CASE REPORT

Craniofacial and Dental Manifestations in Pediatric Patients with Achondroplasia: A Case Report and Clinical View

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Abstract

Aim: The aim of this case report is to describe the dentofacial manifestations of achondroplasia and highlight concerns associated with dental management of pediatric patients with achondroplasia.

Background: Achondroplasia is the most common form of skeletal dysplasia (dwarfism) with clinical manifestations including disproportionate limb shortening and stunted stature. The craniofacial characteristics of achondroplasia are relative macrocephaly, depression of the nasal bridge, and maxillary hypoplasia. Special precautions are necessary during dental management of pediatric patients with achondroplasia due to a large head size, implanted shunts, airway obstruction, and difficulty in head control.

Case description: A 6 years and 7 months male, the patient was diagnosed with achondroplasia, currently receiving vitamin D, no known drug allergy, and a mixed dentition stage with multiple caries, mouth breather, and a high risk of further caries based on a caries risk assessment due to poor oral hygiene. As the patient was uncooperative and required extensive dental care, dental rehabilitation was conducted under general anesthesia using oral intubation due to nasal obstruction. Future examinations were planned for every 3 months.

Conclusion: The current case demonstrated that the characteristics of achondroplasia might cause respiratory, neurological, skeletal, orthodontic, and psychological difficulties. Pediatric dentists who treat these patients must be able to detect these characteristics and difficulties, as dental treatment is limited by practical issues associated with this condition.

Clinical significance: The characteristic features of achondroplasia are attributed to skeletal, respiratory, neurologic, orthodontic, and psychosocial issues. The dentist should be aware of the features of achondroplasia, which can potentially restrict dental management.

Keywords: Achondroplasia, Craniofacial, Fibroblast growth factor receptor.

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Background

Achondroplasia, also termed chondrodystrophia fetalis, is a hereditary autosomal dominant form of chondrodysplasia with complete penetrance. It is considered the most frequent type of short-limb dwarfism.[1,2] The incidence of achondroplasia is one case in 26,000–66,000 births.[3] However, eight out of 10 cases are sporadic. The genetic defect underlying achondroplasia is a point mutation to the *fibroblast growth factor receptor 3 (FGFR3)* gene, located on chromosome 4. This mutation impairs the chondrocytes' differentiation and maturation in the cartilage growth plate, resulting in inadequate bone development. Besides this impairment, approximately 97% of achondroplasia patients carry a common gain-of-function mutation to *FGFR3* that diminishes the endochondral ossification and chondrocyte hypertrophy and qualitatively impacts the cartilage matrix production, resulting in various manifestations and complications.[3,4]

Routine ultrasound for the detection of achondroplasia of a fetus shows shortening of the long bones, which is confirmed by *FGFR3* mutational testing of prenatal specimens.[5] A diagnosis of achondroplasia is sometimes based on clinical manifestations, which include a short stature contrasting with a normal trunk length associated with rhizomelic shortening of the extremities besides other morphotype features of the trunk and the extremities. In the trunk, achondroplasia patients have spinal stenosis, lumbar lordosis, prominent buttocks, and a protuberant abdomen. Regarding the limbs, they have bowed legs and short trident hands characterized by a gap between the third and fourth fingers. Other clinical manifestations include diabetes and obesity.[6] Radiology imaging confirms the skeletal origin of the clinical structural abnormalities and shows further dysmorphic features, notably concerning the vertebrae, and iliac bones, in addition to maxillary hypoplasia and other craniofacial characteristics.[7] These malformations often result in a variety of functional disorders, such as hydrocephaly, higher airway obstruction with difficulty breathing, dental malocclusion, otolaryngeal dysfunction, and recurrent sinusitis and otitis.[8–10]

The treatment of dentofacial deformities of children with achondroplasia is both complicated and difficult, as special precautions are necessary for dental management because of

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macrocephaly, difficulty with shunt implantation, and airway obstruction.[10] Although there is no treatment for achondroplasia, limb lengthening can improve stature,[11] and somatotropin therapy can transiently increase growth but does not significantly increase stature.[12] Most individuals with achondroplasia lead independent and productive lives due to normal intellectual ability.[13] In Saudi Arabia, pediatric patients with genetic disorders, such as achondroplasia, can receive dental care in both general and specialized dental clinics. Therefore, dentists should consider the anatomical and physiological specificities of such patients and be aware of the potential difficulties and complications.

