

# Asymptomatic Tonsillar Herniation in a Neonate With Cleidocranial Dysplasia

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## KEY WORDS

apnea, bone defects, brain imaging, cleidocranial dysplasia, tonsillar herniation

## ABBREVIATION

CCD—cleidocranial dysplasia

Dr Myers drafted the initial manuscript and coordinated revisions; Drs Thomas and Scantlebury reviewed and revised the manuscript; Dr Wei prepared the figures for the manuscript and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

[www.pediatrics.org/cgi/doi/10.1542/peds.2013-0478](http://www.pediatrics.org/cgi/doi/10.1542/peds.2013-0478)

doi:10.1542/peds.2013-0478

Accepted for publication Jul 23, 2013

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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**FINANCIAL DISCLOSURE:** The authors have indicated they have no financial relationships relevant to this article to disclose.

**FUNDING:** No external funding.

**POTENTIAL CONFLICT OF INTEREST:** The authors have indicated they have no potential conflicts of interest to disclose.

## abstract

A male neonate was antenatally diagnosed with cleidocranial dysplasia on the basis of prenatal ultrasound findings and molecular testing of the *RUNX2* gene. The patient presented with urosepsis at 24 days of life and subsequently developed apneas after endoscopic examination of the vocal cords. Computed tomography and MRI studies of the head revealed crowding of the posterior fossa with tonsillar and uncus herniation. Apneas were initially thought to be related to brainstem compression; however, the patient responded immediately to caffeine and subsequently stabilized with antibiotic therapy. To our knowledge, this is the first published MRI study of the brain of a neonate with cleidocranial dysplasia to demonstrate the striking posterior fossa findings seen secondary to the reduced bony skull structures. However, despite the dramatic herniation, brainstem function was not compromised. *Pediatrics* 2014;133:e455–e457

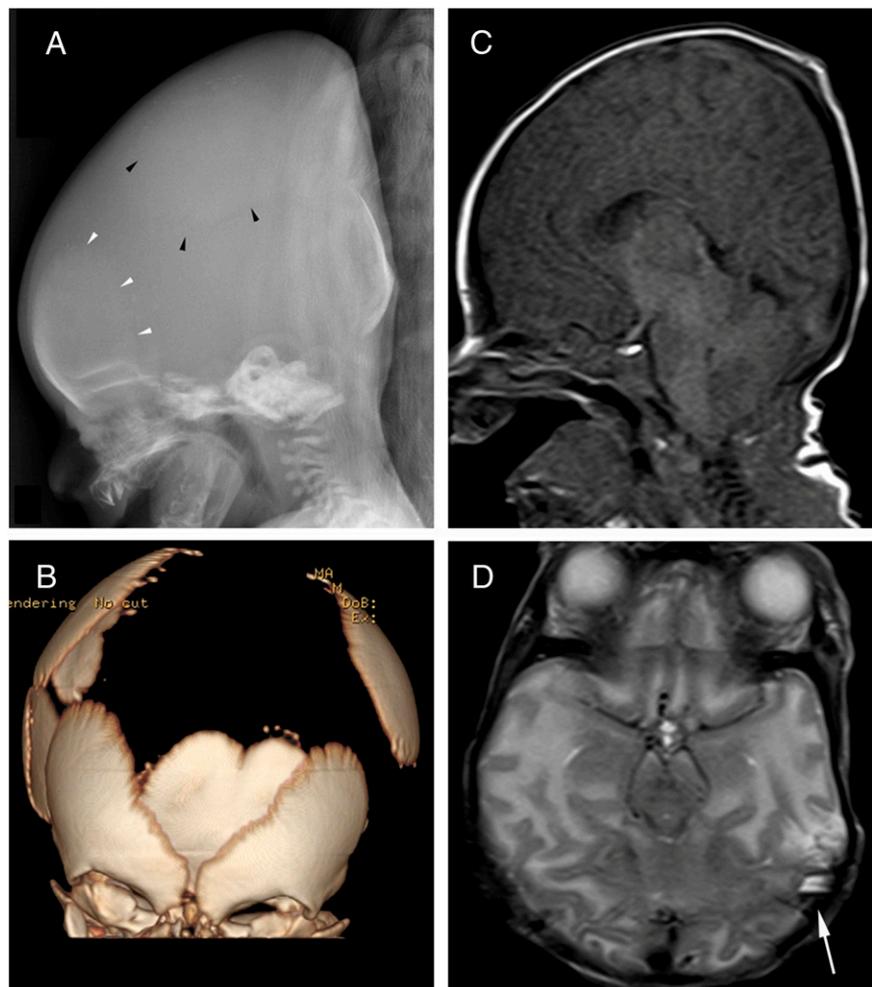
Cleidocranial dysplasia (CCD; Online Mendelian Inheritance in Man no. 119600) is an autosomal dominant inherited disorder of bone formation characterized by hypoplastic or absent clavicles and deficient skull development manifested by open sutures and large fontanels with delayed closure. The early skull anomalies are due to delayed ossification and may persist. Affected individuals may have short stature and a variety of other skeletal or dental anomalies. The brain is not usually affected, and cognitive development is typically normal or near normal.

### PATIENT PRESENTATION

A male fetus was antenatally diagnosed with CCD due to characteristic ultrasound abnormalities and molecular testing of the *RUNX2* gene by amniocentesis, which showed a pathogenic mutation. Postnatal comparative genomic hybridization microarray revealed a 7.76-Mb deletion at the 6p12.1–p12.3 region that confirmed the terminal *RUNX2* gene deletion detected on the initial molecular test. Given the large size of the deletion, numerous other genes were affected; however, none are currently known to be associated with any particular medical condition when deleted. Parental testing was normal, confirming that the deletion was de novo.

