CASE REPORT

Familial Cleidocranial Dysplasia - A Case Series

Amit Mhapuskar[1], Rashmi Agarwal[2], Rohit Behere[3], Darshan Hiremutt[4]

ABSTRACT

Introduction: Cleidocranial dysplasia is a rare hereditary autosomal dominant disorder which presents as a defect of the skeleton and the teeth.

Case Report: The present case is of a 37 year old male patient with a complaint of difficulty in chewing due to multiple missing teeth. On examination, the pathognomonic triad of Cleidocranial Dysplasia, viz., multiple impacted supernumerary teeth, partial absence of clavicles and presence of open fontanelles & cranial sutures were found. Keeping in mind the familial nature of this condition, the patient's son and daughter were also examined. Both the children exhibited nearly all the signs of this condition in varying degrees which confirmed a diagnosis of Familial Cleidocranial Dysplasia. The children and their father were counselled and a comprehensive treatment plan was devised with a multidisciplinary approach.

Conclusion: Though, Cleidocranial Dysplasia is a rare disorder, it should be considered in the differential diagnosis of patients with multiple missing or over retained teeth and further investigations should be advised to confirm the diagnosis.

Keywords: Familial, multiple missing teeth, multiple supernumerary teeth, multiple impacted teeth, multidisciplinary

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INTRODUCTION

Cleidocranial dysplasia (CCD) is a rare dominantly inherited autosomal bone disease which affects the bones undergoing intramembranous ossification which is characterized by delayed closure of fontanelles, presence of open skull sutures, delayed ossification of skull, hypoplastic or aplastic clavicles with narrow thorax, supernumerary teeth, delayed eruption of permanent dentition, wide pubic symphysis, short stature and a variety of other skeletal changes. CCD is also known as Marie-Sainton's disease, Scheuthauer- Marie- Sainton syndrome, mutational dysostosis, and cleidocranial dysostosis. It is caused by mutation in the gene on 6p21 encoding transcription factor CBFA1, i.e. runt−related transcription factor 2(RUNX2).[1]

The most common or the only presenting complaint by these patients is inability to chew due to multiple missing teeth. This denotes the importance of the oral physician in diagnosing this rare disease first by recognizing some typical facial features followed by a more reliable skeletal radiological examination. Early detection of this condition especially in children can help dental professionals to synthesize a comprehensive treatment plan involving multiple disciplines of dentistry. This can lead to a fully functional stable permanent dentition, better facial aesthetics and have positive impact on the psyche of the patients and their parents through early counselling. This case series is presented to summarize the findings seen in Cleidocranial Dysplasia and highlight the familial nature of this condition. It also shows the importance of a thorough investigation of a suspected condition in spite of only a single finding being evident at first.

CASE DESCRIPTION

Case 1

A 37 year old male patient reported to the Department of Oral Medicine & Radiology with a complaint of difficulty in chewing due to multiple missing teeth. He did not give any history of extraction of teeth. On examination, he was found to have pronounced orbital ridges, fronto-parietal & occipital bossing, a significantly depressed nasal bridge and a large ala base. He

was of thin built and a small stature, with short and stout fingers along with hyoplastic fingernails (Figure 1). He also demonstrated moderate hypermobility of shoulders. On clinical palpation, it was possible to feel the absence of the clavicle on the right side. Intra-oral examination showed multiple over-retained deciduous teeth with multiple unerupted permanent teeth. A provisional diagnosis of Cleidocranial Dysplasia and a differential diagnosis of Congenital pseudoarthrosis was made. A panoramic radiograph of the jaws (Figure 2) revealed a total of 54 teeth including multiple impacted supernumerary teeth particularly clustered around the incisor and bicuspid area. The anterior and posterior borders of the rami were seen to be parallel to each other. The left zygomatic arch was seen to have a severe downward tilt. Frontal and lateral skull radiographs (Figure 2) showed a thickened calvarium, an open fontanelle and open sutures. A chest radiograph (Figure 3, top) showed that the left clavicle was hypoplastic and the right clavicle was absent.