The present case report describes the dental and maxillofacial manifestations of achondroplasia in a 6-year-old child and highlights the major concerns associated with the dental management of pediatric achondroplasia patients.

Case Description

A 6-year-old Saudi male presented to the Department of Pediatric and Preventive Dentistry of King Saud Medical City (KSMC) for treatment of multiple dental caries. The child was born by cesarean section to nonconsanguineous parents in Jazan, Saudi Arabia. Further medical history included achondroplasia and the use of calcium and vitamin D supplements. The caesarean section was probably indicated for cephalopelvic disproportion. The patient underwent surgery for the implantation of eight proximal lateral plates for epiphysiodesis for bilateral genu varum (Fig. 1). He is the youngest among eight siblings. Neither parent exhibited dysmorphia, nor the family members had achondroplasia.

On the initial visit, the patient appeared to have a healthy state and good intellectual function. His height was 96 cm, and his weight was 16 kg (below the 5th percentile for age).

Genetic Method and Results

Whole exome sequencing of the patient was conducted at the Molecular Diagnostic Laboratory of KSMC using a SureSelectXT Target Enrichment System (Agilent Technologies, Inc., Santa Clara, California, United States of America) to capture regions of interest from a deoxyribonucleic acid (DNA) fragment library and the Illumina HiSeq 2500 sequencing system (Illumina, Inc., San Diego, California, United States of America) with a minimum coverage of 30× of 95% of the target regions. The proband's exome DNA sequences were mapped and compared to the human genome build University of California Santa Cruz human genome version 19 reference sequence using an in-house pipeline. The coverage and quality of the targeted coding exons of the known protein-coding RefSeq genes were assessed. Exome analyses of thousands of genetic variants were performed using proprietary databases customized to Arab populations. A subset of the genetic variants was characterized in accordance with the guidelines of the American College of Medical Genetics and Genomics to clarify potential clinical relevance. Unless otherwise noted, all variants identified in this report were validated by Sanger sequencing.

A pathogenic heterozygous variant of *FGFR3* (NM_000142:exon9:c.1138G>A:p.G380R) was identified in this patient.

Fig. 1: Photographs of the patient before and after the insertion of eight proximal lateral plates for epiphysiodesis

Extraoral Examination

The patient presented common manifestations of achondroplasia in the trunk and extremities. Nevertheless, he had marked facial dysmorphic features, including saddle nose, severe midface hypoplasia, and an overall face concaveness. However, the mandible and chin were normally constituted. In addition to mouth breathing, the patient exhibited an interlabial gap of 13 mm at rest (Fig. 2). Other remarkable manifestations included long bone bowing, shortening of the elbow with thick proximity and a thin distal end, and limited hip extension.

