CASE REPORT

Cleidocranial Dysplasia Affecting Three Generations in a Family: A Unique Case Report

Vathsala Patil[1], Keerthilatha M. Pai[1], Yogesh Chhaparwal[1], Shubha Chhaparwal[2]*

[1]Department of Oral Medicine and Radiology, [2]Department of Conservative Dentistry and Endodontics, Manipal College of Dental Sciences, Manipal, Manipal Academy of Higher Education, Manipal-576104 (Karnataka), India

Abstract:

Cleidocranial Dysplasia (CCD) is a rare autosomal dominant syndrome that occurs in approximately 1 per million individuals worldwide. This syndrome is characterized by skeletal, orofacial, and dental manifestations like hypoplastic or aplastic clavicle, shoulder hypermobility, patent or delayed closure of fontanelles, and multiple impacted supernumerary teeth with delayed eruption pattern. Early diagnosis and management with a comprehensive team approach are crucial for an overall better prognosis. In this paper, we describe three generations of cleidocranial dysplasia presented in the same family with their clinical features and treatment strategies.

Keywords: Cleidocranial Dysplasia, Familial, Supernumerary Teeth

Introduction:

Cleidocranial Dysplasia (CCD) is a rare syndrome that occurs in approximately 1 per million individuals worldwide [1]. This condition was first coined by Martin in 1765, and its thorough description was proposed by Marie and Sainton in 1898, thus CCD is also called Marie and Sanitons disease [2]. Formerly, the disease was called cleidocranial dysostosis due to its involvement of skeletal structures that undergo intramembranous ossification like the skull, clavicles, and flat bones. Later, it was reported that the disease also involves the bones formed by endochondral ossification, and the patients with this disease exhibit abnormality in their overall skeletal system. Therefore to describe the broad spectrum of symptoms the disease was re-named as cleidocranial dysplasia [1].

CCD is an autosomal dominant condition caused due to the point mutation or deletion of the RUNX2 gene on 6p21 chromosome [3]. This gene controls osteoblastic differentiation and is required for appropriate bone formation. Its mutation results in early developmental disorder of mesenchyme and connective tissue causing retarded ossification or failure of ossification of skeletal structures [1]. This syndrome is characterized by skeletal, orofacial, and dental manifestations like hypoplastic or aplastic clavicle, shoulder hypermobility, patent or delayed closure of fontanelles, and multiple impacted supernumerary teeth with delayed eruption pattern [4]. Early diagnosis and management with a comprehensive team approach are crucial for an overall better prognosis. The parents of the CCD syndrome generally harbor the same genetic mutation, however, some cases with unaffected parents have also been reported [4-6]. In this paper, we describe three cases of cleidocranial dysplasia presented in the same family with their clinical features and treatment strategies.

Case Report:

A 24-year-old otherwise healthy Indian female reported to us with a chief complaint of pain in the upper left back tooth region for two months and multiple over-retained milk teeth since childhood. Pain was dull aching type started gradually, localized, and got aggravated on having food. Her pre-natal, post-natal, past medical, and social history was non-contributory. On general examination, she had short stature, a height of 4.8 feet which is below the 5th percentile, short and sloping shoulders that could be shrugged unusually close together (Fig. 1). Extraoral examination revealed a leptoproscopic and concave facial profile with a broad forehead and marked midline depression, slanting eyelids, hypertelorism, and low set ears, midfacial hypoplasia, and long neck (Fig. 1). Her family history stated that her mother and maternal grandmother also had similar features (Fig. 1). On intraoral examination, she had a mixed dentition status with over-retained maxillary and mandibular deciduous canines and molars, a high arched palate, and a class three malocclusion. The teeth 64, 65 had a deep-seated temporary restoration with secondary caries and partially erupted 37. Soft tissue examination revealed inflamed gingiva with tenderness on palpation and the pus discharge around and distal to 37.