Congenital pseudoarthrosis was considered due to the missing clavicles before radiographs were made. However, the dental abnormalities and radiologic appearance of the skull eliminated that possibility. The absence of osteosclerosis and presence of supernumerary teeth ruled out the possibility of Pyknodysostosis.[2] Delayed fontanelle closure is seen in many conditions like hypothyroidism, rickets, hypophosphatasia, osteogenesis imperfecta and other syndromes such as Apert syndrome, Dubowitz syndrome, Russell-Silver syndrome, Down's syndrome, and Crouzon syndrome.[3] However, along with open fontanelles, presence of multiple impacted supernumerary teeth and absence of clavicles was pathognomonic of Cleidocranial Dysplasia. Keeping in mind the familial nature of this condition, the patient's daughter and son were evaluated as well.

Case 2

The seven year old son of the patient in Case 1 was examined. On general examination, just like his father, he was found to have pronounced orbital ridges, depressed nasal bridge, a flattened mid-face, prominent forehead and pronounced occipital bossing producing the typical appearance of a globular (Arnold) head (Figure 4). He demonstrated marked shoulder hypermobility. On clinical palpation, it was possible to feel the absence of the clavicle on both the sides. Intra-oral examination showed multiple carious teeth. A panoramic radiograph of the jaws revealed two supernumerary impacted teeth in the mandibular bicuspid region and parallel borders of the ascending rami. Frontal and lateral skull radiographs (Figure 4) showed a thickened calvarium, an open fontanelle and open sutures. A chest radiograph (Figure 3, middle) showed absence of both clavicles. This confirmed the diagnosis of Cleidocranial Dysplasia. After proper counselling of the father and the son, a comprehensive treatment plan for the son was devised with a multidisciplinary approach involving Pediatric Dentistry, Oral Surgery, Prosthodontics and Orthodontics.

Case 3

The 13 year old daughter of the patient in Case 1 was also examined. The general and facial examination revealed a milder presentation in her case with presence of a prominent forehead and depressed nasal bridge. However, there was severe shoulder hypermobility. On clinical palpation, it was possible to feel the absence of the clavicle on both the sides. Intra-oral examination showed multiple missing permanent teeth. Similar to Case 1, a panoramic radiograph of the jaws (Figure 5) revealed a total of 47 teeth, including multiple supernumerary impacted teeth particularly clustered around the incisor and bicuspid area. The anterior and posterior borders of the rami were seen to be parallel to each other. Frontal and lateral skull radiographs (Figure 6) showed a thickened calvarium, an open fontanelle and open sutures. A chest radiograph (Figure 3, bottom) showed absence of both clavicles. This confirmed the diagnosis of Familial Cleidocranial Dysplasia.

After proper counselling of the father and the daughter, a comprehensive treatment plan for the daughter was devised with a multidisciplinary approach involving Pediatric Dentistry, Oral Surgery, Prosthodontics and Orthodontics.

DISCUSSION

Although rare, a first description of cleidocranial dysplasia (CCD) is believed to be found in Homer's Iliad in a character named Thersites, who had rounded shoulders stooping together over his chest.[4] CCD, also known as Marie and Sainton Disease, Scheuthauer Marie-Sainton Syndrome, and Mutational dysostosis, is a rare disease which can occur either spontaneously or by a dominant autosomal inheritance. It is shown to have high penetrance and a wide range of expressivity, with a frequency of one per million individuals. The variable expression of CCD was evident in our case-series as the father, son, and daughter all had different degrees of shoulder hypermobility and number of supernumerary teeth. CCD mainly affects bones undergoing intra-membranous ossification; especially skull, clavicle and other flat bones.[5] This condition is familial in nature and is

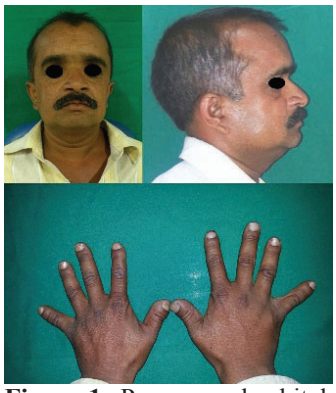

Figure-1: Pronounced orbital ridges, fronto-parietal & occipital bossing, depressed nasal bridge, large ala base & short and stout fingers with hyoplastic fingernails