Intraoral Examination

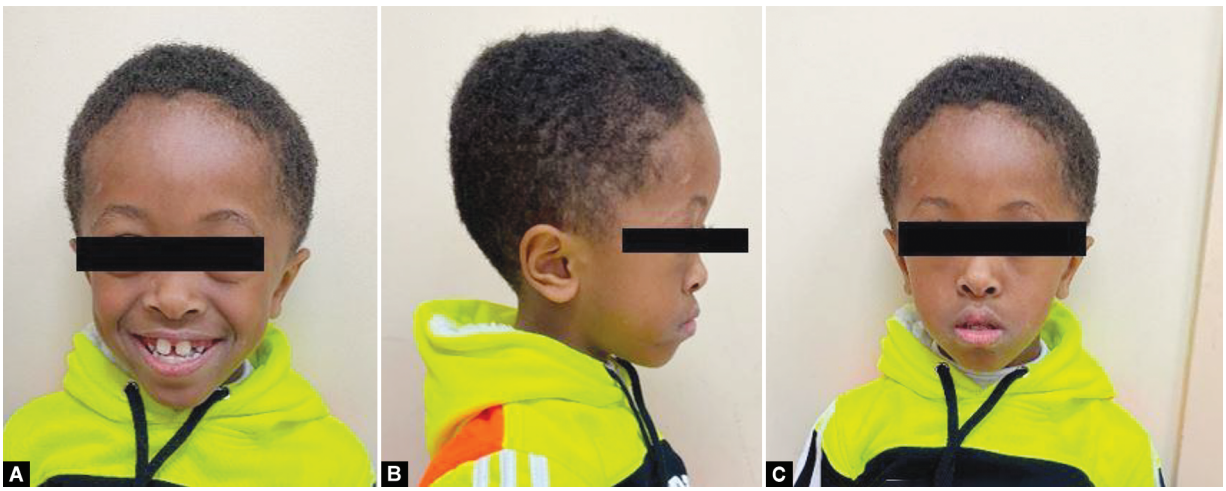
Intraoral examination revealed macroglossia and tongue thrust swallowing with mixed dentition stage (class III canine relation), mesial step molar relationship, and anterior edge-to-edge relationship with a large diastema. The patient had poor oral hygiene, with evidence of plaque-induced gingivitis and dental caries affecting multiple teeth (Fig. 3). On the other hand, the teeth eruption was compatible with the patient's age.

Radiographic Examination

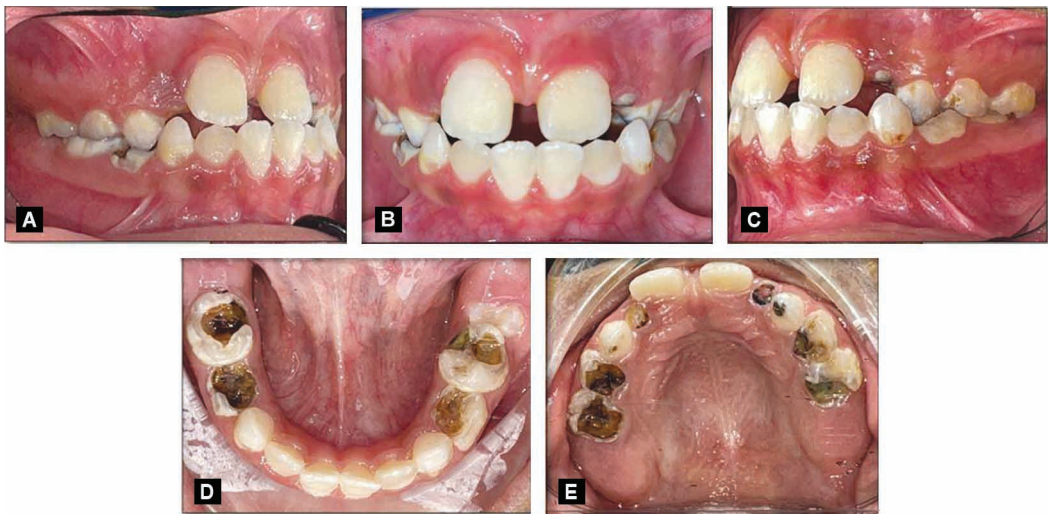
A panoramic radiograph showed normal developing occlusion with no abnormality of the right and left temporomandibular joints. There was a large diastema between the upper central incisors with no supernumerary teeth in the anterior segment and other areas. The lower permanent canines appeared to be erupting normally. However, the upper permanent canines appeared to be erupting with mesial angulation, but no overlapping of the permanent lateral incisors. The dental age was 6 years old. Bitewings and periapical revealed deep caries to teeth numbers #55, 54, 53, 63, 64, 65, 73, 74, 75, 83, 84, and 85 with remaining roots of #52 and 62 (Fig. 4).

