Feeding Abilities in Achondroplasia Patients

Subjects: Primary Health Care

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Achondroplasia is an autosomal dominant genetic disease representing the most common form of human skeletal dysplasia: almost all individuals with achondroplasia have identifiable mutations in the fibroblast growth factor receptor type 3 (*FGFR3*) gene. The cardinal features of this condition and its inheritance have been well-established, but the occurrence of feeding and nutritional complications has received little prominence. In infancy, the presence of floppiness and neurological injury due to foramen magnum stenosis may impair the feeding function of a newborn with achondroplasia. Along with growth, the optimal development of feeding skills may be affected by variable interactions between midface hypoplasia, sleep apnea disturbance, and structural anomalies. Anterior open bite, prognathic mandible, retrognathic maxilla, and relative macroglossia may adversely impact masticatory and respiratory functions. Independence during mealtimes in achondroplasia is usually achieved later than peers. Early supervision of nutritional intake should proceed into adolescence and adulthood because of the increased risk of obesity and respiratory problems and their resulting sequelae.

Keywords: achondroplasia ; feeding ; FGFR3 ; nutrition

1. Introduction

Achondroplasia (ACH) is an autosomal dominant genetic disease representing the most common form of human skeletal dysplasia [1][2] and the most readily recognizable dwarfing disorders [3], accounting for 90% of cases of disproportionate short stature [4]. It has an estimated prevalence in the USA of 0.36–0.6 per 10,000 births [5], affecting at least 250,000 people worldwide [6].

Genetically, approximately 99% of ACH cases are explained by mainly two variants in the *FGFR3* gene: c.1138G > A accounting for 98% of cases, while the remaining 1% of the patients carry the c.1138G > C variant. Both pathogenic variants, mapped on chromosome 4, result in the same glycine to arginine substitution in the *FGFR3* protein (p.Gly380Arg) [3][7][8][9][10][11]. These mutations activate the *FGFR3* receptor in the inhibition of chondrocyte proliferation with subsequent growth restriction and impaired endochondral bone formation [12]. De novo mutations account for most cases (80%) [13], and homozygosity occurrence has been reported seldomly to be compatible with life [14][15]. Its diagnosis is usually suspected prenatally by routine ultrasonographic investigations in the case of the detection of shortened limbs and confirmed by molecular testing [16].

Striking clinical features are macrocephaly, marked limb shortening, exaggerated lumbar lordosis, genu varum, brachydactyly, ligamentous laxity, hypotonia, and hands with a trident appearance. Face appearance is characterized by frontal bossing and mid-face hypoplasia [17].

2. Oral Findings Affecting Feeding

Characteristic clinical features of ACH include muscular hypotonia during infancy and midface hypoplasia.

With regard to floppiness, the medical literature reports that almost all infants with ACH exhibit variable levels of hypotonia during infancy. This common finding is a contributing factor to delayed motor development [18], consistently reported in multiple studies [6][19][20][21]. Hypotonia also negatively influences the optimal development of oral-motor skills by reducing the strength of orofacial muscles. Consequently, jaw movements, lip tightness, tongue positioning, sucking/swallowing/respiration pattern, and general feeding behavior are compromised. In addition, hypotonia of the oral musculature along with midface hypoplasia and enlarged tonsils and/or adenoids is one of the leading causes of the narrowing or even obstruction of the upper airways [22][23], which occasionally requires endotracheal tube placement [24].

The presence of relative macroglossia further contributes to airway obstruction as the tongue encroaches upon and intermittently obstructs the retroglossal airway [25], leading to swallowing difficulties.

Upon closer look, in patients with ACH, muscular weakness can be associated with a tongue thrust swallowing pattern [26]. Normally, between 2 and 4 years, the infantile swallowing pattern changes gradually into a mature swallowing pattern that implies the positioning of the tongue held high on the palate behind the maxillary incisors [27]. In the tongue thrust pattern, instead, the tongue pushes against or between the teeth, leading to open bite and protruded teeth [28].

Moreover, striking ACH facial manifestations, in addition to mouth breathing predisposition, also interfere with the chewing ability [29].

