

## Medical and Orthopedic Management with Growth Hormone and Bone Lengthening in A Patient with Achondroplasia

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**Received:** January 18, 2016; **Published:** February 08, 2016

### Summary

Achondroplasia is a genetic disorder which affects bone growth leading to short stature. It is the most common type of short-limb disproportionate dwarfism (non lethal skeletal dysplasia). The term achondroplasia, implying absent cartilage formation, was first used by Parrot in 1878. It is transmitted as autosomal dominant due to mutations of the FGFR3 gene which codifies the fibroblastic receptor of growth hormone expressed in provisional cartilage. No effective therapies to stimulate bone growth have emerged, but some success has been obtained with growth hormone therapy and orthopedic surgery to correct bone defects. We propose the use of growth hormone in combination with bone lengthening during puberty to improve final height result.

**Keywords:** Achondroplasia; Dwarfism; Elongation surgery; Growth hormone treatment; Short stature

### Introduction

Achondroplasia is a genetic disorder which affects bone growth leading to short stature. It is the most common form of inherited disproportionate short stature. Best estimates are that it occurs in 1:26,000-1:28,000 live births [1] occurring with equal frequency in males and females and in all races. It is transmitted as autosomal dominant defect. In the mid 1990's the molecular pathogenesis of achondroplasia began to be unraveled [2] and the mutation of the transmembrane receptor Fibroblast Growth Factor Receptor 3 (FGFR3) was identified. Achondroplasia presents a distinct clinical phenotype which is evident at birth. Its Characteristic features include short limbs, a relatively large head with frontal bossing and midface hypoplasia, trident hands, muscular hypotonia, patients eventually develop bowed legs and lumbar lordosis, hyperlordosis, small hands, recurrent ear infections, delayed motor milestones, and macrocephaly with high forehead and saddle nose. [3] Neurologic complications are due to narrowing of the vertebral foramen, and craniocervical junction compression increases the risk of death in infancy. [4-5]. Although there is a delayed motor development intelligence is generally normal [5]. Individuals with achondroplasia have short stature caused by rhizomelic shortening of the limbs, characteristic facies with frontal bossing and midfacial retrusion, exaggerated lumbar lordosis, limitation of elbow extension and rotation, genu varum, brachydactyly, and trident appearance of the hands, with the arms and thighs more severely involved than the forearms, legs, hands, and feet. Excess mobility of the knees, hips, and most other joints is common [6]. Direct targeting of therapeutic agents to the growth plate cartilage may enhance efficacy and minimize side effects of these and future therapies. [2]. Many studies have assessed growth hormone (GH) therapy as a possible treatment for the short stature of achondroplasia [7-9]. In general, these and other series show initial acceleration of growth, but with lessening effect over time, and variability of the results .

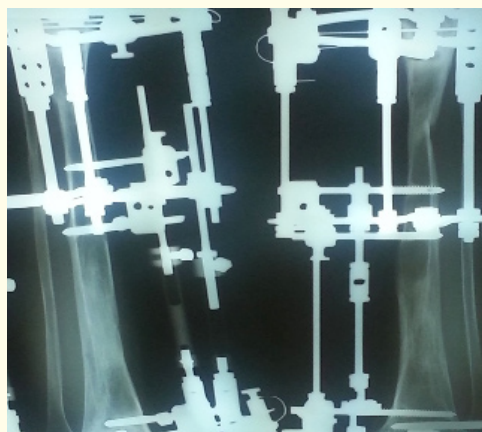
The history of the bone lengthening starts as early as 1904 with Codivilla [10]. There are many techniques and protocols for extended limb lengthening. Increases in height of up to 12-14 inches may be obtained [5,11]. It is proposed to postpone such surgery until the young person is able to participate in making an informed decision. [12,13]

**Citation:** Mejia de Beldjenna Liliana. "Medical and Orthopedic Management with Growth Hormone and Bone Lengthening in a Patient with Achondroplasia". *EC Orthopaedics* 3.1 (2016): 229-232.

**CLINICAL CASE:** I wish to report on a patient with achondroplasia who was treated with growth hormone and bone elongation during puberty. Patient treated by Pediatric Endocrinology from 2 years of age with achondroplasia, hypothyroidism, short stature, dolichocephaly, dental anomalies, shortening of the inferior segment, bilateral genu varus, forearm varus, and trident sign of both hands. RMN showed no evidence of Hydrocephalus. Patient had thelarche at age 11 years old, menarche at 14, 6 years old and surgical elongation of the lower extremities at age 12. She was treated for hypothyroidism with sodium levothyroxine and received growth hormone at a dose of 0.85 mg /kg / week from 4 age until age fourteen. Surgical treatment consists of symmetrical elongation of the lower extremities with Ilisarof distractor at a rate of 1 mm per day for two years with an increase of 21, 5 cm during this period. The simultaneous treatment, growth hormone and elongation of the extremities improved height from 83 cm to 137, 5 cm. Final height was 140 cm. figure 1.fig 2-4 figure bone elongations



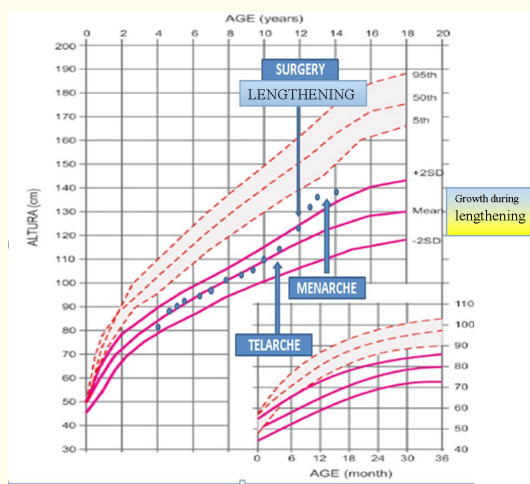
*Figure 1*



*Figure 2*



**Figure 1-2-3:** Bone elongation combined with growth hormone therapy can produced better result in height than growth hormone alone in patient with achondroplasia.



**Figure 4:** Growth curve.

## Discussion

Average adult height for men with achondroplasia is  $131 \pm 5.6$  cm; for women,  $124 \pm 5.9$  cm. [5] Management of disharmonic short stature is complex because of diverse etiology and limited resources. Patients with achondroplasia can benefit from a combination of growth hormone therapy and limb elongation.

Hydrocephaly is a chronic condition which develops early in life and it should be ruled out before beginning growth hormone therapy to prevent complications. At present growth hormone therapy is only approved for the treatment of SHOX deficiency. In other osseous dysplasia such as hypochondroplasia, achondroplasia and osteogenesis imperfect the results have been variable [9, 11, 13]. Surgical limb lengthening is another approach that has been used to increase stature. It involves breaking bones, usually femurs, tibiae, and humerus, followed by slow stretching during the healing process by means of orthopaedic appliances. As much as 15–30 cm has been added to standing height, the procedure is controversial because of the need for repeated surgeries, the extended time that orthopaedic

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appliances must be in place, infections, and complications related to stretching of non-skeletal tissues including nerves and blood vessels [11]. It requires difficult decision making and great commitment of the patient and the family, In our patient the treatment with growth hormone and limb elongation contributed to growth and improved quality of life.

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**Volume 3 Issue 1 February 2016**

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