Diagnosis and Treatment

At the age of 6 years and 7 months, the patient was diagnosed with achondroplasia, currently receiving vitamin D, no known drug allergy, and a mixed dentition stage with multiple caries, mouth breather, and a high risk of further caries based on a caries risk assessment due to poor oral hygiene. The treatment plan included extraction of carious primary teeth (#55, 54, 65, 64, 74, and 84) and restorations (#53, 63, 73, and 75), pulpotomy, and stainless steel crowns (#85 and 75) (Fig. 5). As the patient was uncooperative and required extensive dental care, dental rehabilitation was



Figs 2A to C: Smiling, lateral, and frontal views showing a concave profile, midfacial hypoplasia, flattening of the nasal bridge, and a normal appearing mandible



Figs 3A to E: Intraoral views showing dental caries, anterior reverse overjet, a posterior crossbite, and class III dental malocclusion

conducted under general anesthesia using oral intubation due to nasal obstruction. Follow-up visits were conducted every 3 months, and a high-prevention plan was provided. During the follow-up visit, space analysis was done and showed spaced deficiency in both upper and lower arches (–10 and –11 mm, respectively) (Figs 6 and 7). Orthodontics consultation advised no active treatment is needed at this stage.

Discussion

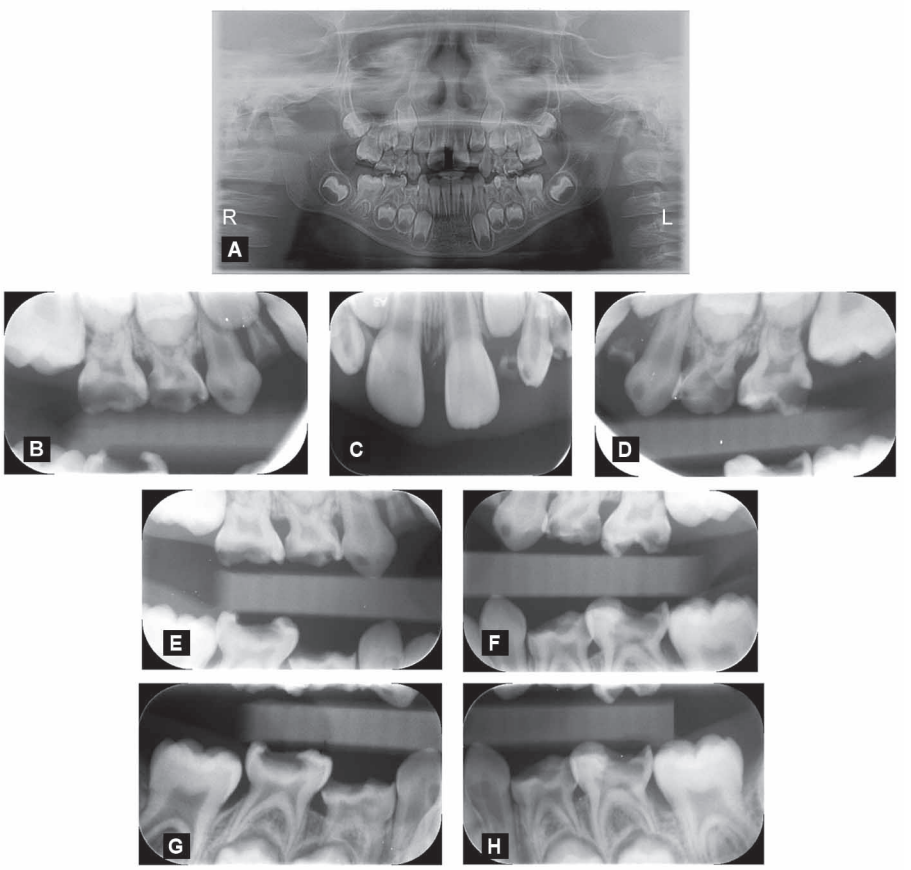
Reports of dentofacial findings, common dental issues, and treatment plans for pediatric patients with achondroplasia are relatively limited.[14,15] The prevalence of achondroplasia was reportedly 2,50,000 cases worldwide in 2007.[16] Achondroplasia is an autosomal dominant form of nonlethal chondrodysplasia caused by defective maturation of the cartilage growth plate of the long bones.[16]