At 36 weeks' gestation, the infant was born via uncomplicated vaginal delivery. Examination showed wide fontanels and clavicular abnormalities characteristic of CCD; however, the infant appeared otherwise well. A lateral skull radiograph taken on day 2 of life showed the expected delayed ossification of skull bones (Fig 1A).

At 24 days of life, the infant presented with poor feeding and lethargy and was diagnosed with *Escherichia coli* urosepsis. A pattern of periodic breathing was noted, prompting an endoscopic study of the vocal cords. After this



**FIGURE 1**

Cranial radiograph, computed tomography (CT), and MRI. A, Lateral radiograph of the skull taken at the age of 2 days shows delayed ossification of the membranous part of the skull. The margins of the ossified portion of the frontal bone (white arrowheads) and parietal bone (black arrowheads) are barely identifiable on this lateral radiography. The cranium is deformed due to lack of bony support. B, On the three-dimensional surface-rendering CT image obtained at 24 days of life, the extremely widened skull sutures are better visualized. C, On the sagittal T1-weighted magnetic resonance image obtained at 24 days of life, a crowded posterior cranial fossa is seen. The fluid spaces including the cisterna magna, prepontine cistern, interpeduncular cistern, and fourth ventricle are all effaced. D, Axial T2-weighted image obtained on the same day shows effaced perimesencephalic cisterns and cerebral sulci. A small extraaxial hematoma with fluid-fluid level is present in the left posterior temporal convexity (arrow).

study the infant developed episodes of apnea (cessation of inspiratory airflow for >20 seconds) and bradycardia (heart rate <80 beats per minute) requiring admission to the PICU. The infant's neurologic examination did not show focal abnormalities at any point. Computed tomography and MRI studies of the brain were performed, and the neurology service was consulted to rule out the possibility that the apneas were of ictal origin. The computed

tomography study revealed the strikingly wide sutures and fontanels characteristic of CCD (Fig 1B). The MRI revealed brain parenchyma with normal myelination; however, the posterior fossa was crowded with tonsillar herniation and effacement of basal cisterns (Fig 1 C and D). An extraaxial hematoma was also noted (Fig 1D).

The infant's apneas and bradycardias improved after treatment with a 4-day course of caffeine and antibiotics for his

urinary tract infection. However, he did return to the PICU briefly at 34 days of life with respiratory distress secondary to a viral upper respiratory illness. There was no need for neurosurgical intervention, and a follow-up pneumogram did not show any evidence of chronic respiratory abnormalities.

## DISCUSSION

This case was interesting in that brainstem compression secondary to herniation initially appeared to be a likely cause of the apneas and bradycardias. This hypothesis became much less likely after the patient displayed rapid clinical improvement after treatment with caffeine. The underlying cause of his respiratory difficulties was ultimately thought to be a combination of intercurrent illness and irritation from the endoscopic examination. The deterioration may have been exacerbated by the combined effects of the other deleted genes, although none have been specifically associated with neonatal respiratory difficulty.

The striking imaging findings were thought to simply represent the brain's normal resting position in a skull with abnormal bone mineralization. The finding of a small extraaxial hematoma without a history of trauma illustrates

the vulnerability to parenchymal damage in individuals with CCD. For this reason, protective helmets are recommended at younger ages.<sup>1</sup>

The abnormal posterior fossa findings in CCD have been recognized for some time, as evidenced by Staffeldt's 1955 description as follows:

"... impeded growth of the basilar part of the skull, especially in the transverse diameter; impression of basis cranii with kyphosis of the basilar part; giving a foramen magnum which is directed forward to a great extent (negative basilar angle) ...."<sup>2</sup>

Despite the long historical understanding of this disorder, to our knowledge there are no neonatal radiologic characterizations of posterior fossa findings in the literature. A review found only 1 neonatal case report including an MRI study and this report did not include views of the posterior fossa.<sup>3</sup> The sequelae of the bony posterior fossa abnormalities have been better characterized in older patients, including reports of Chiari I malformation and syringomyelia,<sup>4–5</sup> as well as atlantoaxial subluxation and subsequent myelopathy.<sup>6</sup>

Patients with CCD generally do well in the neonatal period, although the report from Gardner et al,<sup>3</sup> as well as the patient presented here, suggests that they may be more susceptible

to intracranial hemorrhage. This vulnerability likely relates to the relative lack of brain parenchyma protection due to the underdeveloped skull. Oyer et al<sup>7</sup> described a patient with a CCD phenotype who died in the neonatal period secondary to complications of in utero intraventricular hemorrhage and subsequent hydrocephalus and hypoxic injury; however, there was no clear causal link between CCD and the intraventricular hemorrhage. Isolated respiratory distress and swallowing difficulties have been described in 1 report but are not typical.<sup>8</sup>

## CONCLUSIONS

This is the second published MRI brain imaging of a neonate with CCD and the first to show the striking posterior fossa findings seen secondary to the reduced bony skull structures. Although the imaging suggests brainstem compression, there is no apparent clinical correlate. The most common neurologic sequelae in individuals with CCD are myelopathy and syringomyelia; however, these usually present in adulthood. When neonates with CCD present with respiratory symptoms, an alternative, nonneurologic diagnosis should be considered.

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DOI: 10.1542/peds.2013-0478 originally published online January 20, 2014;

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