthria, ataxic gait, hemiplegia	CT: possible cerebellar infarction Angiogram: basilar occlusion	Marked hemiparesis, bilateral ataxia, and dysarthria at 1 month
Curless (present study)	13	12/F	Sudden flaccid quadriplegia, bilateral VII, aphonic	CT: normal Angiogram: basilar occlusion	Right hemiparesis and mild dysarthria at 1 year
	14	7/M	Drop attack progressing to coma; vertical nystagmus, quadriplegia	CT (at 2 days): multiple infarcts including pons and midbrain Angiogram: basilar occlusion	Quadriplegia and possible "locked-in"; state at 1 month
	15	14/M	Unable to walk or talk within minutes. LMN VII, left gaze preference, left hemiparesis	CT: normal MRI: right pontine infarct Angiogram: normal	Beginning ambulation and dysarthric at 2 weeks

On examination he was comatose with no response to verbal or visual stimuli. Vital signs revealed a normal respiratory pattern and blood pressure of 110/70. Noxious stimulus of the right arm produced flexion withdrawal. Midline noxious stimulation resulted in extension posturing of all extremities. Bilateral extensor plantars were present. Ocular examination revealed normal fundi, skew deviation of the eyes, and upbeating nystagmus, Arachnodactyly was not present.

CT on admission was normal except for a small enhancing area in the right occipital lobe. Four-vessel angiography revealed complete occlusion of the basilar artery, just distal to the anterior inferior cerebellar artery origin. The left posterior cerebral artery was also occluded (Fig. 1). CT scan 2 days following angiography showed areas compatible with infarction in the left thalamus, left occipital lobe, midbrain and pons (Fig. 2). No right occipital abnormality was seen.

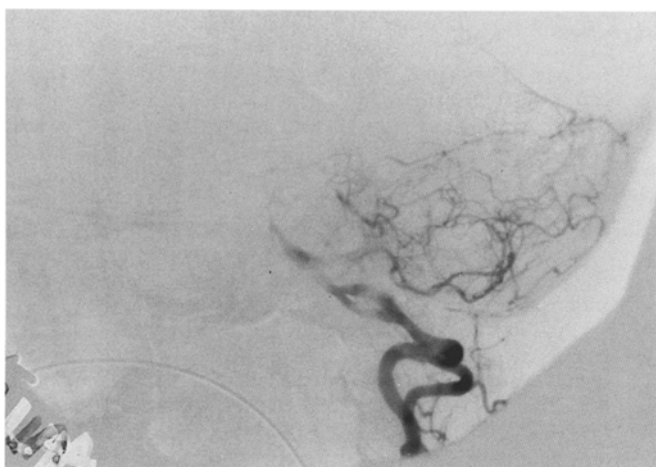
The following laboratory studies were normal: urine for homocystine, hemoglobin electrophoresis, PTT and platelet count, antinuclear antibody (ANA), syphilis serology (FTA -abs; fluorescent

treponemal antibody-absorption), purified protein derivative, serum complement, serum electrolytes, complete blood count and ammonia level. Normal cardiac evaluation included auscultation, ECG and echocardiogram.

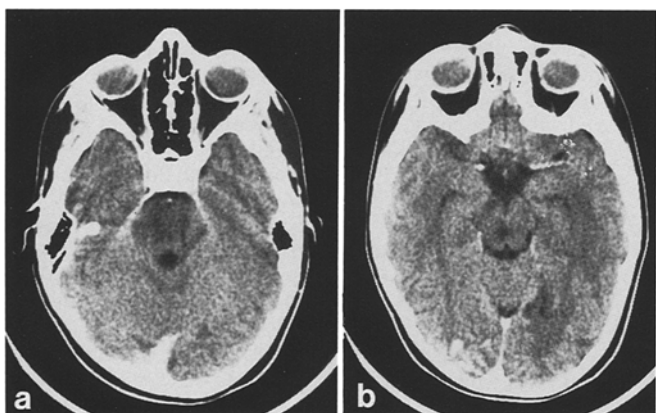
After 1 week he was discharged to a regional center. At that time he was quadriparetic with some characteristics of a deafferented, locked-in syndrome. Evaluation 4 years later revealed spastic lower extremities, left greater than right, and an inability to stand. The right arm was nearly normal in function, but marked spasticity was present in the left arm. Neck strength was poor and moderate dysphagia and dysarthria persisted.

### Case 15

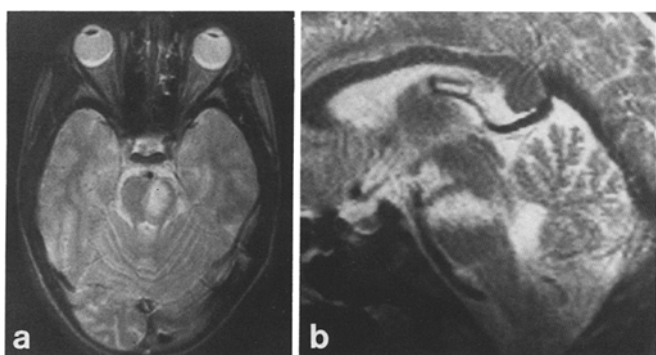
A 14-year-old black male was brought to the emergency room on 12 February 1989 because 1 h earlier, while watching television, he complained of "feeling bad all over." Within a few moments he was unable to speak or stand. There was no history of previous signifi-



**Fig. 1.** Vertebral angiography of case 14 demonstrates a complete occlusion of the basilar artery just distal to the origin of the anterior inferior cerebellar artery



**Fig. 2 a, b.** CT of case 14 with 5-mm cuts through the posterior fossa reveals areas of decreased attenuation in the midbrain (a) and pons (b) compatible with infarctions



**Fig. 3 a, b.** T2-weighted magnetic resonance imaging of case 15 reveals a right pontine lesion of high signal intensity in a transaxial plane (a) and sagittal plane (b) compatible with an infarction

cant medical illnesses. The family history revealed no neurological disorders of childhood or young adults.