In the heterozygous state of achondroplasia, life span, and intellectual ability are normal, but patients have an increased risk of obesity, spinal stenosis, cervicomedullary compression, and obstructive sleep apnea. By contrast, the homozygous form of achondroplasia, which is considered a lethal form, can cause severe rib cage deformities in early life, resulting in respiratory insufficiency.

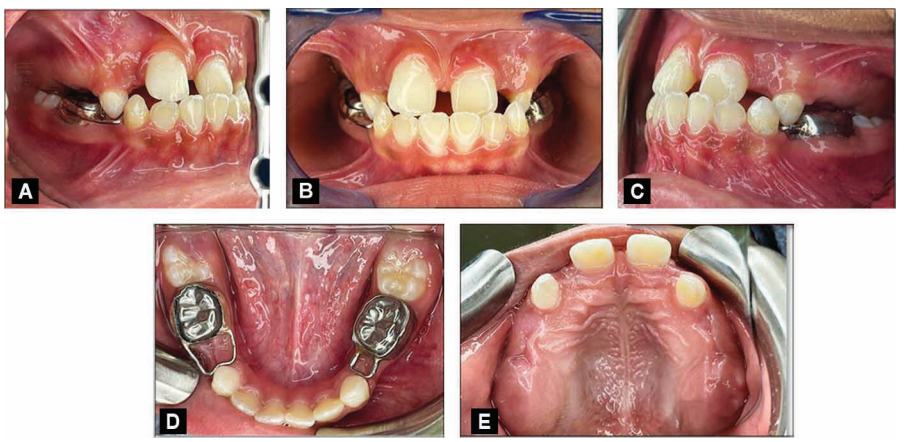
Children with achondroplasia are born with short stature and a slow growth rate throughout their childhood. However, the skull is typically enlarged with a prominent forehead. In addition, the limbs are relatively shortened; especially the upper arms and thighs, and the distal extremities are short and wide. The typical final adult height is 131 and 126 cm for men and women, respectively. Although most affected children are healthy, severe complications appear in one out of 10 of them. Thus, routine examinations are recommended.

Cervicomedullary compression, which can present with episodes of apnea, is a rare complication of achondroplasia. Imaging assessment using a computed tomography scan or magnetic resonance imaging is recommended prior to surgical intervention. The most common symptoms of cervicomedullary compression are numbness or weakness of the legs due to compression of the nerve roots within the canals.[17]

In addition to skeletal deformities, the present case had a class III posterior crossbite, anterior open bite, anterior reversed



Figs 4A to H: Preoperative radiographs showing extensive dental decay affecting all primary molars and canines



