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Neonatal Pontomedullary Disconnection with Aplasia or Destruction of the Lower Brain Stem: A Case of Pontoneocerebellar Hypoplasia?

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Summary: We report a neonate who presented with marked hypotonia and absent suck reflex. MR demonstrated complete absence of the pons as well as absence of a basilar artery flow void. Our case exhibits features similar to those described in previous reports of pontoneocerebellar hypoplasia, but with a more severe degree of pontine involvement. The associated vascular findings suggest a vascular insult to the brain stem as the cause.

Index terms: Brain, abnormalities and anomalies; Infants, newborn

Cerebellar atrophy in conjunction with brain stem atrophy has been reported in adults and children. These finding may be seen in several different disease processes but perhaps best characterize pontoneocerebellar hypoplasia. We report a case with severe cerebellar atrophy and complete absence of the lower pons with disconnection of the upper and lower brain stem. We discuss these findings in our case with respect to previous reports.

Case History

N.B. was a full-term girl born by vaginal delivery at 41 weeks of gestation to a 21-year-old mother who was gravida 2 para 1. Pregnancy was unremarkable, and the mother was rubella positive. Apgar score was 7/7 at 1 and 5 minutes. Birth weight was 3.2 kg. Examination shortly after birth revealed marked temperature instability with swings in temperature from 35°C up to 41°C. There were no particular dysmorphic or neurocutaneous features. Neurologic examination was markedly abnormal. The infant did not visually fixate or follow. Vestibular ocular reflexes were absent on either side. The corneal responses were absent, and there was no sucking or rooting response. The limbs withdrew from pain but were not accompanied by any facial response. There was marked limb hypotonia, which intermittently increased. A urine toxicology screen was negative, and there was no cocaine found in the hair. Investigation for infections was unremarkable, as was the cerebrospinal fluid. Brain stem auditory evoked responses demonstrated no reproducible responses from either ear at a maximum intensity of 90 dB, and somatosensory evoked potentials using the right median nerve showed reasonably well-formed potentials at Erb's point and at the C-2 cervical level, but no reproducible responses were found at the scalp.

Computed tomography demonstrated a widened prepontine cistern and cerebellar hypoplasia (Fig 1A). Magnetic resonance (MR) revealed absence of the pons and vermian as well as cerebellar hemispheric hypoplasia (Fig 1B). There was no evidence of abnormal signal in the brain stem or cerebellum on the T2-weighted images (Fig 1C). No heterotopias were noted. No flow void was visible in the expected region of the basilar artery or distal vertebral arteries (Fig 1D). Based on the T1-weighted images there was evidence of normal myelination for age.

Angiography was refused by the family. The patient was discharged from the hospital and died at home at 6 weeks of age. No autopsy was performed.

Discussion

We attempted to classify this case with respect to previously described entities. There are several we considered. Severe vermian atrophy can be seen with Joubert syndrome, but not severe brain stem atrophy. The low position of the torcula and absence of a posterior fossa cyst in the case we describe also would serve to exclude the more common Dandy-Walker malformation. Olivopontocerebellar atrophy is not thought to occur in the neonatal period, because it reflects a degenerative process occurring over the course of years. There are, however, three entities in which marked brain stem as well as cerebellar hypoplasia have been described in neonates. These are pontoneocerebellar hypoplasia, brain stem necrosis, and Moebius syndrome.

