Case Report

Clinical and Radiological Spectrum in Cleidocranial Dysplasia: A Case Series

FAKIR MOHAN DEBTA[1], KUNAL AGARWAL[1], BASUDHA BERA[1], ROMALI PANDA[1], SEBATI MURMU[1]

[1]*Department of Oral Medicine and Radiology, SCB Dental College and Hospital, Cuttack, Odisha, India*

ABSTRACT: Cleidocranial dysplasia (CCD) is an autosomal dominant disorder caused by a mutation in Runt-related transcription factor 2 (RUNX2), primarily affecting bones undergoing intramembranous ossification, characterized by generalized dysplasia of bones and teeth. Affected individuals exhibit short stature, partial or complete absence of clavicles, delayed fontanel closure, open skull sutures, multiple wormian bones. Dental issues include retention of deciduous teeth, delayed eruption of permanent teeth, supernumerary teeth, absence of cellular cementum. Diagnosis is based on clinical & radiographic findings. Early diagnosis enhances treatment and quality of life. This case series presents spectrum of clinical and radiographic findings of four adult CCD patients with varying dysplasia manifestations.

KEYWORDS: *Cleidocranial dysplasia, Cleidocranial dysostosis, CBFA1, RUNX2, wormian bones.*

Introduction

Heritable skeletal diseases are a group of complex genetic disorders with diverse clinical manifestations indicative of the fundamental mechanisms of skeletal development, cartilage formation, patterning, growth and homeostasis [1].

Cleidocranial dysplasia (CCD) is a rare hereditary skeletal disorder sometimes referred to as Scheuthauer Marie-Sainton syndrome, Marie and Sainton disease, and mutational dysostosis [1-3].

It is a rare bone condition with mostly an autosomal dominant inheritance pattern characterized by clavicular aplasia, delayed cranial ossification, occasional stunting of long bones and other skeletal abnormalities.

However, it occurs sporadically in 20-40% cases [2,4].

It affects one million people worldwide, regardless of gender or ethnicity [2,5].

The main oral manifestations are delayed exfoliation of primary teeth, multiple supernumerary and impacted permanent teeth [6].

This article aims to present four cases of CCD depicting their clinical and radiological features and emphasizing the dental and maxillofacial implications with suggested management strategies.

Case Presentation

In this case series, four adult female patients with cleidocranial dysplasia presented to the outpatient department, all exhibiting short stature and hypermobility of shoulders.

Three patients demonstrated complete shoulder hypermobility, with the ability to approximate the shoulders at the midline while one patient showed partial mobility.

Clinical examination revealed a hypertelorism, frontal and parietal bossing, brachycephalic skull, and sloping of shoulders in most of cases.

Figure 1. (a) showing short stature (b) showing sloping of shoulders, hypermobility of shoulders (c) showing facial profile showing frontal bossing and hypertelorism flat nasal bridge hypoplastic maxilla, prognathic mandible (d) Case 4 showing absence of frontal bossing and hypertelorism flat nasal bridge (e) showing upper and lower extremities were short and broad (f) showing multiple clinically missing teeth, retained deciduous teeth and multiple impacted teeth. "V shaped palate".

10.12865/CHSJ.51.02.14

This is an open-access article distributed under the terms of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Public License, which permits unrestricted use, adaptation, distribution and reproduction in any medium, non-commercially, provided the new creations are licensed under identical terms as the original work and the original work is properly cited.

Notably, frontal and parietal bossing was absent in Case 3, while Case 4 exhibited only a brachycephalic skull.

The facial appearance was generally symmetrical, with midfacial deficiency resulting in a concave profile with competent lips.

Intraoral findings included a high-arched, V-shaped palate and multiple retained deciduous teeth.

On radiographical investigation, Orthopantomogram (OPG) revealed multiple supernumerary teeth and unerupted permanent teeth involving maxilla and mandible.

Posteroanterior (PA) view of skull and lateral cephalogram revealed depressed skull, open fontanelles, multiple wormian bones and hypoplastic maxilla and prognathic mandible.