A periapical radiograph was taken of 64,65 (over-retained deciduous molars of the second quadrant) revealed deep secondary caries approximating pulp. Her panoramic radiograph showed a total of fifty-seven impacted permanent and super-numerary teeth including both maxilla and mandible. Incidentally, a well-defined radiolucent lesion was seen around the crown of impacted mandibular left third molar measuring roughly 2 × 2 cm (Fig. 2). Considering her short stature and sloping shoulders, a chest X-ray and PA skull were also advised where the skull X-ray showed the presence of wormion bone and the chest X-ray showed the incomplete formation of the clavicle (Figs. 3, 4). This confirmed that the oral and skeletal features presented by her were due to underlying syndrome-CCD. As her presenting complaint was in deciduous teeth, our main goal was to restore the deciduous teeth and her normal

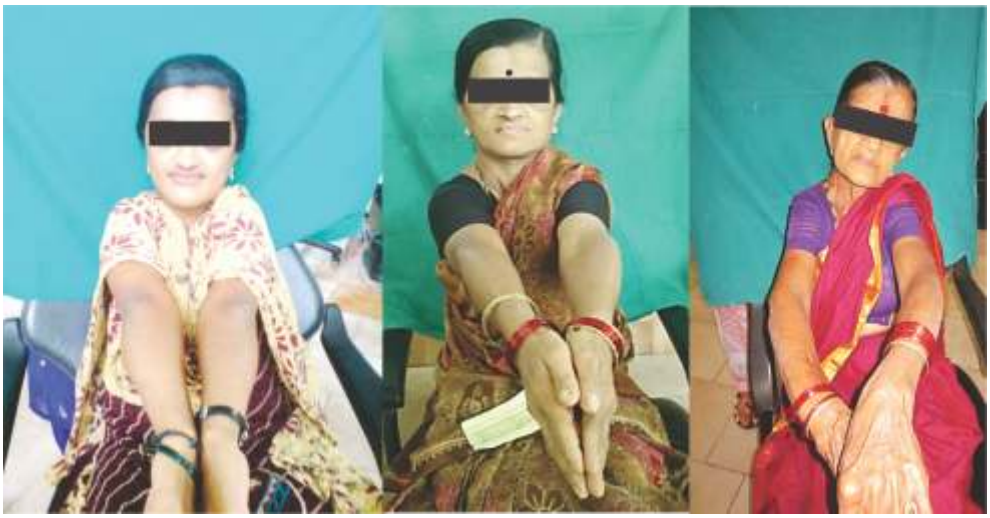
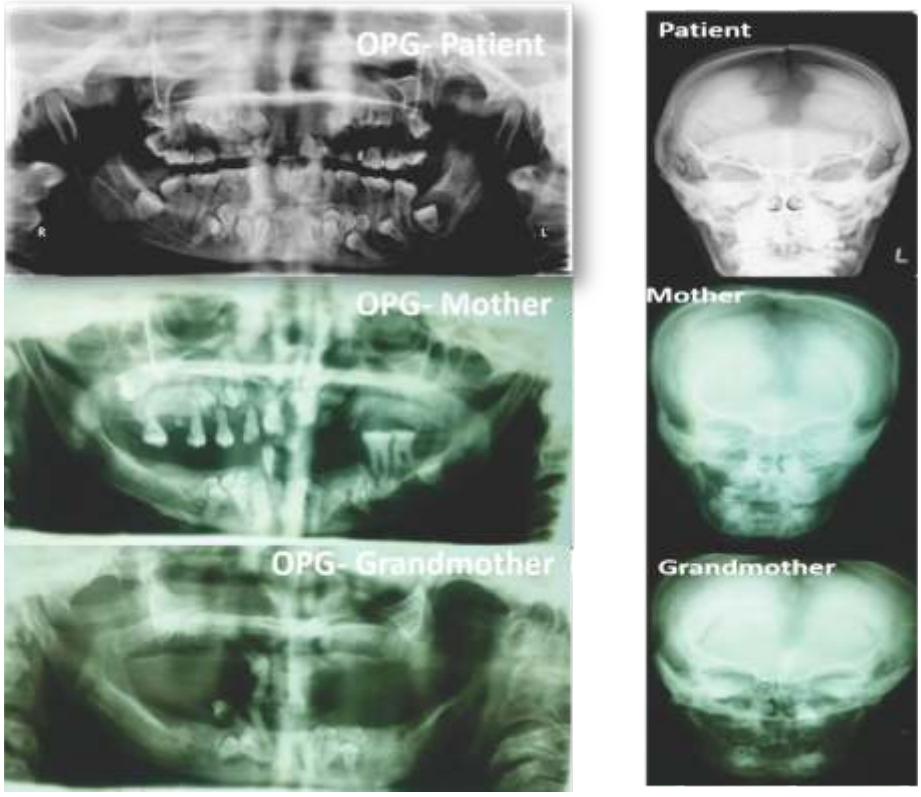
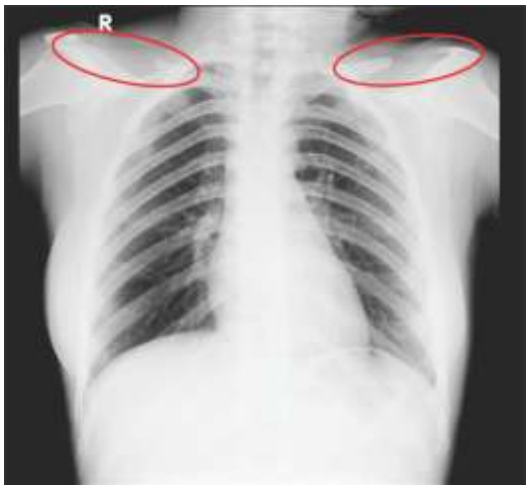


