Orthopaedic and other medical problems in adults with achondroplasia

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Achondroplasia is the most common genetic condition causing disproportionate short stature with an incidence of 1:20 000 – 30 000 live births [1, 2]. The genetic defect in achondroplasia results in ligand-independent activation of FGFR3 with subsequent inhibition of chondrocyte proliferation and differentiation. Cartilage cells, especially in the long tubular bones in the arms and legs, the vertebrae and the skull are affected, with reduced standing height being the most striking clinical feature of the disease. The average height in adults is around 123–125 centimeters for women and 130–134 centimeters for men.

Other typical clinical features include: rhizomelic disproportion, deformities in the upper- and lower limbs, joint hyperlaxity, thoraco-lumbar kyphosis, midface hypoplasia and macrocephaly. Lower limb deformities and joint hyperlaxity lead to specific gait alterations including reduced walking speed and step length, flexion pattern in the sagittal plane at the pelvis and the knee and the increased varus malalignment during gait compared with the radiologically measured varus malalignment in the knee [3, 4].

Besides thoraco-lumbar kyphosis other spinal obstacles include foramen magnum stenosis and spinal stenosis. The midtface anomalies and adenotonsillar hypertrophy

in these patients may lead to sleep apnea, recurrent upper airway and otitis media with possible subsequent hearing loss if chronic ear infection is present [5]. Impaired hearing reported in 33%-55% of adults with achondroplasia [6].

Due to multiple aspects of the disease including both orthopaedic and other medical problems, treatment approach should be multidisciplinary during childhood, and if possible, also in adulthood. Adults may face several orthopaedic and medical problems, which influence physical function, psycho-social function and quality of life.

The level of independence to carry out activities of daily living may be significantly reduced. In a study by Alade et al. (2013) 64% of adults with achondroplasia reported daily pain[7]. In this study self-reported pain on different sites of the body in patients with skeletal dysplasia showed that two-thirds had pain in three or more locations, with the most common being the lower back (>50%), followed by hips, posterior neck, knees and the ankles/feet [7]. Furthermore, this study showed a marked decrease of physical function for the categories of ambulation and ADLs from childhood to adulthood. More specifically 20% could not walk the length of one city block and 13% were categorized as having "poor" walking ability, 11% were not able to bath or dress and 11% could not toilet independently 16% could not cook or do basic housework tasks 16% could not shop for groceries [7].

The natural history of the disease shows that in adults with achondroplasia pain prevalence is increasing with age markedly impairing independent ambulation and daily function. Overall mortality rate is increased in adults with life expectancy being decreased by 10 years, whereas main causes of death are: heart disease, neurological complications, and accidents [6]. Chronic pain is known to be associated with poor mental health and a substantial percentage of adults with achondroplasia suffer from anxiety and depression [8]. A literature review by Constantinides et al. (2022) revealed that a reduction of the mental component or psychosocial domains compared to the generel population was found in 4 studies and work participation and establishing family was reported as challenging. Education level was comparable or lower than in the general population [8].

The natural history of the disease with marked impairment of function and pain at several sites of the body, raises the question on what could be done in childhood and adolescence to ensure best possible function in adulthood. Valgus and varus malalignment of the knee are known to increase the risk of osteoarthritis in the general population [9, 10]. However, despite the presence of varus malalignment in the knee in 50-60% of individuals with achondroplasia [11], degenerative knee arthritis occurs rarely [2, 11, 12]. Despite this, knee pain is one of the main complaints in adults with achondroplasia [7], and gait analysis studies showed that varus malalignment further increases during gait [3, 4]. It should therefore be considered to address coronal plane deformities during childhood. Hemiepifysiodesis, a minor surgery, might be considered when there is sufficient remaining growth (at least two years). The method is effective in children with achondroplasia, although treatment time is longer and various results are reported for the rate of complications and effectivity of the procedure [13-15]. If guided growth procedures are not effective, corrective osteotomies in the femur and/or tibia can be considered.

Ankle varus malalignment with limited eversion ability is also frequently present in achondroplasia leading to increased loading of the lateral aspects of the plantar. Knee varus malalignment might further pronounce gait problems due to ankle varus.

In a recently published cohort study by Won Seok Choi and colleagues (2024) the prevalence of ankle osteoarthritis in adults with achondroplasia was 29% [16]. However, they could not find any differences in the prevalence of ankle osteoarthritis in patients who had undergone correction of knee malalignment

compared with untreated patients.
The prevalence of ankle osteoarthritis is relatively high in adult individuals with achondroplasia (29%), and 13,5% report pain in the ankle/feet [7, 16]. However, the decision whether to correct an existing deformity in childhood should be considered individually, based on the patient's pain and gait disturbances.
Coronal malalignment in the knee and ankle joint in achondroplasia might be correlated to fibular overgrowth [12]. Beals and Stanley (2005) compared three different surgical groups for correction of varus knees. In one group proximal closed wedge osteotomy was combined with epiphysiodesis in the proximal fibula, in the second group proximal open wedge tibia osteotomy was done without simultaneous epiphysiodesis in the proximal fibula, and in a third group an Ilizarov fixator was used to do axis correction and 3 cm lengthening and at the same time distalisation of the fibula [17]. They found the Ilizarov procedure to be most effective and they also recommend fibula shortening when correcting distal bowlegs. Apart from this article there is, to my knowledge, no published literature which addresses the possibility to perform a proximal and/or distal fibula epiphysiodesis to avoid fibula overgrowth and its possible contribution to varus deformity and knee instability.
Obesity is believed to aggravate skeletal symptoms, including lumbar spine symptoms, limb deformity and joint pain. Thus, early detection of obesity in children and adults with achondroplasia is important and nutrition counselling should be provided at an early stage [18].
Spine problems in these patients include foramen magnum stenosis, thoraco-lumbar kyphosis and spinal stenosis. Whereas, foramen magnum stenosis and kyphosis will be addressed at a very early stage, spinal stenosis becomes symptomatic later. Lower back pain and claudication seem to be one of the main problems in adults with achondroplasia. It is therefore of great importance to be aware of symptoms related to spinal stenosis in these patients.
Limb lengthening in both the upper and lower extremity are an option in these patients. However, there is an ongoing debate whether these procedures increase function, the level of independence, and quality of life. There is no evidence that indicates that limb lengthening procedures should be done in childhood to avoid/reduce musculo-skeletal problems later in live.
The focus when treating these patients with the aim to avoid late musculo-skeletal complications should be on lower limb deformity correction, nutrition counselling to avoid obesity and early detection and timely treatment of spinal complications. An interdisciplinary approach is crucial for both children and adults with achondroplasia.

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