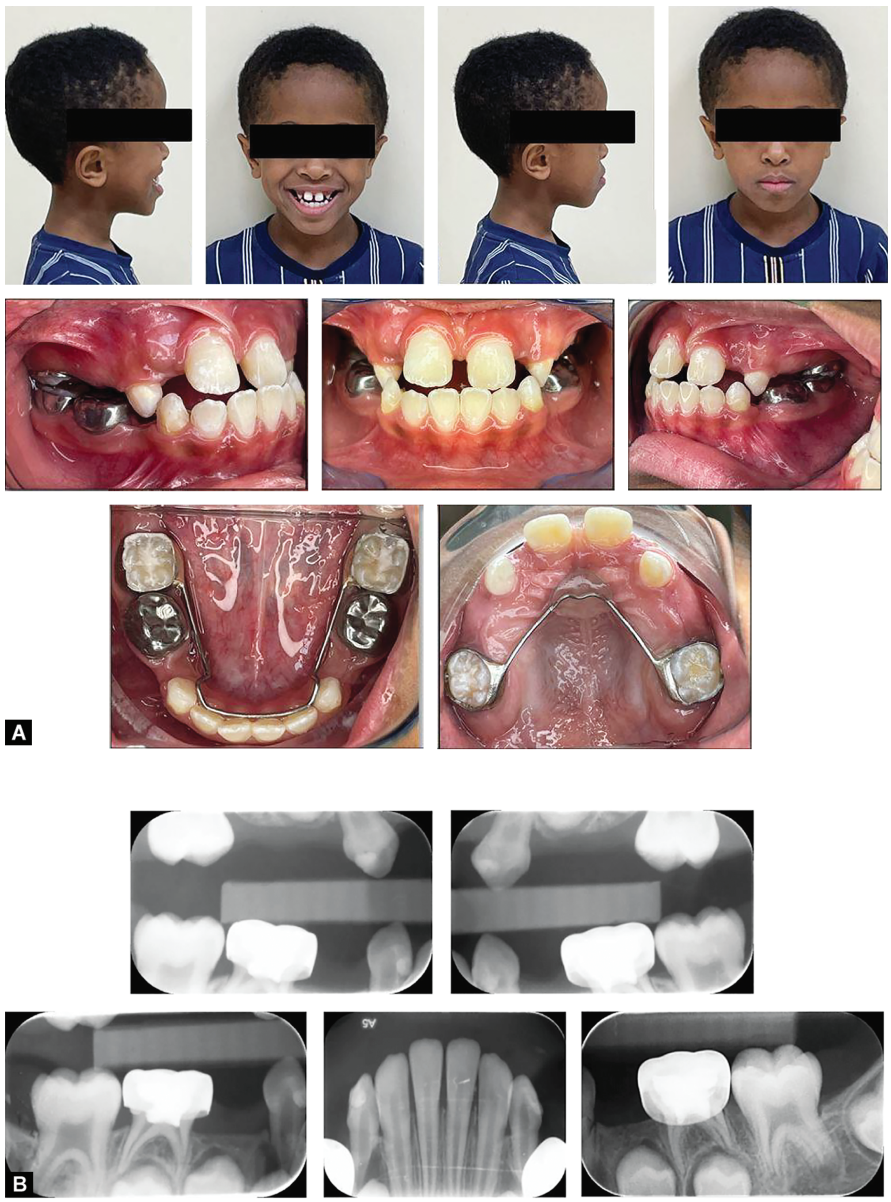
Figs 5A to E: Photographs at 3 months after dental rehabilitation under general anesthesia

overjet due to midface hypoplasia, and a normal mandible. Rohilla et al.[18] reported that these characteristics resulted from inadequate endochondral ossification with normal membranous ossification. On the other hand, since the condylar cartilage is produced by periosteal chondrogenesis, the growth of the mandibula is conserved, consistent with the present case.

Achondroplasia children usually present mild or moderate muscular hypotonia and motor skills retardation.[19] Our patient began to walk at the age of 2 years but had bowing of the tibias, which is defined as a distance of more than 5 cm between the knees with the legs straight and ankles apposed.[20] Based on these criteria, by the age of 5 years, 9.7% of individuals have bowed tibias, which continues to develop throughout childhood and into adulthood in 41.6% of patients. Tibial osteotomy is a valid treatment option for these individuals. At the age of 6 years, our patient had normal intelligence, although hydrocephalus and complications with the central nervous system are known complications.[13]

In pediatric patients with achondroplasia, dental development may be delayed due to altered bone growth,[21] while the eruption of both primary and permanent teeth occurs with no delay,[22] as in the present case.