Fig. 1: Shows the Extraoral Features and Shoulder Hypermobility in Three Generations

occlusion and extraction of 38 with cyst enucleation with histopathological examination. Root canal was initiated for tooth 64 under local anaesthesia LA and deep caries management was done for tooth 65. On access cavity preparation for 64 palatal and disto-buccal canal could be located but the mesiobuccal was found to be calcified. After shaping and cleaning were done canal was then obturated using Mineral Trioxide Aggregate (MTA). Genetic counseling about her condition and the future care needed for her over-retained deciduous teeth was provided. During the next visit, we also examined her mother and maternal grandmother. Mother had only 8 teeth in the oral cavity which were mobile and interfered with her normal chewing. Her panoramic radiograph revealed thirty impacted teeth (Fig. 2). Her maternal grandmother also presented with 5 teeth in the oral cavity which were periodontally compromised and 17 impacted teeth in the panoramic radiograph (Fig. 2). Both of them presented with similar orofacial and skeletal features as that of our patient (Figs. 1, 2 and 3). They underwent extraction and full mouth rehabilitation with a complete denture, which took care of their esthetic and masticatory function. All of them are on regular follow up and are following the oral hygiene instructions given to them.



Figs. 2 & 3: Panoramic Radiograph and PA Skull of the Patient, Mother, and Grandmother showing Multiple Impacted Teeth and Incomplete Closure of Fontanelle with Wormion Bones.



Figs. 4: Chest X-ray of the Patient showing Incomplete Clavicle Formation

Discussion:

In addition to the major unique features like underdeveloped or absence of clavicles, open sutures with wormion or immature bones, and wide interparietal diameter, a myriad of other skeletal deformities are also seen in CCD. They present with overall growth retardation, short stature, narrow or bell-shaped thorax, deformities of the pelvis, scoliosis, kyphosis, missing ribs, clinodactyly, onychodystrophy, midfacial hypoplasia with frontal bossing, paranasal sinus abnormalities, narrow and high arched palate, and skeletal class 3 malocclusion [1]. All the three-generations in our case presented were short stature with a height below 5 ft (percentile). They exhibited shoulder hypermobility similar to the facial features of a broad forehead and midline depression. Chest X-ray also confirmed the absence / undeveloped clavicle in these patients.

