Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2016; 4(3A):679-682 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com DOI: 10.36347/sjams.2016.v04i03.010

Case Report

Oral Manifestation of Achondroplasia -A Case Report

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Abstract: Achondroplasia is a disorder of bone growth that causes the most common type of dwarfism. It belongs to a group of disorders called chondrodystrophies or osteochondrodysplasias. It is a congenital genetic disorder resulting in rhizomedic dwarfism and is the most common skeletal dysplasia. This case report highlights the oral manifestation of a 3 year old male patient with achondroplasia.
Keywords: Achondroplasia, Mutation, Short stature.

INTRODUCTION

Achondroplasia is a genetic (inherited) condition that results in abnormally short stature and is the most common cause of short stature with dyspropotionately short limbs. The average height of an adult with achondroplasia is 131cm (4 feet 4 inches) in males and 124cm (4 feet 1 inch) in females. The frequency of achondroplasia is estimated to range from about 1 in 10,000 births in Latin America to about 12 in 77,000 in Denmark. An average figure worldwide is approximately 1 in 25,000 births with males affected frequently than females [1].

It occurs due to sporadic mutation in the majority of cases but can be inherited as an autosomal dominant condition. Homozygous achondroplasia is lethal. Although achondroplasia literally means "without cartilage formation",the defect in achondroplasia is not in forming cartilage but in converting into bone, particularly in long bones.It is a genetic disorder of bone growth and inherited as a dominant trait but 80% of cases are due to new mutation (neither parent has achondroplasia). It can be diagnosed before birth and the intelligence is normal in people with achondroplasia [2]. The present article describes a case of achondroplasia disorder, diagnosed and successfully treated in a 3 year old male patient.

CASE REPORT

A 3year old male patient reported with a chief complaint of decayed teeth in the upper anterior teethfor the past one year. No history of fever, rashes, jointpain, lymphadenopathy, hypertension, diabetes mellitus or medication. The natal and post natal history revealed that the patient was delivered by caessarian section. Post natal physiological events were in normal range. Family history showed the patient born to non-consangunious parents. Medical history revealed that the patient was a known case of achondroplasia.

Fig. 1: Achondroplasia patient with short stature with rhizhomelic shortening of arms and legs

Anthrometry expressed a height of 70cm and weight of 25kg.The gross motor developmental milestones were delayed significantly,which might be due to the large head but fine motor developmental and language milestones were found to be normal at a 3years old level.

The patient appeared to be well adjusted healthy and intelligent. General physical examination showed short stature, rhizomelic shortening of the arms and legs and a trident hard configuration. Extraoral examination revealed facial features such as bracycephaly, midfacialhypopasia, flat nasal bridge,

frontal bossing and competent lips.A concave facial profile was also noticed,however the mandible appeared to be normal and the chin was not prominent. Intraoral examination revealed primary dentition. The size, number and form of the teeth were normal with straight flush terminal relationship with spacing in anterior teeth. The periodontium was found to be healthy and decayed teeth in 51,52,61,62 were present. The plain computed tomogram (CT) of the brain that was performed at the age of one and half years showed moderate degree of hyrdocephalus. The lateral cephalogram revealed bracycephally and midfacial hypoplasia. The panaromic radiograph showed complete set of primary dentition with normal development and spacing in the upper and lower anterior teeth. The handwrist radiograph revealed the trident hand configuration and according to the fisher's skeletal maturityindex, the patient was in stage3. Radiograph of the lower limb anteroposterior (AP)view showed shortening and increased apparent thickness of the femur,tibia and fibula bilaterally with flaring of the acetabulla, also there was shortening of the long bones of the upper extremities,proximal more than distal. The thoracic and lumbar vertebrae reveleddecreased APdiameter of the vertebral border with increased apparent thickness of the discs. Based on the history,clinical examination and radiological investigation, a final diagnosis was arrived as achondroplasia. The patient and parent were psychologically counselled for the general good prognosis of the condition.

Fig-2: Lateral view showing concave profile, midfacial hypoplasia, flat nasal bridge and normal appearing mandible

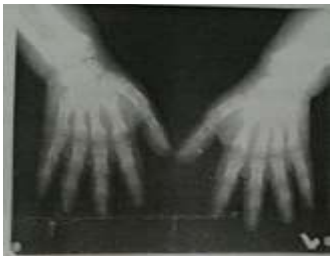

Fig-3: Hand wrist radiograph showing trident hand configuration

As the treatment part oral prophylaxis and composite restoration were done in relation to 51,52,61,and 62done. Oral hygiene of the patient was found to be satisfactory.An oral hygiene instruction was given and the patient was counseled and motivated for regular follow up.

DISCUSSION

Achondroplasia is a disorder of bone growth that causes the most common type of dwarfism. It belongs to a group of disorders called chondrodystrophies or osteochondrodysplasias. It may be inherited as an autosomal dominant trait, which means that if one parent has achondroplasia, the infant has 50% choice of inheriting the disorder and if both parents have the condition the infant's chances being affected increase to 75%. However most cases appear as spontaneous mutation which means that an achondroplastic child can have normal parents [3, 4].