Paranasal sinus view (Water's view) revealed possible hypoplastic bilateral maxillary sinus, multiple wormian bones and open sagittal suture.

Chest radiographs revealed a barrel-shaped thorax with hypoplastic clavicles in three patients.

Case 4 exhibited right clavicular aplasia and left clavicular hypoplasia.

The history, clinical examination and radiographical findings all supported the diagnosis of cleidocranial dysplasia.

The four cases that reported to the outpatient department showing a range of extraoral and intraoral manifestations in the CCD spectrum, are shown in Figure 1 and the radiological observations are highlighted in Figure 2.

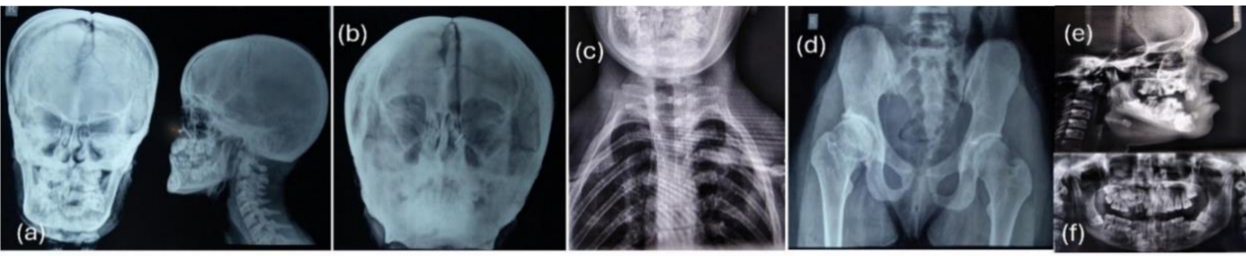

Figure 2. (a) Anteroposterior view of skull showing sunken sutures and depressed calvaria, Lateral view of skull shows open coronal suture, hypoplastic maxilla, prognathic mandible, frontal bossing (b) Paranasal sinus view showed possible hypoplastic bilateral maxillary sinus, multiple Wormian bones, open sagittal suture (c) Postero-anterior chest radiograph showing hypoplastic clavicles. Two separate hypoplastic segment noted in left side. Oblique orientation of ribs. Narrow bony thorax. (d) Radiograph of pelvis revealed wide pubic symphyseal space and shortened neck of right femur with osteoarthritic changes in right hip joint (e) Lateral cephalometric showing multiple unerupted permanent teeth, supernumerary teeth Hypoplastic maxilla and prognathic mandible and midface deficiency (f) OPG shows supernumerary teeth, multiple impacted teeth and over retained primary teeth.

Discussion

Cleidocranial dysplasia (CCD) is a genetic condition marked by significant and distinctive orofacial characteristics and varying degrees of pan-skeletal abnormalities [3].

Derived from Greek origin cleido means collar bone, kranion means head and dysplasia means abnormal formation [4].

The descriptive term "dysostose cléido crânienne héréditaire" was first coined by Marie and Saiton in 1897.

It was first reported by Martin in 1765 [7,4].

A heterozygous Runt-related transcription factor 2 (RUNX2) gene mutation on chromosome 6p21 short arm encoding runt-related transcription factor 2, also termed as Core-Binding Factor Alpha 1 (CBFA1) is suggested to be the underlying cause behind this condition, though only in 65% cases this mutation is seen [1,8-9].

Being a transcription factor this gene is essential for osteoblast differentiation as well as bone growth and maintenance [10].

Abnormalities in this gene causes abnormalities in formation of membranous and endochondral bone, as it is required for stem cell differentiation into osteoblasts.

This affects endochondral formation of long bones, intramembranous bones and midline ossification [6,11].

Individuals with CCD have distinctive pathognomic clinical features. In 1967, Keats reported involvement of the long bones, spine, and base of skull, followed by a detailed assessment of bone abnormalities in 1974 with Jarvis [11,12].

They frequently have a short stature, pronounced parietal and frontal bossing separated by metopic groove and brachycephalic head [1].

