Primary Snoring and Growth Failure in a Patient With Cystic Fibrosis

Kelvin D MacDonald MD RRT, Brian M McGinley MD, David J Brown MD, Laura M Sterni MD, Beryl J Rosenstein MD, and Peter J Mogayzel Jr MD PhD

An 8-year-old female with pancreatic-insufficiency cystic fibrosis presented with recurrent pharyngitis, and reduction in body mass index and height velocity during the previous 2 years. Her symptoms (eg, snoring and restless sleep) suggested obstructive sleep apnea, and physical examination revealed tonsillar hypertrophy. While her respiratory disturbance index on nocturnal polysomnography was normal, there was evidence of prolonged periods of snoring, associated with hypercapnia. Adenotonsillectomy decreased the snoring, improved her sleep, and in the 18-month follow-up period she had substantial weight-gain and growth improvement. This case demonstrates that adenotonsillar hypertrophy associated with recurrent pharyngitis and primary snoring might hinder growth in a patient with cystic fibrosis. Key words: pancreatic insufficiency, cystic fibrosis, pharyngitis, snoring, sleep disturbance, obstructive sleep apnea, tonsillar hypertrophy, somnography, adenotonsillectomy, growth. [Respir Care 2009;54(12):1727–1731. © 2009 Daedalus Enterprises]

Introduction

Cystic fibrosis (CF) is the most common autosomal recessive life-span-shortening disease in persons of European descent. The disease currently affects approximately 30,000 people in the United States. Symptoms of CF usually begin in childhood. Seventy percent of persons with CF are homozygous for the F508del CF transmembrane regulator mutation. In CF, exocrine glands in secretory epithelia produce abnormally viscous mucus, which accumulates and obstructs the lumens of pancreatic ducts, airways, and biliary and reproductive tracts. Decreased pancreatic secretion impairs nutrient and caloric absorption, resulting in nutritional failure. Mucociliary clearance in the lung becomes impaired, and bacteria permanently infect the airways and cause permanent lung injury. Pulmonary CF exacerbations are treated aggressively with antimicrobials, but bacterial infection is never completely eradicated, and obstructive lung disease becomes irreversible.1,2

Children with CF often have difficulty gaining weight because of pancreatic insufficiency, higher caloric need, CF-related diabetes, and (less commonly) sleep-disordered breathing. Habitual (primary) snoring starts the continuum of pediatric sleep-disordered breathing that ends in obstructive sleep apnea (OSA).3 In children, sleep-disordered breathing is associated with growth failure.4 Though the etiology of pediatric sleep-disordered breathing is not completely understood, it is commonly associated with adenotonsillar hypertrophy. Adenotonsillectomy alleviates OSA symptoms approximately 80% of the time,5 and frequently is associated with growth spurt.6 Other indications for adenotonsillectomy include recurrent pharyngitis, tonsillitis and failure to thrive.7

Children with CF have frequent sleep complaints and substantial alteration of sleep architecture, which correlates with the severity of the lung disease.8 Children with CF are at risk of nocturnal hypoxia and hypoventilation solely on the basis of the CF lung disease,9,10 which can hinder growth. We present a child with CF, primary snoring, and impaired growth, who responded to tonsillectomy, as evidenced by subjective reports of improved sleep quality, decreased snoring, and marked weight gain.
**Case Report**

The patient was an 8-year-old child homozygous for the F508del CF transmembrane regulator mutation, and with pancreatic insufficiency. Her CF was complicated by juvenile rheumatoid arthritis, which had been asymptomatic recently but required long-term anti-inflammatories. From birth until 6 years of age her height and weight had been above the 50th percentile for age, on a standard growth chart, but in her 7th and 8th years of life her body mass index fell from the 25th percentile to below the 3rd percentile, despite progressive increases in pancreatic lipase supplementation (up to 2,300 units/kg/meal) and recurrent interventions with the nutritionist. Her gastrointestinal symptom was periodic constipation. She denied dysphagia. She had had few CF pulmonary exacerbations (defined as acute weight loss, increased cough, change in sputum, or acute decline in lung function), all of which had been managed on an out-patient basis. She had a history of recurrent pharyngitis, multiple ear infections, and upper-respiratory-tract infections, including an episode of acute sinusitis, which were all treated with oral antimicrobials. Her parents reported that she had nightly snoring, restless sleep, and mouth breathing, but no other symptoms of sleep-disordered breathing, such as daytime somnolence or impaired school performance.

Physical examination demonstrated normal vital signs, normal voice quality, and no hoarseness, stridor, or muffling. The tympanic membranes were intact and without effusions. Her tonsils occupied more than 75% of the lateral dimension of the oral pharynx (grade 4). There was no tonsillar erythema or exudate. She had clear rhinorrhea bilaterally, no sinus polyps, and no tenderness to sinus palpation. Her neck had full range of motion, without thyromegaly or tracheal deviation. She had palpable non-tender bilateral anterior cervical lymph nodes, less than 1 cm in size. Her forced vital capacity was 1.80 L (103% of predicted), and her forced expiratory volume in the first...
second (FEV₁) was 1.45 L (95% of predicted). She had no response to bronchodilator. Surveillance throat culture routinely found *Staphylococcus aureus*.

At the Johns Hopkins Medical Institutions we routinely use polysomnography to assess the severity of sleep-disordered breathing in all children with suspected OSA. Overnight polysomnography demonstrated normal baseline oxygen saturation, with a nadir of 92%. Sleep efficiency and architecture were normal. Her respiratory disturbance index was 0.2 events per hour of sleep, all of which were hypopneas and consistent with normal values. She had inspiratory flow limitation (snoring) during parts of the somnography, specifically, when she slept supine, compared to a side-lying position. The inspiratory flow limitation was associated with a prolonged inspiratory time and shortened expiratory time, and with mild elevation of end-tidal CO₂, from 45 mm Hg to 50–54 mm Hg for 12% of sleep time (Fig. 1). The caregiver accompanying the child, however, thought that the somnography night’s sleep was atypical; specifically, the child snored less, slept on her side more, and slept better than usual.

