https://doi.org/10.5664/jcsm.8650

JCSM | Journal of Clinical Sleep Medicine

CASE REPORTS

# Central sleep apnea and Chiari 1 malformation in a pediatric patient with Klippel-Feil syndrome

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Klippel-Feil sequence (KFS) is a rare congenital condition that presents with congenital cervical spine fusion, reduced cervical spine flexion, and low posterior hairline. Chiari malformation type 1 and sleep-disordered breathing (SDB) are frequent comorbidities of KFS. The pathologic basis of the connection between Chiari malformation type 1 and SDB in the setting of KFS is not clearly understood. Here we report a pediatric patient with KFS, SDB, and drooling who also had Chiari malformation type 1. Posterior fossa decompression of this patient significantly improved most symptoms including sleep disturbances. Repeat polysomnogram 8 weeks after posterior fossa decompression revealed worsening central sleep apnea despite the patient being clinically asymptomatic. Taken together, this case highlights the point that, although it is critical to recognize the association of SDB in the setting of KFS, decompression alone may not be sufficient to completely alleviate SDB and certain neurologic symptoms.

**Keywords:** Klippel-Feil sequence, sleep apnea, sleep-disordered breathing, decompression

**Citation:** Martirosyan Z, Malhotra S. Central sleep apnea and Chiari 1 malformation in a pediatric patient with Klippel-Feil syndrome. *J Clin Sleep Med*. 2020;16(10):1805–1807.

## INTRODUCTION

Klippel-Feil sequence (KFS) is a rare congenital condition affecting 1 in 42,000 births. It classically presents with a triad of congenital cervical spine fusion, reduced cervical spine flexion, and low posterior hairline. KFS has been associated with several comorbidities that are not part of the major diagnostic criteria. These include congenital heart defects, hearing loss, renal dysfunction, Chiari type 1 malformation (CM1; herniation of a portion of the cerebellum through the foramen magnum), and, more recently, central sleep apnea (CSA) and obstructive sleep apnea. The short neck and cervical spine fusion with protrusion leading to airway narrowing along with scoliosis could potentially result in obstructive sleep apnea. Sleep-disordered breathing (SDB) of variable severity has been described in several individuals presenting with KFS.[1,2]

The co-occurrence of SDB and CM1 has been reported in multiple individuals.[3,4] The prevalence of CSA in patients with CM1 ranges from 17.6% to 48%.[5,6] There are reports of significant SDB in patients with CM1 malformations. Taken together, CM1, if present in a patient with KFS, may significantly increase the risk for SDB. However, the pathologic basis of the connection between CM1 and SDB is not clearly understood. There is little doubt regarding the use of polysomnogram (PSG) in patients with KFS.

A related question is whether detection of CSA in KFS should prompt magnetic resonance imaging (MRI) of the brain. The evidence for this is mixed at best. In 1 study of 59 children with SDB, MRI revealed Chiari malformation as the most common finding.[7] Although the evidence is based on only a few studies, MRI findings guide the subsequent management of patients with KFS with Chiari malformation (eg, posterior fossa decompression [PFD] for CM1).

Here we present a pediatric case report of a patient with KFS, SDB, and drooling/dysphagia whose MRI revealed CM1. PFD of this patient significantly improved most symptoms, namely the drooling, nocturnal cough, and dysphagia. However, unexpectedly, a repeat PSG 8 weeks after PFD revealed worsening CSA despite the patient being clinically asymptomatic. This observation is consistent with the hypothesis that SDB in the setting of KFS is multifactorial and the pathophysiology is not clearly understood.

## REPORT OF CASE

A 9-year-old Hispanic boy presented with congenital fusion of cervical spine and scoliosis that were consistent with KFS. He also exhibited oropharyngeal dysphagia, congenital heart defects (atrial septal defect and ventricular septal defects), status post repair with primary atrial septal defect closure, patch ventricular septal defects closure, and tricuspid valve veloplasty, and developmental delay. The palatine tonsils were not enlarged, and he was on montelukast and fluticasone for allergies. Family history was not contributory other than a 2-year-old sister with febrile seizures. Chromosomal microarray studies revealed a loss of a 1-Mb region in chromosome 19 (19p13.11). This loss includes a gene that has previously been associated with intellectual disability and cardiovascular malformations. However, the other features remained unexplained by genetics. The physical examination was significant for body mass index of 25 kg/m$^2$ (98 percentile), short neck, scoliosis, oral anatomy consistent with Mallampati class 2, and drooling.

The patient was referred to our pediatric sleep medicine clinic for evaluation of nocturnal cough, snoring, and choking in his sleep, which his mother attributed to inability to clear secretions. He began drooling 3 years ago, but symptoms significantly worsened over the last 1 year. The mother described him as restless sleeper with frequent jerks and arousals since early childhood. Sleep assessment revealed a regular sleep schedule with an average of 9 hours of sleep per night and 1–3 nightly awakenings in the later part of the night. His pediatric daytime sleepiness scale score was 16 (significant values > 15). Baseline PSG showed SDB with apnea-hypopnea index of 6.06 events/hr of sleep, which comprised of central apnea index of 4.81 central events/hr of sleep and obstructive apnea index of 1.28 obstructive events/hr of sleep. The lowest oxygen saturation ($SpO_2$) was 89%, and the $SpO_2$ was below 90% for 1.5% of the total sleep time. Transcutaneous $CO_2$ was not elevated, with maximum transcutaneous $CO_2$ of 47 mm Hg. He also exhibited significantly poor sleep efficiency of 54.2% (normal > 85%). Rapid eye movement sleep stage was 13.2% of the total sleep time (normal range, 18%–25%). Cardiopulomonary evaluations were normal.