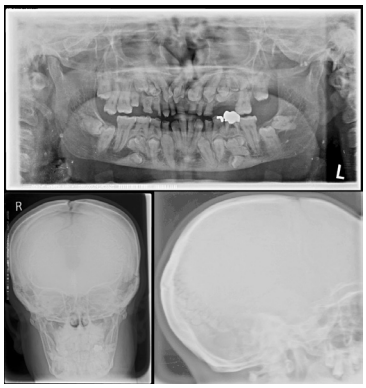

Figure-2: Panoramic radiograph of the father showing multiple impacted supernumerary teeth & downward tilt of left zygomatic arch and frontal & lateral skull radiographs showing thickened calvarium, open fontanelle and open sutures

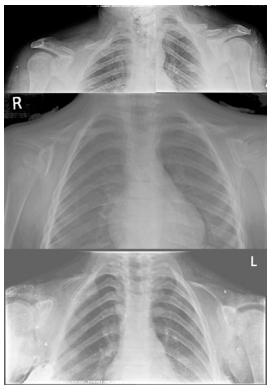

Figure-3: Chest radiographs of all the three cases showing partial/complete absence of clavicles

caused by a mutation of the Runt-related transcription factor 2 ($RUNX_2$) gene, which encodes a protein necessary for the correct functioning of osteoblasts and dental cell differentiation, and thus is responsible for normal bone and tooth formation.[6] For a definitive diagnosis of CCD, the following pathognomonic triad needs to be identified: multiple impacted supernumerary teeth, partial or complete absence of clavicles and presence

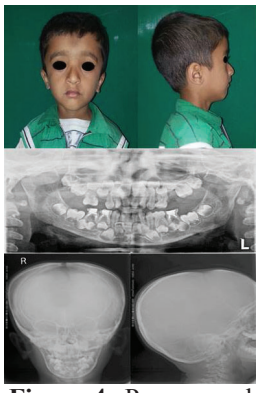

Figure-4: Pronounced orbital ridges, fronto-parietal & occipital bossing showing 'Arnold Head' appearance and Panoramic radiograph of the son showing parallel borders of the ascending ramii and frontal & lateral skull radiographs showing thickened calvarium, open fontanelle and open sutures

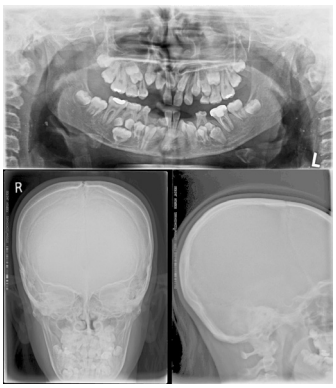

Figure-5: Panoramic radiograph of the daughter showing multiple impacted supernumerary teeth and frontal & lateral skull radiographs showing thickened calvarium, open fontanelle & open sutures

of open fontanelles & cranial sutures.[5]

In CCD patients, genetic disturbances in dental cell differentiation give rise to an abnormal dentition with over-retained deciduous teeth (due to delay in root resorption) and unerupted and/or impacted supernumerary teeth (due to lack of eruption potential and presence of physical barriers). The father and the daughter in our case series both had multiple impacted supernumerary teeth with the father having multiple over-retained deciduous teeth as well. The clavicle which is the first bone to ossify (5^{th} to 6^{th} week of fetal life), is seen to be totally absent in 10% of all CCD cases.[5] In our case series, both the children had missing clavicles while the father had a hypoplastic clavicle on one side. In CCD, there is an early developmental disorder of mesenchyme or connective tissue, causing retarded ossification of bone precursors, especially at junctions, which can lead to defective ossification or even failure

of ossification of some portions of skeletal structures. The syndesmoses between cranial bones are basically connective tissue junctions, which is the reason for open fontanelles and open sutures being a very common finding in CCD.[2] This was seen very prominently in all the three cases in our series.