Examination demonstrated normal vital signs including a blood pressure of 120/60. He was stuporous, followed simple commands, but refused or was unable to speak. Cranial nerve examination demonstrated a left facial weakness. By the 3rd hospital day this was identified as a lower motor neuron deficit. He had a left conjugate

gaze preference and a left hemiparesis. There was no arachnoidactyly.

CT scan was normal, but magnetic resonance imaging (MRI) revealed a right pontine lesion compatible with an ischemic infarct (Fig. 3). Four-vessel angiography was normal. The following studies were also normal: ECG, echocardiogram with bubble technique, prothrombin time and PTT, platelet aggregation studies, anticardiolipin antibody, ANA and a double-stranded DNA, plasma lipid profile, urine amino acids, and an electroencephalogram. A cardiac Holter monitor revealed frequent premature ventricular contractions.

Gradual neurological improvement was noted over a 10-day hospitalization. He was discharged to a rehabilitation facility with dysarthria, a left hemiparesis and early attempts at ambulation. Eighteen months after the stroke no neurological deficit could be found. The patient indicated complete recovery 2 months following discharge from the hospital.

## Discussion

These cases are examples of idiopathic brain-stem infarction without clinical evidence for cerebellar or cerebellar outflow involvement. Two additional children with brain-stem infarctions were discovered in reviewing 13 years of our records, but both had identifiable etiologies: one had chronic, repeated, self-inflicted neck trauma producing a vascular abnormality of the vertebral artery, and the other had CNS tuberculosis. A third case was excluded because the diagnosis was complicated migraine, and only a cerebellar lesion was demonstrated in spite of prominent brain-stem signs combined with ataxia. The clinical description suggested basilar artery migraine progressing from transient ischemic attacks to an infarction [5, 9].

A 20-year review of the literature combined with our 3 cases produced 15 examples of idiopathic brain-stem ischemia with or without cerebellar symptoms and signs developing prior to 16 years of age (Table 1) [1, 3, 4, 8, 14, 16, 18, 21, 22, 24]. Only 2 of these were females: a 16-year-old with a basilar artery occlusion (case 12), and a similar lesion at 12 years of age in the current report (case 13). The age ranged from 3 to 16 years with a relatively even distribution except for a cluster of 4 cases at ages 6 and 7.

Because of the time covered by the review, a variety of radiographic techniques were relied upon to confirm the diagnosis. Case 15 is the only one in which MRI was used, and in this patient the CT and angiogram were normal. In 9 of the 15 neither CT nor MRI was available so the diagnosis was a combination of clinical examination with posterior circulation angiography or a post-mortem examination as in case 1. Of the remaining 6, 5 had abnormal angiograms and 4 of these had abnormal CTs. Angiography in case 13 demonstrated a basilar artery occlusion, but the early-generation CT failed to reveal an abnormality. As noted earlier, case 15 had a normal CT and angiogram, but a large pontine lesion was seen on MRI.

Of the 12 cases with abnormal angiograms, 5 involved a vertebral artery, 5 had basilar artery occlusions. Both females had basilar artery occlusions. As expected, MRI provided the clearest image of the brain stem, and in case 15 demonstrated a structural lesion in the absence of

a CT abnormality. Angiography failed to identify evidence for vasculitis or a vascular malformation.

Of the 6 cases with computerized imaging studies (cases 10–15) 3 had pontine lesions, 1 had both a pontine and midbrain lesion, 1 had a questionable cerebellar lesion, and 1 was normal. On follow-up, 2 of the patients with pontine lesions demonstrated only a mild residual deficit, but the remaining 4 retained a severe disability. Unfortunately the follow-up duration was short in many cases.

The etiology of non-embolic brain infarcts in children includes sickle cell disease, homocystinuria, vascular malformations and vasculitis [6, 28]. Recent descriptions add chronic disorders such as nephrotic syndrome [12], neoplasia [23], mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke (MELAS) [25], and toxins including cocaine [17] and phenylpropanolamine [7]. Other mechanisms for stroke in children include the hypercoagulable states of protein C and S deficiency [13, 20, 26, 27, 29], antiphospholipid antibodies [15, 19] and platelet dysfunction [2]. Two-dimensional echocardiography revealing silent atrial septal defects responsible for central embolization without symptomatic distal venous thrombosis has been reported in adults but not in children [11]. Studies for a hypercoagulable state and two-dimensional echocardiography were not done on any of the cases obtained from the literature the first two cases in this report. A careful history and examination will provide clues to many of these etiologies, but without an awareness of the diagnostic possibilities, the questions asked and laboratory studies obtained will be inadequate.

In the presence of platelet dysfunction, we recommend aspirin and or dipyridamole therapy as prophylaxis following an idiopathic infarction. The adult dose for aspirin is 5 grains once a day and for persantin 75 mg 3 times a day. Halving these adult dosages is recommended for children weighing less than 30 kg. Unfortunately, there is no long-term follow-up study which proves the effectiveness of this treatment. New radiographical techniques including MRI angiography provide non-invasive methods for localizing the lesion, but much more information regarding pathogenesis is needed before effective prophylactic or therapeutic measures can be contemplated.

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