Achondroplasia is the most common form of skeletal dysplasia affecting growth of tubular bones, spine and skull. It is an autosomal dominant disorder with complete penetrance. The gene for achondroplasia is localized to 4p 16.3.Subsequently mutation of fibroblast growth factor receptor 3 (FGFR3) gene within the region 4p 16.3 is reported as a cause of achondroplasia [5].

Achondroplasia has recently been shown to result from a Glycine to Arginine substitution in the transmembrane domain of the new receptor thyrosine kinase, with the transmembrane domains of wild-type and mutant FGFR3, the Arginine 380 mutation in FGFR3 is shown to activate both the kinase and transforming activities of this chimeric receptor [6].

Residues with side chains capable of participating Glu,Asp and to a lesser extent, Gln, Hisland Lys, are able to substitute for the activating Arg 380 mutation. The Arg 380 point mutation also causeslig-and-independent stim-ulation of the Tyrosine kinase activity of FGFR3 itself and greatly increased constituent level of phospotyrosine on the receptor. As a result it limits the formation of bone from cartilage, particularly in long bones. FGFR3 also plays an important role in cell growth and division, determination of cell type, formation of blood vessels,wound healing and embryo development [7, 8].

FGFR3 is one of the key FGF binding tyrosine kinase receptors and is highly conserved in both human and mice. The human FGFR3 gene is located on chromosome 4q 16.3. Research has shown that FGFR3 is expressed in different tissues including cartilage, the brain, kidneys and the intestine in different stages of development. FGFR3 is a single pass trans membrane

receptor and is involved in regulating cartilage and varied aspects of long bone development including chondrocyte proliferation and cartilage matrix calcification. The FGFR3 gene is 15kb and contains 19 exons and 18 introns. Numerous functional domains are encoded by FGFR3 gene including an extracellular glycosylation ligand-binding domain, a hydrophobic transmembrane domain and an intracellular tyrosine kinase catalytic domain. Mutation of FGFR3 in the hydrophobic transmembrane domain in patients with achondroplasia according to polymerase chain reaction (PCR) combined with single strand conformation polymorphism (SSCP) [9].

Genetically around 99% of achondroplasia cases are caused by the c.1138G A and c.1138G C mutations. Both mutations convert glysine (Gly) into arginine (Arg) on the 380th amino acid, leading to dysfunctional proteins. In 1995, Swedish and Japanese research groups found a third base mutation C.1123G T - in individual cases and one family, but the incidence of this mutation is very low(about 1-2% of all mutation). Recently another noval mutation was reported, Gly to Glu on the 346th of amino acid [10].

In Hetrozygous state, achondroplasia is non-lethal with normal lifespan and normal intelligence. However they are at risk like cervicomedullary compression, spinal stenosis, obesity, obstructive sleep problems. There is a disturbance in the division and the maturation of growth plate. Chondroblasts causing deficiency of chondroid and an inhibition of normal endochondral growth. The limb bones are affected but the trunk is relatively normal. In homozygous state achondroplasia is a lethal condition in the early few months of life because of severe rib cage deformity that results in respiratory insufficiency [11].

Achondroplasia is the most common condition associated with severe disproportionate short stature. The diagnosis can usually be made on the basis of clinical characteristics and very specific features on radiographs which include contracted base of the skull, square shape of the pelvis with a small sacrosciatic notch, short pedicles of the vertebrae, rizhomelic shortening of the long bones, trident hands, a normal length trunk,proximal femoral radiolucency and a characteristic chevron shape of the distal femoral ephiphysis. Other rhizomelic dwarfing disorders such as hypochondroplasia, thanatophoric dysplasia, achondrogenesis, campto-melicdysplasia, Ellis-van, Creveld syndrome are the part of the differential diagnosis [12].

The average adult height in acondroplasia is approximately 4ft for men and women. The most common complication occuring in adulthood is related to lumbosacral spinal stenosis with compression of the spinal cord or nerve roots. This complication is usually treated by surgical decompression if it is diagnosed at an early stage [13].

Most of the children with achondroplasiado well. However children affected with achondroplasia with commonly have delayed milestones, otitismedia and bowing of the lower legs. Less commonly infants and children may have serious health consequences related to hydrocephalus, craniocervical junction compression, upper airway obstruction or thoracolumbar kyphosis. Although they are less common anticipatory case should be directed at identifying children who are at high risk and intervening to prevent serious sequelae [14].

Obesity can be a significant problem in people with achondroplasia. The excessive weight gain usually occurs during childhood. When obesity is present, the back and joint problems that are characteristic of this condition worsen in severity. The child with achondroplasia must not be allowed to become overweight. Adults with achondroplasia showed also monitor and control their weight [15].

Dental development can be delayed in achondroplastic children due to altered bone growth. Several odontostomatological manifestations like skeletal and dental class III maloclussion, normal maxilla, macroglossia, posterior open bite had been reported with acchondroplastic children. Treatment with human growth hormone which is still considered experimental, had been primarily reported to increase the growth rate after treatment, but studies were not yet demonstrated the adult height is increase by this treatment [16].

CONCLUSION

Dealing with achondroplastic children needs special psychological management during dental treatment, as the presence of disproportionate short stature can cause a number of psycosocial and social problems. Patient with chondroplasia not only required specific medical management but also need special attention with definite dental management along with psychological support to help him lead a normal life and cope up with medical and social challenges of life.

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