Neurologic examination did not reveal anything significant in the patient except for drooling. Given that >50% of the apnea-hypopnea index was attributed to CSA and the patient had worsening symptoms of drooling over the last 3 years, a brain MRI was performed. Although the MRI revealed no evidence of prior infarcts, it showed crowding of the cerebrospinal fluid spaces at the cranio-cervical junction compared with a prior brain MRI. There was mild prominence of the intracranial subarachnoid spaces and ventricles and a complex bony abnormality at the cranio-cervical junction and upper cervical spine, consistent with KFS. The MRI also revealed CM1 with syrinx at the upper cervical spine, adjacent cord edema, and effacement of the surrounding subarachnoid spaces. Additionally, a dysmorphic C2 vertebrae was noted that was impinging (tilting and indenting) on the spinal cord and the cerebellar tonsils, resulting in crowding of cerebrospinal fluid spaces at the cranio-cervical junction.

The patient's neurologic symptoms (gagging, dysphagia, drooling) and CSA were thought to be attributed to the MRI findings above. The patient underwent PFD. His symptoms improved significantly after surgery with resolution of choking, nocturnal gagging, and drooling. Additionally, the mother reported improved sleep quality with less restless movements, awakenings, coughing, and snoring. Indeed, there was some improvement in daytime sleepiness as reported by a pediatric daytime sleepiness scale score of 12. Repeat PSG was ordered 7 weeks after neurosurgical decompression to assess severity of CSA. We expected improvement in CSA. EEG leads were unremarkable for epileptiform abnormalities. He did not have a full electroencephalogram. However, he did not have signs or symptoms suggestive of seizures. Additionally, the electroencephalogram leads from the sleep study did not show epileptiform abnormality or focal lateralizing features. However, PSG revealed severe CSA with 41.6 central sleep apneic events/hr of sleep and $O_2$ nadir of 81% with <2.2% of total sleep time below 90%. Transcutaneous $CO_2$ was not significantly elevated during the study. Given the severity of CSA, the patient was started on bilevel positive airway pressure in spontaneous timed mode with a setting of 10/6 $cmH_2O$ with a backup rate of 12 breaths/min. At this pressure setting, central apnea index was 0.0, snoring was not attenuated, the oxygen nadir was 93%, and the highest transcutaneous $CO_2$ was 52 mm Hg.

Repeat MRI was obtained 8 weeks after the surgery in search of a possible explanation for the worsened CSA. The MRI showed decompressed CM1 with decreased crowding of the cranio-cervical junction. Central syrinx at C2-C3 and mild edema extending from the posterosuperior to posteroinferior region was without significant change since the previous MRI.

## DISCUSSION

Both obstructive sleep apnea and CSA have been reported in patients in the setting of KFS, and in certain cases, decompression has been reported to provide alleviation of most clinical symptoms. For example, a prospective study of adult patients with Chiari malformation suggested that PFD surgery results in a decrease in central apnea index.[5] However, there are also case reports of patients with KFS where a foramen magnum decompression resulted in partial improvement of CSA.[8] There is evidence for pathophysiologic heterogeneity in CSA in patients with CM1.[9] Consistent with this, decompression did not alleviate SDB in our patient. It remains possible that the findings in Botelho et al[5] may not necessarily be the same for children with complex genetic diseases such as our patient.

This patient, with initially moderate SDB, CM1, and neurologic symptoms of drooling, highlights the importance of testing for SDB and CM1 in a patient diagnosed with KFS. The case also demonstrates that, contrary to expectations, decompression did not alleviate the SDB; however, it did reduce, to a certain degree, other neurologic symptoms. This is consistent with previous reports of variable pathophysiology of SDB under different settings of CM1. Indeed, it has been shown that morbidity of patients with congenital heart defects is higher if they also have SDB.[10] Our patient with a complex genetic condition including congenital heart defects, developmental delay, KFS, and SDB highlights the variability in pathophysiology. It remains possible that that a pleiotropic genetic defect acting earlier in development may contribute to CSA/SBD and congenital heart defects. One possible explanation could be that the repeat PSG was done too soon in postoperative period. As noted in repeat MRI, edema did not resolve completely and could be a possible explanation for exacerbating CSA.

Taken together, this case highlights the point that, although it is critical to recognize the association of SDB in the setting of KFS, decompression alone, while necessary in certain cases, may not be sufficient to completely alleviate SDB and/or certain neurologic symptoms such as nocturnal coughing.

## ABBREVIATIONS

CM1, Chiari malformation 1
CSA, central sleep apnea
KFS, Klippel-Feil sequence

MRI, magnetic resonance imaging
PFD, posterior fossa decompression
PSG, polysomnogram
SDB, sleep-disordered breathing

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## SUBMISSION & CORRESPONDENCE INFORMATION

**Submitted for publication February 11, 2020**
**Submitted in final revised form June 12, 2020**
**Accepted for publication June 16, 2020**
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## DISCLOSURE STATEMENT

All authors have seen and approved the manuscript. This case report was originally presented in abstract form at SLEEP 2020, the annual meeting of the Associated Professional Sleep Societies. Work for this study was performed at Texas Children's Hospital and Baylor College of Medicine. The authors report no conflicts of interest.