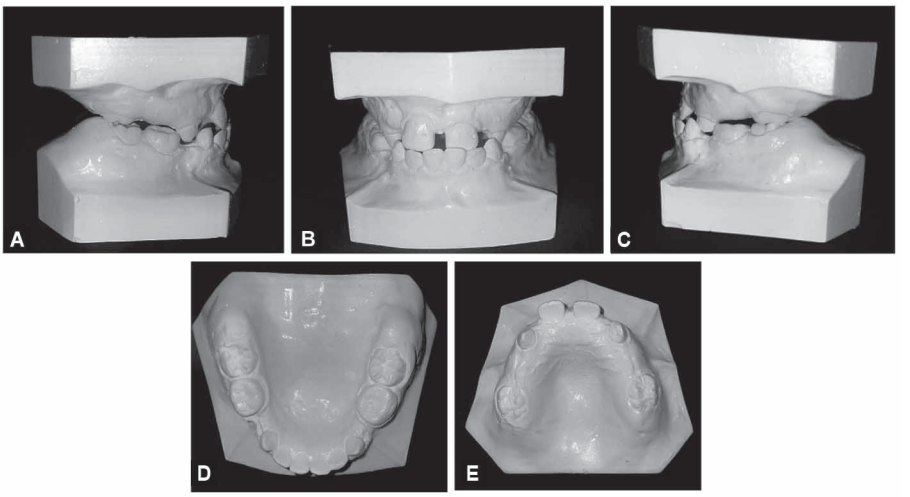
There is no report in the literature on the risk and incidence of dental caries in pediatric patients with achondroplasia. Our patient



Figs 6A and B: (A) Photographs after 6 months; (B) Radiographs after 6 months

had an increased risk of dental decay because of the malocclusion, in addition to high sugar intake and poor oral hygiene. Dunbar et al.[22] reported that class III malocclusion is the most common orthodontic condition associated with achondroplasia. It is critical to consider early orthodontic assessments for pediatric patients with achondroplasia. Our patient should be followed-up until the complete eruption of the permanent first molars and incisors.[22,23] A review of orthodontic problems after the age of 5 years is recommended by the American Academy of Pediatrics. A short stature causes a variety of psychosocial and social issues in pediatric patients with achondroplasia. Thus psychological management might be necessary throughout the dental treatment.[19] Shunts are placed in some pediatric patients with achondroplasia for treatment of hydrocephalus.[20,23] which could complicate head management and require antibiotic prophylaxis prior to dental care, although shunt implantation was not necessary in the present case.

Specific precautions for head management during dental interventions may be necessary because of the eventual craniocervical instability and other abnormalities that may increase the risk of respiratory complications, such as foramen magnum stenosis and restricted neck extension. Precautions are particularly important for uncooperative pediatric patients with achondroplasia.[24] Mouth breathing is reportedly a common feature of pediatric patients with achondroplasia due to upper airway obstruction.[24,25] Our patient was uncooperative; thus, the dental interventions were performed under general anesthesia. Although the clinical and radiographic findings of pediatric patients with achondroplasia vary, endotracheal intubation is usually not problematic.[26] However, certain complications can arise from intubation because of the relatively narrownasal pharynx and larynx, anteriorly placed epiglottis, and small chest size.[27,28] Therefore, it is necessary for specialists dealing with pediatric dental care to screen for eventual factors and complications that may require specific precautions during sedation or anesthesia of such patients.



Figs 7A to E: Dental cast after 6 months showing spaced deficiency in both the upper and lower arches (–10 and –11 mm, respectively)

Imaging assessment of the foramen magnum, oxygen therapy prior to anesthesia using appropriately sized endotracheal tubes, oral intubation, and oxygenation after extubation are recommended during dental treatment.[26]

Clinical Significance

Besides the skeletal features, achondroplasia encompasses several system dysfunctions, including respiratory, neurologic, and orthodontic, besides the psychosocial impact. The present report highlighted the potential complications that might arise during the dental care of pediatric patients with achondroplasia. The dentist should consider assessing and managing the anatomical and functional features of achondroplasia that can potentially restrict dental management.

Patient Consent Statement

The author(s) have obtained written informed consent from the patient's parents/legal guardians for publication of the case report details and related images.

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