Concerning the typical oro-cranio-facial findings in ACH children, they include macrocephaly, prominent forehead and frontal bossing, and underdevelopment of the cartilaginous bones of the face. These characteristics result in midface hypoplasia, collapsed midface, and an elongated lower face and concave profile [30]. In turn, oral findings include posterior crossbite, anterior open bite, prognathic mandible, and retrognathic maxilla with reverse overjet and high-arched palate [31][32]. In this specific genetic condition, maxillary hypoplasia typically results in an Angle class III malocclusion with anterior open bite [30]. To note, the deviation from normal mandible growth can strongly affect the masticatory and respiratory functions [33].

Finally, the development of adequate chewing ability in children can be affected by a delayed eruption of teeth and oligodontia due to altered bone growth [34][35][36]. In adults, instead, a deterioration of chewing function can be caused by progressive teeth loss due to cartilage formation impairment, as observed by Swathi et al. in a 50 year-old-man with partial edentulism [32], and to dental mobility, as observed by Chawla et al. in a 31-year-old female patient with severe periodontal disease [37].

3. Respiratory Findings Affecting Feeding

Many infants and children with ACH present respiratory complications due to several factors, namely, upper airway obstruction, neurological dysfunction, and rib cage deformity [38]. This latter feature is one of the main causes of respiratory decompensation in ACH [39]. In normal infants, the thorax is circular at birth with minimal difference between the thoracic width and depth. With growth, the transverse posterior diameter becomes larger than the anterior–posterior one, giving an elliptical appearance to the thorax. At the end of growth, the thoracic width and depth represent approximately 30% and 20% of sitting height, respectively [40]. Conversely, because of irregular rib development, ACH infants have a small thorax with short flared ribs, the thorax is frequently bell-shaped, and has reduced anterior–posterior diameter [39].

Infants with decreased total lung capacity commonly have a rapid and shallow respiratory pattern because of increased respiratory frequency and diminished tidal volume: these infants often exhibit increased work in breathing, which is a distinctive feature of syndromes with short rib dysplasia and tachypnea [41]. Of note, persistent marked tachypnea can cause secondary feeding difficulties [3] and increase the risk for aspiration [42]. Furthermore, Dessoffy et al. first established an estimated frequency of 5.5% for airway malacia in the ACH population, which is considerably higher than the cumulative frequency in average statured children (from 0.5% to 1.5%) [43]. The presence of laryngomalacia or trachea-bronchomalacia negatively influences swallowing and feeding functions [44], commonly causing regurgitation, choking, and slow feedings [45][46]. Empirically, laryngomalacia involves a collapse of the supraglottic structure during inspiration: it contributes to a failure of sucking, swallowing and breathing coordinated pattern, and airway protection. Therefore, laryngeal penetration and aspiration are common findings [47]. Meanwhile, trachea-bronchomalacia, due to the softening of the tracheobronchial tree, can cause a wide range of respiratory and feeding problems including dysphagia, cough, and cyanosis [48][49].

4. Neurological Findings Affecting Feeding

ACH is characterized by impaired enchondral ossification, which gives rise to neurologic abnormalities including foramen magnum stenosis (FMS). FMS may be common in ACH, and in about 10–20% of infants leads to cervico-medullary myelopathy and a range of symptoms including poor suck, poor weight gain, and weakness [50].

Therefore, swallowing difficulties, in addition to lower cranial nerve palsies, hyperreflexia, generalized hypotonia, weakness, and clonus, can suggest a cervical myelopathy [4][51].

Another neurological manifestation in infants with ACH is hydrocephalus, occurring in 15–50% of patients [52]. Hydrocephalus is due to increased intracranial venous pressure secondary to stenosis of the jugular foramina [4] and, if occurring, may further contribute to poor feeding [6].

In the study by Ireland et al. [6], the authors first described the development of feeding skills in 20 Australasian children diagnosed with ACH. Using a retrospective questionnaire covering the progression in the introduction of food texture, the authors found an overall adequate sucking ability with a preference for exclusive breastfeeding over bottle-feeding in half cases. Moreover, the timing of the introduction of semi-solid food textures (median: 5 months) in children with ACH was in line with those in the general population.

