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CASE REPORTS

# Sleep Apnea in Hurler Syndrome: Looking Beyond the Upper Airway

Sumera Shaikh Solaiman, MD[1]; Daniel Scott Rifkin, MD[2]; Harish Rao, MD[3]

*[1]Department of Pediatrics, Pennsylvania State University Children's Hospital, Hershey, PA; [2]Division of Pediatric Pulmonology, Pennsylvania State University Children's Hospital, Hershey, PA; [3]Sleep Disorders Center, Pennsylvania State University, Hershey, PA*

This case involves a 13-month-old male with Hurler syndrome. Due to oxygen desaturations during sleep, this patient was referred for polysomnography, which revealed severe mixed sleep apnea (apnea-hypopnea index [AHI] 72 events/h). Because sleep apnea in patients with Hurler syndrome is frequently attributed to upper airway obstruction, he was referred to otolaryngology. Prior to his evaluation by otolaryngology, he underwent ventriculoperitoneal (VP) shunt placement, which had been scheduled due to hydrocephalus on brain magnetic resonance imaging (MRI). After VP shunt placement, his oxygen desaturations during sleep resolved. Repeat polysomnogram revealed mild sleep apnea (AHI 1.9). The etiology of his sleep apnea was likely his hydrocephalus. This is the first report of a patient with Hurler syndrome with sleep apnea which markedly improved with ventriculostomy and VP shunt placement. This highlights the importance of considering neurological etiologies for sleep apnea in Hurler's patients, despite their predisposition for airway obstruction.

**Keywords:** Hurler's, hydrocephalus, polysomnography, mucopolysaccharidosis, sleep apnea

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## INTRODUCTION

Hurler syndrome (mucopolysaccharidosis type 1) is an inherited progressive multisystem lysosomal storage disease caused by deficiency of the enzyme alpha-L-iduronidase.[1] Glycosaminoglycans accumulate due to inability to degrade them in lysosomes. Patients with Hurler syndrome display high prevalence of obstructive sleep apnea, often with moderate to high severity.[2] They have narrow nasal passages, enlarged tongues, short and immobile necks, hypoplastic mandibles, increased tonsillar and adenoid size, engorged soft tissues of the nasopharynx, and narrowed trachea with thickened epiglottis and vocal cords, causing upper and lower airway obstruction and restrictive lung disease.[3,4] Although sleep apnea in these patients is frequently attributed to upper airway obstruction, we report a case of sleep apnea in this population caused by hydrocephalus.

## REPORT OF CASE

Our patient was a 13-month-old male with Hurler syndrome. During admission for pre-stem cell transplant evaluation, he exhibited oxygen desaturations at night while on continuous pulse oximetry, in addition to periods of apnea and retractions during sleep. These signs and symptoms led to referral for polysomnography. His study revealed severe mixed sleep apnea (AHI 72 events/h). He was referred to otolaryngology for evaluation of possible airway obstruction. Prior to this evaluation, however, he underwent ventriculostomy and VP shunt placement for hydrocephalus, which had been found on brain MRI as part of his pre-stem cell transplant evaluation for treatment of Hurler syndrome. Following this intervention, there was significant improvement in overnight oxygen saturation. One week later, repeat polysomnography was ordered, revealing only mild sleep apnea (AHI 1.9 events/h), a marked improvement from his initial sleep study (**Table 1**).

## DISCUSSION

Although obstructive sleep apnea and its pathophysiology in Hurler syndrome is well described, this is the first report of a patient with Hurler syndrome with sleep apnea which markedly improved with ventriculostomy and VP shunt placement. The association between hydrocephalus and mucopolysaccharidoses is well documented in the literature.[5–7] In some types of mucopolysaccharidoses, hydrocephalus is rare, as in type 2, but it is common in type 1 (Hurler syndrome).[8] There is also an association between central sleep apnea and hydrocephalus.[9] Despite these associations in the literature, this is the first report of a patient with Hurler syndrome with hydrocephalus and sleep apnea that markedly improved after VP shunt placement.

In Hurler syndrome, there is impaired degradation of glycosaminoglycans in the lysosomes, leading to their accumulation. Over time, this accumulation of storage material leads to engorgement of the arachnoid granulations and obliteration of the subarachnoid space. This infiltration of the subarachnoid space could lead to impaired cerebrospinal fluid absorption, resulting in hydrocephalus.[10] Venous hypertension has been proposed as one of the possible causes responsible for ventricular and sulci enlargement in these patients.[4]

The improvement in obstructive sleep apnea in this case can be attributed to improvement in vocal cord function or motor innervation of upper airway musculature, such as the pharyngeal

**Table 1**—Polysomnogram findings before and after VP shunt placement.

| Parameters | Before VP Shunt | After VP Shunt |
|---|---|---|
| Sleep efficiency (%) | 69.0 | 98.0 |
| % REM sleep (%) | 4.7 | 16.3 |
| Obstructive apneas (events) | 24.0 | 5.0 |
| Central apneas (events) | 42.0 | 6.0 |
| Mixed apneas (events) | 1.0 | 0.0 |
| Hypopneas (events) | 420.0 | 6.0 |
| AHI (events/h) | 72.7 | 1.9 |
| Time with $SpO_2$ < 90% (% of TST) | 67.2 | 1.2 |
| Time with $EtCO_2$ > 51 (% of TST) | 4.5 | 0.0 |
| PLM index (events/h) | 14.6 | 40.7 |

AHI, apnea-hypopnea index; $EtCO_2$, end-tidal carbon dioxide; PLM, periodic limb movement; REM, rapid eye movement; $SpO_2$, oxygen saturation; TST, total sleep time; VP, ventriculoperitoneal.

dilators, which could have previously been compromised by nerve compression from the patient's hydrocephalus. Surgical options for the obstructive sleep apnea in this patient would have been limited given the nonfocal anatomic obstructions. The pediatric otolaryngologist would likely be limited to offering either tracheostomy or CPAP. The improvement in central apneas could be secondary to resolution of increased intracranial pressure with consequent relief in compression of brain stem neurons responsible for regulation of respiration. It was difficult to differentiate central from obstructive hypopneas for this case due to lack of esophageal manometry, which is the gold standard for scoring central versus obstructive hypopneas.

This case highlights the importance of considering neurological etiologies for sleep apnea in patients with Hurler syndrome, despite their predisposition for airway obstruction. Hydrocephalus should be considered in the differential for sleep apnea in patients with Hurler syndrome, as surgical shunting can lead to marked clinical improvement. These findings are applicable, not only to patients with Hurler syndrome, but to any patient with mucopolysaccharidosis.

## ABBREVIATIONS

AHI, apnea-hypopnea index
$EtCO_2$, end-tidal carbon dioxide
MRI, magnetic resonance imaging
PLM, periodic limb movement
REM, rapid eye movement
$SpO_2$, oxygen saturation
TST, total sleep time
VP, ventriculoperitoneal

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Address correspondence to: Sumera Shaikh Solaiman, MD, Pennsylvania State University Children's Hospital, Department of Pediatrics, Mail Code H085, 500 University Drive, Hershey, PA 17033; Tel: (717) 531-5685; Fax: (717) 531-0856; Email: sshaikh0512@gmail.com

## DISCLOSURE STATEMENT

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