The manifestation of over-retained deciduous teeth, with failure of eruption of permanent teeth and multiple impacted supernumerary teeth, is another representative feature of this condition. Our case had 57 impacted supernumerary teeth. Mother and grandmother presented with 30 and 17 impacted teeth respectively. So far the highest number of impacted teeth reported was 63 by Yamamoto *et al*. [7]. Premature closure of the gubernacular canal, absence of cellular cementum, and increased acellular cementum has been attributed to the loss of eruptive force and non-eruption of permanent teeth in the affected persons [8]. Reduced vertical facial growth with poor alveolar bone development can also be attributed to multiple impacted teeth [9]. Yamachika *et al*. reported an association of CCD with cleft palate [10]. Our cases, however, did not present with cleft lip and palate issues.

Few conditions like Noonan syndrome, Turners syndrome, hypothyroidism can mimic the clinical features of CCD, before the diagnosis is confirmed radiologically [11]. Conventional dental radiographs are very valuable tools for establishing the diagnosis. It exhibits two major features of the standard triad considered pathognomonic for the diagnosis: multiple supernumerary teeth and open suture at fontanels of the skull. The third sign - partial or complete absence of the clavicles can be confirmed through a chest X-ray [12].

Planning of treatment for CCD patients is complicated and depends on many factors like chronological and dental age, the time of diagnosis, and the social and economic circumstances of the patient. Time of diagnosis is important to determine the treatment prognosis, minimize the extent of later surgical and orthodontic intervention. As most of the striking features of CCD become apparent after the pubertal growth spurt of the mandible, it often goes missing during early

childhood and results in a bad prognosis as seen in our patient, who was unaware of her underlying syndrome. Early diagnosis of CCD by ultrasound morphometric evaluation of the clavicle of the fetus may help in early diagnosis of congenital defects, such as clavicular hypoplasia, and cleidocranial dysplasia [9, 13-14].

A holistic multidisciplinary approach is essential for the management of this case. The goal of the treatment is to achieve an esthetic facial appearance and well-functioning dentition, along with motivation and psychological support to the patient as the facial appearance in this condition can also cause psychological discomfort. In our patient, it was planned that the deciduous teeth should be retained to provide esthetic as well as the functional need of the patient. MTA has excellent properties such as radiopacity, resistance to moisture, good seal ability against bacterial microleakage, and bioinduction [15-16]. O'Sullivan and Hartwell have reported successful treatment using MTA as a root canal filling material in the primary tooth with no successor permanent tooth [17]. Hence in the present case, MTA was chosen as the material of choice for obturation.

Conclusion:

CCD is an autosomal dominant skeletal disorder caused due to defect in osteoblastic differentiation. They present with heterogenous clinical characteristics ranging from mild dental abnormalities to severe defects, like the complete absence of ossification of parietal bones. Few patients can also manifest respiratory complications and loss of hearing. A long-term follow-up and appropriate treatment plan are needed by a multidisciplinary team as more symptoms can become apparent during growth and different stages of childhood.