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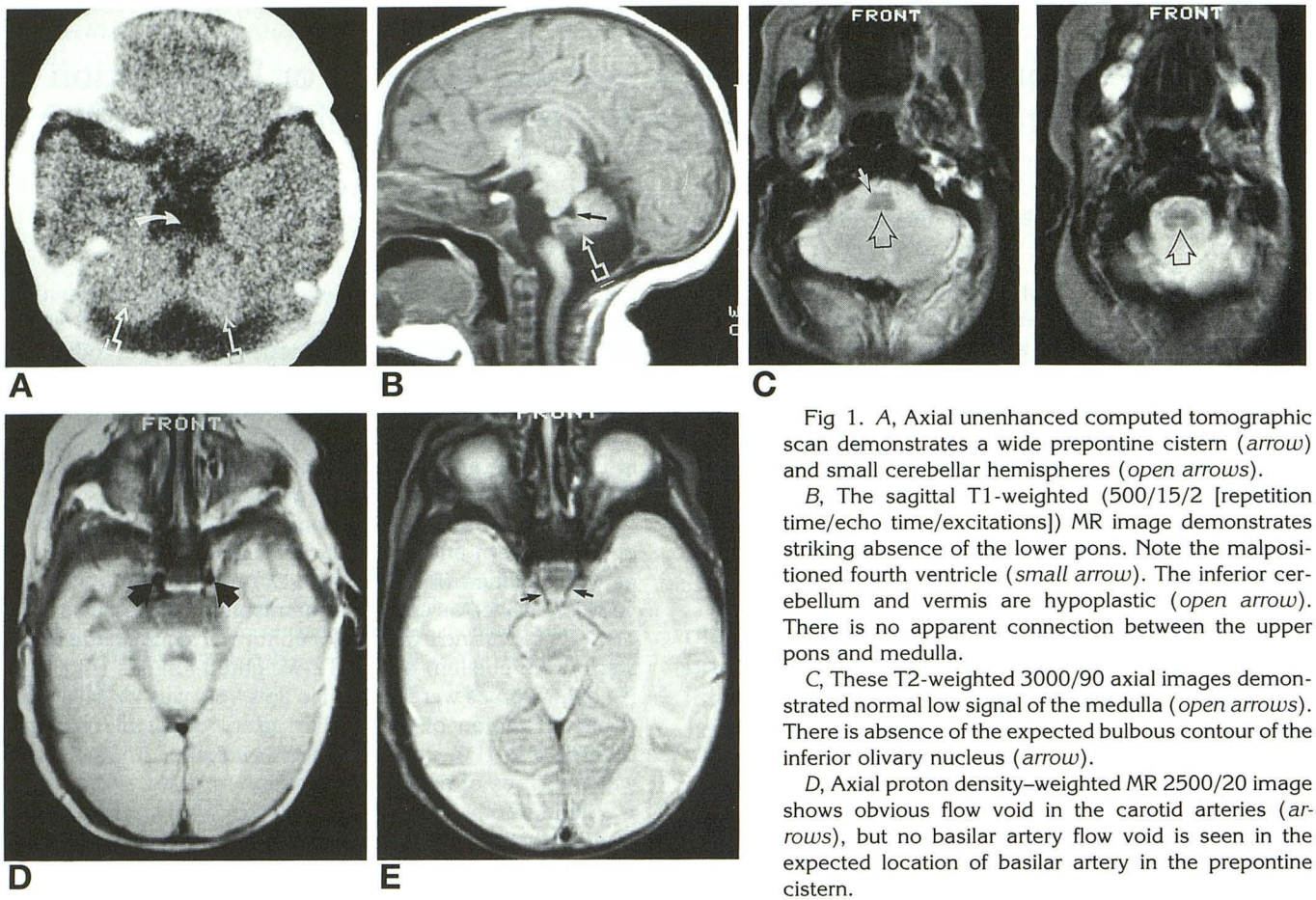

Fig 1. *A*, Axial unenhanced computed tomographic scan demonstrates a wide prepontine cistern (*arrow*) and small cerebellar hemispheres (*open arrows*).

B, The sagittal T1-weighted (500/15/2 [repetition time/echo time/excitations]) MR image demonstrates striking absence of the lower pons. Note the malpositioned fourth ventricle (*small arrow*). The inferior cerebellum and vermis are hypoplastic (*open arrow*). There is no apparent connection between the upper pons and medulla.

C, These T2-weighted 3000/90 axial images demonstrated normal low signal of the medulla (*open arrows*). There is absence of the expected bulbous contour of the inferior olivary nucleus (*arrow*).