In contrast, self-feeding with a spoon (median: 20.5 months), cup drinking (median: 20 months), and finger-feeding skill (median: 15 months) attainment faced a delay if compared with the general population.

5. Feeding Management

The primary goals of the management of feeding-related issues in the ACH population are to prevent complications and introduce personalized treatments in a timely manner with constant involvement of the family in decision-making. As previously outlined, midface hypoplasia is universal in the ACH population as the result of impaired endochondral bone formation and normal membranous ossification [53]. Therefore, maxillary hypoplasia, relative mandibular prognathism, and class III malocclusion accompanied by oral muscle dysfunction are consistent features [54]. The American Academy of Pediatrics recommends a review of orthodontic problems in ACH after 5 years of age [55]. The main goal of orthodontics is primarily to enhance maxillary and restrict mandibular growth. As proposed by Pineau et al., there is a need in this specific population to correct the anterior crossbite and open bite, improve the skeletal class III jaw-base relationship, create proper overjet and overbite, and establish an acceptable occlusion with a functional class I occlusion [30]. Correction of malocclusion with orthodontic strategies and myofunctional therapy go hand in hand, with the latter therapy lasting throughout the orthodontic treatment [56]. Generally, myofunctional strategies include exercises involving the cervical and facial muscles aimed at improving proprioception, tone, and mobility. The myofunctional approach, in turn, results in neuromuscular re-education of the muscles involved in swallowing, tongue motion, oral breathing as well as the rest posture of the tongue, lips, and cheeks [28]. In this specific context, myofunctional strategies are intended to stop the tongue-thrusting habits, optimize glossal muscle tone, and correct its positioning and functioning. A further management strategy consisting of personalized craniofacial surgery may also be needed in some selected cases [30]. Usually, although with increasing age there is a spontaneous improvement in oral motor function, a lack of autonomy achievement during feeding may result in greater caregiver dependence. Therefore, multidisciplinary assessment should focus on areas of vulnerability and appropriately promote the support of the entire family in all aspects of the patients' daily life.

Due to the anatomical features of ACH infants, management guidelines recently developed by the European Achondroplasia Forum (EAF) and the American Academy of Pediatrics (AAP) indicate considerations for early infant handling including breast- and bottle-feeding positioning. In everyday practice, when breastfeeding, it is recommended to support the infant head and neck and use a firm support for kyphosis. If bottle feeding, it is recommended to support the infant's back using a pillow with a firm hand on the lower back. With growth, there is still the need to support the children's kyphosis [57][58].

The presence of restrictive pulmonary disease may cause tachypnea, consequent feeding difficulties, and failure to thrive. Therefore, the management of these latter aspects cannot be separated from the assessment of respiratory functioning. Polysomnography and daytime spot oximetry during active alert time and, particularly during feedings, for example, may be helpful [3].

As previously described, tracheo and bronchomalacia are commonly present after the neonatal period with airway symptoms including cough, stridor, airway obstruction, frequent infections, and wheezing [45]. It is recommended that a multidisciplinary team of clinicians is involved in the counseling of families and caregivers to better define the most appropriate management of airway malacia including supraglottoplasty or more conservative options [47]. Concerning the management of neurological findings, the cranio-cervical junction constriction, of which poor feeding is an indirect symptom, is a major concern in ACH patients. Indeed, the comprehensive history and physical exam for foramen magnum stenosis should include the evaluation of weak suck and feeding difficulty [50]. Following the American Academy of Pediatrics guidelines on health supervision for children with ACH, magnetic resonance imaging (MRI) of the cervical–cranium region is strongly advised to screen all infants with ACH [54]. International experts recommend a neurological evaluation from infancy [recommendation #34] [59] with special attention also on symptomatic hydrocephalus. Since birth, all children with ACH should have routine circumference measurements plotted on ACH-specific head circumference

charts [3][8] and further neurosurgical evaluation if rapid growth and other clinical or neuroradiological signs are observed [59].

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