References

1. Roberts T, Stephen L, Beighton P. Cleidocranial dysplasia: A review of the dental, historical, and practical implications with an overview of the South African experience. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2013;115(1): 46-55.
2. Nagarathna C, Shakuntala BS, Mathew S, Krishnamurthy NH, Yumkham R. Cleidocranial dysplasia presenting with retained deciduous teeth in a 15-year-old girl: A case report. *J Med Case Rep* 2012;6: 25.
3. Bufalino A, Paranaíba LMR, Gouvêa AF, Gueiros LA, Martelli-Júnior H, Junior JJ, *et al*. Cleidocranial dysplasia: Oral features and genetic analysis of 11 patients. *Oral Dis* 2012;18(2): 184-190.
4. Xu W, Chen Q, Liu C, Chen J, Xiong F, Wu B. A novel, complex RUNX2 gene mutation causes cleidocranial dysplasia. *BMC Med Genet* 2017;18(1): 1-7.
5. Suda N, Hattori M, Kosaki K, Banshodani A, Kozai K, Tanimoto K, *et al*. Correlation between genotype and supernumerary tooth formation in cleidocranial dysplasia. *Orthod Craniofacial Res* 2010;13(4): 197-202.
6. Takaki N, Mori J, Matsuo S, Osamura T, Michigami T. Cleidocranial dysplasia with growth hormone deficiency: A case report. *BMC Pediatr* 2020;20(1): 2-5.
7. Garg RK, Agrawal P. Clinical spectrum of cleidocranial dysplasia: a case report. *Cases J* 2008;1(1):377.
8. Manjunath K, Kavitha B, Saraswathi T, Sivapathasundharam B, Manikandhan R. Cementum analysis in cleidocranial dysostosis. *Indian J Dent Res* 2008; 19(3): 253-256.
9. Golan I, Baumert U, Hrala BP, Müßig D. Dentomaxillofacial variability of cleidocranial dysplasia: Clinicoradiological presentation and systematic review. *Dentomaxillofacial Radiol* 2003;32(6): 347-354.
10. Yamachika E, Tsujigiwa H, Ishiwari Y, Mizukawa N, Nagai N, Sugahara T. Identification of a stop codon mutation in the CBFA1 runt domain from a patient with cleidocranial dysplasia and cleft lip. *J Oral Pathol Med* 2001;30(6):381-383.
11. Jindal M, Verma R, Maheshwari S. Familial Cleidocranial Dysplasia. *Int J Clin Pediatr Dent* 2010;3(1): 57–61.

12. Dalessandri D, Laffranchi L, Tonni I, Zotti F, Piancino MG, Paganelli C, *et al*. Advantages of cone beam computed tomography (CBCT) in the orthodontic treatment planning of cleidocranial dysplasia patients: A case report. *Head Face Med* 2011;7: 1-9.
13. Wiśniewski M, Baumgart M, Grzonkowska M, Małkowski B, Flisiński P, Dombek M, *et al*. Quantitative anatomy of the growing clavicle in the human fetus: CT, digital image analysis, and statistical study. *Surg Radiol Anat* 2017;39(8): 827-835.
14. Shekhawat V, Gulati Y. Cleidocranial dysplasia – A case report discussing the clinical and radiological manifestations. *J Mar Med Soc* 2020;22(2):238-240.
15. Bogen G, Kuttler S. Mineral trioxide aggregate obturation: a review and case series. *J Endod* 2009;35(6): 777–790.
16. Yildirim T, Oruçoğlu H, Çobankara FK. Long-term evaluation of the influence of smear layer on the apical sealing ability of MTA. *J Endod* 2008;34(12): 1537–1540.
17. O'Sullivan SM, Hartwell GR. Obturation of a retained primary mandibular second molar using mineral trioxide aggregate: A case report. *J Endod* 2001; 27(11): 703–705.

Author for Correspondence:
Dr. Yogesh Chhaparwal, Department of Oral Medicine and Radiology, Manipal College of Dental Sciences, Manipal, Manipal Academy of Higher Education, Manipal, Karnataka, India- 576104 Email: yogesh.omr@gmail.com Cell:9986454730

How to cite this article:
Patil V, Pai KM, Chhaparwal Y, Chhaparwal S. Cleidocranial Dysplasia Affecting Three Generations in a Family: A Unique Case Report. *J Krishna Inst Med Sci Univ* 2021; 10(2):150-155

Submitted: *10-Feb-2021* ***Accepted:*** *16-Mar-2021* ***Published:*** *01-Apr-2021*