Her history of recurrent pharyngitis, snoring, growth failure, and CF led us to recommend elective adenotonsillectomy. Intraoperatively we found tonsillitis. The adenoid tissue obstructed less than 25% of the choana. Two months after surgery she and her family reported substantial improvement in her sleeping pattern and more restful sleep. She also reported improved taste sensation and appetite. There were no changes in her postoperative nutritional regimen. Fourteen months after surgery her body mass index returned to the 25th percentile (Fig. 2), her forced vital capacity was 2.01 L (102% of predicted), and her FEV₁ had improved by 15%, to 1.87 L (109% of predicted) (Fig. 3).

**Discussion**

Growth failure is common in children with pancreatic-insufficient CF because of malabsorption of calories and nutrients. Despite our efforts to increase her calorie intake, and the use of pancreatic enzyme supplements, our patient had a declining body mass index. We excluded other causes of growth failure in CF, such as severe lung disease and hypoxia, recurrent severe lung infections, CF liver disease, or CF-related diabetes; but she had signs and symptoms of sleep-disordered breathing, including snoring, restless sleep, and adenotonsillar hypertrophy. Thus, this case demonstrates the need for maintaining a broad differential for growth failure in children with chronic medical conditions such as CF. Acute weight loss, anorexia, increased cough, change in sputum, and acute reduction in lung function are easily recognized classic findings of CF pulmonary exacerbation. Symptoms of sleep-disordered breathing can be subtle and require clinician awareness and diligence in asking about signs of sleep difficulty, such as snoring, mouth breathing, witnessed pauses in respiration, restless sleep, frequent awakening, daytime hypersomnolence, secondary nocturnal enuresis, and poor school performance.6 The American Academy of Pediatrics12 recommends polysomnography for diagnosing sleep-disordered breathing when the index of clinical suspicion is high. The basis of the recommendation is two-fold. First, > 10% of the pediatric population has primary snoring, whereas 2% of children have true OSA, so additional diagnostic testing is needed with a habitually snoring child before considering surgery. Second, polysomnography is useful for identifying patients at risk of adverse outcomes from surgery (eg, profound hypoxia). Surprisingly little is known about the impact of sleep-disordered breathing on inflammation in pediatric chronic conditions such as CF, inflammatory bowel disease, or arthritis.

Adenotonsillar hypertrophy is associated with recurrent tonsillitis, reduced dietary intake, and a higher risk of upper-airway obstruction during sleep. In our patient it was unclear what were the relative contributions of the upper-airway obstruction, gas-exchange perturbance, adenotonsillar hypertrophy/inflammation, and recurrent infection to her poor growth. However, applying the Pittsburgh criteria14 for tonsillectomy, our patient would have been classified as high-risk and predicted to benefit substantially from tonsillectomy.

It is not clear how upper-airway obstruction impairs growth. A hormonal mechanism of decreased insulin growth factor-1 has been proposed to explain slow growth in children with OSA. Another possibility is that upper-
Airway obstruction increases respiratory effort during sleep and thus increases metabolic expenditure. The combination of those 2 mechanisms might be more profound in a child with coexisting chronic illness. We think the degree of upper-airway obstruction in our patient might have been underestimated in the polysomnography, because she demonstrated inspiratory flow limitation only while supine. Body position influences upper-airway obstruction during sleep, and the supine position worsens sleep-disordered breathing. The limited amount of time our patient spent supine during the somnography might have also accounted for the parent’s report that she slept better than usual during the somnography. A recent prospective trial found that a single-night somnography study is adequate 85% of the time.

Our patient’s postoperative lung-function improvement is interesting. She had a sustained improvement of > 15% in percent-of-predicted FEV₁ during the 18-month postoperative follow-up period. A recent case-control series that compared pulmonary function in normal children to those with adenotonsillar hypertrophy found abnormal pulmonary function in the adenotonsillar-hypertrophy group prior to elective adenotonsillectomy, and improved pulmonary function after the surgery.

Moreover, Hayes described improved pulmonary function after adenotonsillectomy in a 6-year-old, pancreatic-sufficient patient who had CF and an abnormal sleep study. He postulated a relationship between OSA and lower-airway inflammation in CF. Goldbart et al found that tonsillar tissue in children with OSA had more cysteinyl leukotriene receptors 1 and 2. Additionally, both interleukin-1 beta and tumor necrosis factor alpha are significantly greater in hypertrophic tonsillar tissue than in the corresponding serum sample, which suggests a local inflammatory stimulus. The “unified airway” theory suggests that inflammatory processes can be spread from the upper airway to the lower respiratory tract. In our patient, elective adenotonsillectomy decreased her snoring and improved her sleep, and thus possibly reduced the inflammatory stimulus associated with upper-airway obstruction (snoring) and recurrent pharyngitis.

We conclude that in our patient, disturbed sleep, primary snoring, adenotonsillar hypertrophy, and recurrent pharyngitis all contributed to growth failure, which resolved after adenotonsillectomy. This case suggests that even mildly sleep-disordered breathing (including primary snoring) in the presence of important pediatric chronic illness such as CF may result in marked comorbid outcomes, such as growth failure. Practitioners caring for children with chronic medical conditions should consider sleep-disordered breathing in the differential diagnosis of growth failure. The impact of primary snoring, chronic adenotonsillar hypertrophy, and disturbed sleep quality deserves further attention in the pediatric CF population.

REFERENCES