D, Axial proton density–weighted MR 2500/20 image shows obvious flow void in the carotid arteries (*arrows*), but no basilar artery flow void is seen in the expected location of basilar artery in the prepontine cistern.

E, Axial proton density–weighted MR 2500/20 image shows flow in patent posterior communicating arteries bilaterally (*arrows*) supplying the posterior cerebral arteries.

In a 1917 paper, Brun described a case with features he characterized as "ponto-neocerebellar hypoplasia" (1). Since that time there have been many reports in the literature of similar cases. Although pathologic findings vary considerably in these cases, there are some consistent features characterizing this entity: marked reduction in the number of neurons in the pontine, arcuate, inferior olivary, and dentate nuclei, and atrophy of the middle cerebellar peduncle, basis pontis, and neocerebellar white matter. The involvement of the dentate nuclei may be severe, with a fetal pattern of clusters or islets of cells. Clinically, all cases demonstrated mental retardation.

Previous reports describe both familial cases (2–5) and isolated ones more likely caused by prenatal insult (1, 6–8). The later seem more relevant to our case. Several mechanisms have been proposed for the pathologic findings in such cases. These seem roughly divided into early and late in utero insults. This differentiation seems based on the appearance of the dentate nucleus. In the case Brun described, there was a fetal pattern of clustering of cells, which suggested to him an early insult. Later reports do not support this observation and argue for a later, second or third trimester insult of uncertain nature (7, 8).

There were several features we believe differentiate our case from previous reports of similar cases. Previous cases of pontoneocerebellar hypoplasia demonstrated poor suck, as compared with the absent suck in our case, and presented later, after the neonatal period. Although the name *pontoneocerebellar hypoplasia* emphasizes the greater involvement of the cerebellar hemispheres as compared with vermis, we found just the opposite in this case.

There is one report of two cases of fetal brain stem necrosis associated with cerebellar atrophy (9). These patients were noted to be markedly impaired at birth. This is different from pontoneocerebellar hypoplasia, in which the

earliest reported clinical presentation was 9 days. Focal brain stem necrosis has been described after cardiac arrest and severe hypotension (10). Based on the location and character of the lesions in these two cases, the mechanism was presumed to be an ischemic or anoxic insult to the brain stem.

Our third consideration was Moebius syndrome. Clinically our case does not fit the classic description of this syndrome: facial palsy and external opthalmoplegia without gross structural brain abnormalities. However, there are exceptions described in the literature in which there was atrophy of the pons, cerebellum, or both (11–13). In one case there was marked hypotonia and hypoplasia of the descending tracts (12). Although there seem to be several mechanisms that may cause this syndrome, many authors argue for a primary vascular insult to the brain stem. One case was felt to have findings at autopsy most consistent with basilar artery occlusion (14).

There are two important features of this case that differentiate it from these previously described cases. First, although brain stem atrophy was noted in many cases, we could find no report of a case in which there was complete absence of the upper brain stem. Second, by MR criteria, there was no evidence of vertebrobasilar flow in this patient. Although one could argue this reflects diminished flow in response to reduced demand secondary to brain stem parenchymal loss, it seems unlikely because the vertebrobasilar circulation supports the midbrain, thalamus, and occipital lobes as well. The posterior cerebral artery is a major branch of the internal carotid artery in approximately one third of all individuals, but unilaterally. Although the posterior fossa is supplied by the carotid artery in early fetal development, the adult pattern of circulation is established by 9½ weeks in utero. There was MR evidence of carotid flow to the posterior cerebral arteries by way of patent bilateral posterior communicating arteries (Fig 1E). This could supply the superior cerebellar arteries either by way of reflux through the basilar tip or by direct anastamotic connections. This might explain the greater involvement of the inferior cerebellar hemispheres.

It remains conjecture whether our case represents an entirely new entity or a severe variation of one of these previously described syndromes, several of which are thought to reflect a late in utero ischemic insult to brain stem nuclei. We believe that in our case MR demonstrated severe brain stem and cerebellar atrophy in conjuction with absent vertebrobasilar flow, suggesting a vascular cause.

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