Other common features of this condition are a bell-shaped thorax, enlargement of the frontal and occipital bones, hypoplasia of the pelvis and distal phalanges, and short stature. Less common findings of CCD patients include shortened or absent nasal bones, reduced or absent paranasal sinuses, hypertelorism, deafness, thickening of some segments of the calvaria, underdevelopment of the maxilla and delayed union of the mandibular symphysis.[2] Campos reported a case of CCD causing acute upper limb ischemia by means of mechanical damage to the axillary-subclavian arteries.[7] Absence of acellular cementum was noted in the ground section of an exfoliated deciduous molar in a case of familial CCD.[8]

Other radiographic findings include scoliosis, vertebral anomalies, spina bifida occulta[2], a wide pubic symphyseal space with a "chef's hat" appearance of the femoral head[9], long second metacarpals and short tapering distal phalanges on both hands. In the present case, the vertebral and hand wrist radiographs revealed no pathologic features.

In our case series, other features seen were pronounced orbital ridges, depressed nasal bridge, a flattened midface, prominent forehead, pronounced occipital bossing, parallel borders of the ramii, a downward tilt of the zygomatic arches and thickened calvarium particularly in the occipital region. In CCD patients, there is hypotrophy of the masseter muscles, which may be caused by discontinuity of the zygomatic arch. This hypoplasia of the masseter muscles leads to hyper-function of the temporal muscles.[2] Consequently, in such CCD patients, the anterior border of the mandibular ramus is usually parallel to the posterior border as seen in all three cases in our series.

The diagnosis of CCD is possible through family history, demonstration of hypermobility of shoulders, palpation of clavicle and maxillofacial and chest radiographs. Computed tomography may be useful in patients with CCD because it clearly delineates the open fontanelle, unlike the conventional anteroposterior skull radiograph in which the opened fontanelle is superimposed on the occipital bone.[6]

Common complications of CCD include pes planus, genu valgum, shoulder and hip dislocation, recurrent sinusitis, upper airway complications, recurrent ear infection, hearing loss, dental caries, osteomyelitis of the mandible or maxilla, respiratory distress in early infancy etc. Even with these complications the life span in such patients is normal. None of the above mentioned complications were found in the present case series.[10]

The treatment of CCD patients needs a multi-disciplinary approach and should be planned keeping the dental and chronological age of the patient in mind. Along with physical ramifications, this condition can also have an adverse impact on the psychology of these patients. Thus proper motivation and psychological support of patients and their parents is of utmost importance. The goal of treatment is to achieve a stable functional occlusion and pleasing aesthetics.

In conclusion, recognizing the features of CCD can establish an early diagnosis of this rare condition and prompt early treatment would lead to better long-term results.

REFERENCES

1. Diseases of Bone and Joints, 994-997 In: Shafer's Textbook of Oral Pathology, 5th edition. Rajendran and Sivapathasundharam, Elsevier 2006.
2. Tanaka JL, Ono E, Filho EM, Castilho JC, Moraes LC and Moraes ME (2006). Cleidocranial dysplasia: importance of radiographic images in diagnosis of the condition. J Oral Sci 48:161-6.
3. Karagüzel G, Aktürk FA, Okur E, Gümele HR, Gedik Y and Okten A (2010). Cleidocranial Dysplasia: A Case Report. J Clin Res Ped Endo 2:134-6.
4. Issever AS, Diederichs G and Tuischer J (2007). Diagnosis of Cleidocranial Dysplasia in Routine Chest Radiograph. Circulation 116:e116-8.
5. Mehta DN, Vachhani RV and Patel MB (2011). Cleidocranial dysplasia: a report of two cases. J Indian Soc Pedod Prev Dent 29:251-4.
6. Mohan RP, Suma GN, Vashishth S and Goel S (2010). Cleidocranial dysplasia: clinico-radiological illustration of a rare case. J Oral Sci 52:161-6.
7. Campos Júnior W, Cardoso RM, Fidelis R, Silva ES and Ramos R (2005). A familial case of cleidocranial dysostosis presenting upper limb ischemia. Sao Paulo Med J 123:292-4.
8. Chelvan HT, Malathi N, Kailasam V and Ponnudurai A (2009). Cleidocranial dysplasia: a family report. J Indian Soc Pedod Prev Dent 27:249-52.
9. Aktas S, Wheeler D, Sussman MD (2000) The "chef's hat" appearance of the femoral head in cleidocranial dysplasia. J Bone Joint Surg Br 82, 404-408.
10. Kumar VV, Nithyanand S, Kumar V. Cleidocranial dysplasia: a case report of a rare anomaly. Nepal Journal of Medical sciences 2012;1:135-7.