A Three-Month-Old Achondroplastic Baby with both Obstructive Apneas and Central Apneas

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A 3-month-old infant girl with achondroplasia presented with a 2-month history of snoring without breathing pauses, nasal flaring, chest retraction, or cyanosis. The baby was born at 38 weeks gestation to a 33-year-old mother via elective cesarean section. Apgar score was 9. The father is achondroplastic. At 6 months gestation, fetal ultrasound was consistent with achondroplasia; prenatal and perinatal history was otherwise unremarkable.

Physical exam revealed an alert playful baby with macrocephaly, head circumference of 44 cm (50% percentile achondroplasia chart)¹; mid-face hypoplasia; and large anterior and posterior fontanelles. Upper airway was Mallampati IV with 2+ tonsillar enlargement. No excessive palatal arching was noted. Neurologic exam revealed mild hypotonia, lumbar kyphosis, and normal deep tendon reflexes throughout. The remainder of the exam was normal.

Computerized tomography (CT) of the head with 3-dimensional reconstruction showed widening of the metopic, coronal, and sagittal sutures, with pat-

ent anterior and posterior fontanelles. Mild foramen magnum narrowing was noted without evidence of cervicomedullary junction stenosis (**Figure 1**). Diagnostic polysomnogram (PSG) revealed a total sleep time (TST) apnea-hypopnea index (AHI) of 4, with 15 obstructive apneas and 15 central apneas; NREM AHI of 1.8; and REM AHI of 11.6. The apneas were not associated with bradycardia; the lowest heart rate for the night was 95 bpm. The apneas were brief and met American Academy of Sleep Medicine Scoring Manual criteria for duration with 2 missed breaths. The central apneas were associated with 3% oxygen desaturation. The minimum oxygen saturation was 91%. There was no evidence of hypoventilation. The end-tidal CO₂ remained below 50 mm Hg for the entirety of the night, with an average of 35 mm Hg.

QUESTION:

Which of the findings mentioned above have been commonly associated with achondroplasia?

Figure 1—Three-dimensional reconstructed computerized tomography of the head in a patient with achondroplasia

(A) Open anterior fontanelle with a transverse diameter of 80 mm and an anterior-posterior diameter of 127 mm. (B) Open posterior fontanelle with a transverse diameter of 46 mm and an anterior-posterior diameter of 19 mm. (C) Small short cranial base with mild narrowing of the foramen magnum: 16.8 mm by 18.8 mm.

ANSWER:

The following findings are common in children with achondroplasia: macrocephaly; mid-face hypoplasia; persistent open fontanelles; lumbar kyphosis; hypotonia; narrow cervicomedullary junction (CMJ), and both central apneas and obstructive apneas.

DISCUSSION

Achondroplasia is an autosomal dominant mutation in the fibroblastic growth factor receptor-3 (FGFR3) gene that affects 1 in 30,000 children and leads to underdevelopment of the long bones formed by endochondral ossification.² Achondroplasia is a clinical diagnosis based on history, physical examination and skeletal radiography. Prenatal diagnosis is possible through ultrasound or by DNA testing. Most cases are sporadic and associated with increased paternal age. Skeletal features include: macrocephaly with frontal bossing, short stature, proximal short limbs (rhizomelia), midface hypoplasia, and large fontanelles.

A large fontanelle diameter, rapidly increasing head circumference, or radiologic evidence of ventriculomegaly should prompt evaluation for hydrocephalus. In most cases of achondroplasia, a communicating hydrocephalus develops from venous outflow obstruction at the base of the skull and does not require shunting.³ Hydrocephalus has been found in 28% of achondroplastics with obstructive sleep apnea (OSA), suggesting a link between hydrocephalus and sleep disordered breathing (SDB) in patients with achondroplasia.⁴

Midface hypoplasia and skull base deformities in achondroplasia due to abnormal ossification may predispose these children to SDB and otologic complications. Otologic complications occur in 68% of achondroplastics and include recurrent acute otitis media, chronic otitis media, tympanic membrane perforation, and hearing loss.⁵ Up to 75% of achondroplastic children have SDB consisting of obstructive apneas, central apneas, or both. Obstructive apneas are thought to be associated with mid-face hypoplasia and reduction in the nasopharyngeal space.⁶ Nocturnal hypoxemia ($\text{SpO}_2 < 90\%$) without apnea has been found in up to 44% of children with achondroplasia and may represent restrictive lung disease, secondary to a combination of hypotonia, thoracolumbar kyphosis, and a small thoracic cavity.⁷

