

Achondroplasia and disordered breathing in sleep

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- OSAS

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SUMMARY. **Background** The occurrence of obstructive sleep apnoea in children with achondroplasia has already been described. **Objectives** To investigate the association between achondroplasia and obstructive sleep apnoea syndrome (OSAS) in adult patients. **Subjects and methods** Three women aged 43-59 years with achondroplasia were studied. They all complained of snoring, daytime somnolence and chronic fatigue. Their past history included tonsillectomy and adenoidectomy. Polysomnography, spirometry, blood gases and blood biochemistry analysis were performed. **Results** All three women had OSAS, with RDI 42.8/h, 23.3/h, 40.1/h respectively. Spirometry and arterial blood gases were within normal limits, but blood biochemistry showed hyperlipidaemia in all the women. Cephalometry showed middle face hypoplasia. Neck CT-MRI demonstrated constriction of the foramen magnum and stenosis of the oropharynx and hypopharynx. **Conclusions** OSAS should always be suspected in adult patients with achondroplasia, as well as in patients with skeletal deformities of the face and upper airway soft tissue abnormalities. *Pneumon 2008; 21(4):384-387*

INTRODUCTION

Achondroplasia is a genetic disorder characterised by a defect in endochondrial bone formation¹. It is the most common skeletal dysplasia, inherited as an autosomal dominant trait, but most cases appear to represent a new mutation in the gene FGFR3^{2,3}.

Patients with achondroplastic suffer from dwarfism with typical features in the head (macrocephaly, frontal bossing) and limbs (rhizomelia), and kyphosis³ (Figure 1).

Most children with achondroplasia do well. Individuals with achondroplasia are of normal intelligence and are able to lead independent and productive lives². Infrequently, infants and children with achondroplasia may have serious health consequences related to hydrocephalus, cranio-cervical junction compression, upper airway obstruction or thoracolumbar kyphosis².

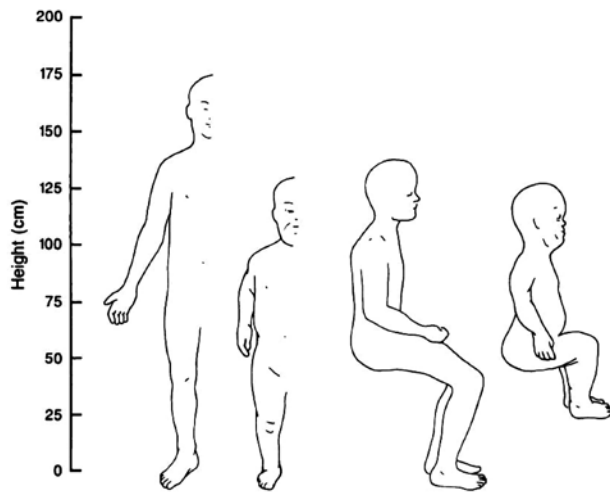


FIGURE 1.

Between 10% and 85% of infants and children with achondroplasia present for treatment because of major respiratory difficulty, such as obstructive sleep apnoea, waking cyanotic episodes and chronic respiratory insufficiency and failure³⁻⁶. Although such problems are not uncommon in other forms of dwarfism, there are specific developmental abnormalities in achondroplasia that may predispose to these sometimes life-threatening symptoms, including midfacial hypoplasia and upper airway obstruction, dysplasia of the basiocciput, exoccipital bone and craniovertebral junction with foramen magnum stenosis and cervicomedullary cord compression, and possible thoracic cage restriction^{4,7}.

Aim of the study

In this context, the cases are reported of three women aged 43-59 years with achondroplasia and breathing problems, with a review of the the association between achondroplasia and obstructive sleep apnoea syndrome (OSAS) in adults.

SUBJECTS AND METHODS

Three women with achondroplasia aged 43, 51, 59 years old, were investigated in the Sleep Unit (Figure 2).

The first woman was complaining of snoring, daytime somnolence and cognitive impairment (loss of memory).

The second woman reported unrefreshing sleep, nocturnal gasping and choking and daytime somnolence.

The third woman complained of unquiet sleep, loud

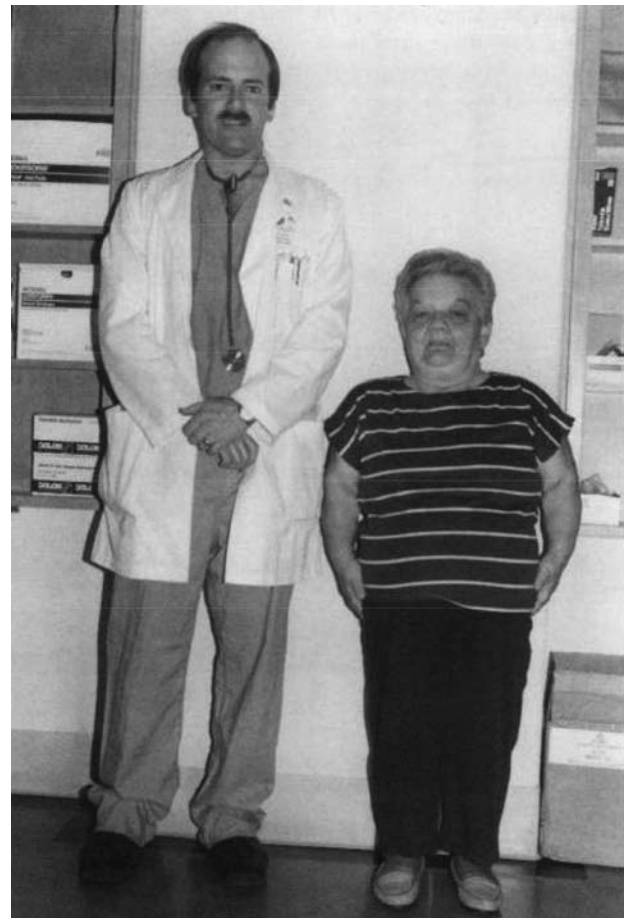


FIGURE 2.