Babies with achondroplasia have significantly smaller foramen magnum diameters than unaffected babies, and this difference persists across the lifespan.⁸ Both obstructive apneas and central apneas have been reported in achondroplastics with foramen magnum stenosis. Compression of the lower motor neurons innervating the respiratory muscles may result in obstructive apneas, while compression of the medullary respiratory centers may lead to central apnea. The increased apneic events, paired with a decreased arousal response may contribute to the increased risk of sudden death, reported in up to 5% of achondroplastics.

Other neurologic consequences of cervicomedullary compression (CMC) include myelopathy with mono-, hemi-, para- or quadriplegia and hyperreflexia/clonus, hypotonia, and dysphagia due to unilateral or bilateral pharyngeal paresis. It

is unclear whether the absolute dimension of the foramen magnum is helpful in determining which patient will benefit from decompression.⁹ The American Academy of Pediatrics recommends an initial evaluation with a thorough neurologic history, complete physical examination, neuroimaging, and polysomnography, with subsequent annual screening for hyperreflexia and sleep apnea.¹ No specific recommendations are given regarding home apnea monitors.

Symptomatic patients with notable CMC on neuroimaging (i.e., a narrow foramen magnum and/or T2 weighted image hyperintensity on magnetic resonance imaging [MRI] of the brainstem/cervical spinal cord) should undergo cervicomedullary decompression (CMD).¹⁰ CMD has shown to improve the central apneas and the degree of oxygen desaturation.⁷ The most common surgical complication of CMD is CSF leak and infection. Recurrence of stenosis has also been reported.⁹

Management of SDB with tonsillectomy/adenoidectomy or continuous positive airway pressure (CPAP) therapy has shown improvement in respiratory indices, arousal indices, oxygen saturation, and hypercapnia.^{4,7} Treatment of SDB may also have neurocognitive benefits in some patients.¹¹ Oxygen supplementation has been used in premature babies or children with restrictive lung disease. Tracheostomy is effective in severe or emergent cases.⁷

Respiratory stimulants such as caffeine and doxapram, commonly used for apnea of prematurity and respiratory depression after anesthesia, could be a future treatment option in babies with achondroplasia, due to the stimulation of breathing on the medullary respiratory centers and carotid bodies; however, they have not been evaluated for use in this patient population.¹²

Our patient underwent three-dimensional computerized tomography (CT) of the cervicomedullary junction without sedation instead of MRI with sedation, because of faster image acquisition time with CT than MRI, and the risks associated with sedating an infant patient with SDB in order to acquire MRI images.

Benefits and risk of CPAP and CMD were discussed with the parents; both the parents and sleep medicine physicians preferred to wait a few months and obtain a repeat PSG. PSG performed 3 months later showed AHI of 0.4, and minimum oxygen saturation of 95%. The improvement in AHI may be attributed to maturity of the brainstem. Prior studies have demonstrated that SDB is more prevalent in infants younger than 12 weeks of age.¹³

It is the opinion of the authors that in a neurologically asymptomatic baby with achondroplasia, evaluation of apnea with a PSG should be delayed until at least 6 months of age. Our patient is currently stable, does not show signs or symptoms of medullary compression, and continues close follow-up by a multidisciplinary medical team (neurologist, sleep medicine physician, pediatrician, and geneticist).

CLINICAL PEARLS

1. The American Academy of Pediatrics recommends that every infant with achondroplasia should be screened for CMC. The assessment should include a thorough neurologic history, physical, neuroimaging (CT or MRI), and polysomnography.

2. Repeating neuroimaging should be considered for evaluation of hydrocephalus or symptoms of CMC.
3. SDB in patients with achondroplasia can include central apnea, obstructive apnea, and hypoventilation
4. Treatment options for SDB in achondroplasia include: cervicomedullary decompression, tonsillectomy and adenoidectomy, CPAP, oxygen supplementation, and tracheostomy.
5. Infants with achondroplasia will benefit from the intervention of a multidisciplinary team of pediatricians, geneticists, sleep medicine physicians, pulmonologists, neurologists, otolaryngologists, neuroradiologists, and neurosurgeons.

CITATION

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