snoring, witnessed apnoeas, sweating during sleep, nocturia, headache and chronic fatigue.

Height (H) and body mass index (BMI) were measured in all three women.

1st woman: H:1.19m, BMI: 34 kg/m²; 2nd woman: H:1.18m, BMI: 38 kg/m², 3rd woman: H:1.35m, BMI: 43.9kg/m².

They all underwent night polysomnography, spirometry, measurement of arterial blood gases, biochemistry screening tests and upper airways imaging (cephalometric radiograph and pharyngeal CT- MRI) (Figure 3).

RESULTS

Diagnostic polysomnography revealed OSAS, for all three of the women (table 1):

Table 1. Polysomnography findings on the three women with achondroplasia.

Spirometry and arterial blood gases were all within



FIGURE 3.

normal limits, but blood biochemistry showed hyperlipidemia for the three of them. There was no evidence of pulmonary hypertension, according to the ECG.

Cephalometry revealed middle face hypoplasia. Neck CT – MRI showed constriction of the foramen magnum

TABLE 1.

| | Patient 1 | Patient 2 | Patient 3 |
|-------------------------|-------------|-------------|-------------|
| CA (TST) | 6 | 1 | 2 |
| OA (TST) | 93 | 47 | 21 |
| MA (TST) | 8 | 1 | 1 |
| HYP (TST) | 106 | 205 | 71 |
| AHI REM/h | 75,3 | 59,4 | 37,5 |
| AHI NREM/h | 40,3 | 37 | 22,8 |
| AHI TST/h | 42,8 | 40,1 | 23,3 |
| SatO ₂ <90% | 4 min | 12,5 min | 13,5 min |
| Min satO ₂ % | 80 | 81 | 76 |

CA: central apnoea, OA: obstructive apnea

MA: mixed apnea, HYP: hypopnea,

AHI: apnea – hypopnea index/h sleep,

TST: total sleep time

and stenosis of the oropharynx and hypopharynx in all three (fig. 3).

DISCUSSION

The occurrence of obstructive sleep apnoea (OSA) in achondroplasia has already been described^{5,8-10,16}. Such obstruction may be caused by the associated anatomical abnormalities such as mid-facial hypoplasia and/or adenotonsillar hypertrophy, or by variable pathophysiological changes occurring in the nasopharyngeal or glossal muscle tone⁷.

The skeletal abnormalities associated with achondroplasia include stenosis of the spinal canal and of the foramen magnum (8-10), and these may cause bone impingement on the brain stem and spinal cord. This compression can result in functional neurological^{11,12} and respiratory abnormalities^{13,14}, including OSA.

The orofacial abnormalities in achondroplasia that may also cause OSA include small mid-facial dimensions and a small upper airway^{13,15}.

There appear to be three distinctive phenotypes for the achondroplasia respiratory difficulty syndrome^{4,7}. In one form (*phenotype 1*), there is simply 'relative' adenotonsillar hypertrophy caused by a degree of mid-facial hypoplasia, but which results in OSA that is clinically resolved by adenotonsillectomy.

In a second form (*phenotype 2*), there is muscular upper airway obstruction with progressive hydrocephalus, which could have jugular foramen stenosis as a common aetiology,.

In the third form (*phenotype 3*), there is muscular

upper airway obstruction, but without hydrocephalus. This could be explained by hypoglossal canal stenosis with or without foramen magnum compression, but no jugular foramen stenosis.

The muscles of the nasopharynx and tongue are supplied by cranial nerves IX-XII¹⁴. The hypoglossal nerve (XII) originates in the medulla: the rootlets form two bundles that perforate the dura mater separately, opposite the hypoglossal canal in the occipital bone and which then unite after traversing it. The motor portion of the nerve supplies all the muscles of the tongue except the palatoglossus. Nerve fibres from the nucleus ambiguus form cranial nerves IX, X, and XI, which supply the striated musculature of the pharynx, the larynx, and the upper part of the oesophagus. These three nerves leave the cranium via the jugular foramen. The simplest 'muscular' explanation consistent with these findings, would be that abnormal muscle tone is exacerbated during active sleep^{4,6,7}.

In phenotype 3 patients, a restrictive hypoglossal canal with or without foramen magnum stenosis and medullary compression results in, at the least, impaired hypoglossal function. In phenotype 2 patients, isolated jugular foramen restriction results in both vertebral venous hypertension with hydrocephalus, and impaired pharyngeal and laryngeal function.

CONCLUSION

OSAS should always be suspected in adult patients with achondroplasia, as in all patients with skeletal deformities of the face and upper airways soft tissue abnormalities.

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