Short tapered fingers and anomalies of the phalangeal, carpal, metacarpal, tarsal and

 10.12865/CHSJ.51.02.14

metatarsal bones, and various vertebral and dental abnormalities are frequently noted.

Adults with CCD often have delayed fontanelle closure, while some also have open fontanels.

The nose has broad base with depressed bridge, and the eyes are wide apart.

Middle phalanges of the fifth fingers are usually short along with various spinal and dental abnormalities.

The shoulders are narrow and slope downward, giving the appearance of a long neck [13,14].

The hallmark of this syndrome is the partial or full absence of one or both clavicles, which occurs often (10%).

Clavicle being the first bone to ossify in the sixth week of intrauterine life, it is mostly affected [6].

Other deformities include a flat foot, narrow bell-shaped thorax, genu valgum, a wide symphysis pubis and problems in the spine such as scoliosis [15].

Even within families, the clinical spectrum varies greatly, ranging from mild cases with merely dental abnormalities to severe cases with noticeable skeletal deformities [4].

Dental alterations are very characteristic and common in CCD. Clefts involving the hard and soft palates have been reported, and the palate is frequently very arched.

Deciduous dentition is often retained while the permanent teeth erupt later.

Root formation is delayed in permanent teeth, and eruptive potential is diminished but not completely gone.

One of the most noticeable dental findings in CCD is the enormous number of extra teeth that make up a more or less a full third dentition (up to 30 extra teeth in certain cases) [1].

An underdeveloped maxilla and malformed paranasal sinuses are also seen.

The unhindered growth of the skeletal Class III tendency and prognathism of mandible in CCD can be ascribed to the hypoplasia of maxilla and upward and forward mandibular rotation [16].

Because of the abnormal eruption patterns, several supernumerary teeth, and involvement of the facial bones, this disorder is clinically significant to dentists [16,17].

Radiological evaluation, including panoramic radiography, projections of full skull, chest, pelvis, long bones, lumbar spine, hands and feet should be requested by the clinician when CCD is suspected.

Genetic analysis can help confirm the diagnosis of CCD in cases when it is not readily apparent from clinical or radiographic evidence [5].

PA, cephalometric and panoramic radiographs are the most commonly used imaging for the diagnosis of CCD as they enable the observation of two key features of the syndrome: presence of multiple supernumerary teeth and the absence of closure of cranial sutures and fontanelles.

Chest radiographs are also highly helpful in diagnosis as they can reveal the absence or hypoplasticity of the clavicles either unilateral or bilateral [15].

A U-shaped sigmoid notch, sclerosis of the alveolar bone, a thick bone trabeculae, increased bone density, and presence of multiple supernumerary teeth are some of the distinctive radiographic features that can be seen in OPG.

The ascending ramus of mandible also has a shape abnormality where the anterior and posterior margins are parallel.

Table 1. Clinical findings of all cases.

Clinical findings	Case 1	Case 2	Case 3	Case 4
Age (in years)	35	27	22	24
Sex	Female	Female	Female	Female
Frontal and parietal bossing	Yes	Yes	No	No
Hypertelorism	Yes	Yes	Yes	No
Broad nasal bridge	Yes	Yes	Yes	No
Depressed malar process	Yes	Yes	Yes	No
Relative mandibular prognathism	Yes	Yes	Yes	
Skull	Brachycephalic	Brachycephalic	Brachycephalic	Brachycephalic
Shoulder hypermobility	Complete	Complete	Complete	Partial
Intraoral findings				
Retained primary teeth	12	7	8	3
Erupted permanent teeth	3	11	15	17

Table 2. Radiological findings of all cases.

Radiological findings	Case 1	Case 2	Case 3	Case 4
Open skull sutures	Present	Present	Absent	Absent
Wide, open fontanels	Present	Present	Present	Absent
Aplasia/hypoplasia of clavicle	Aplasia	Aplasia	Hypoplasia	Aplasia on right side and hypoplasia on left side
OPG findings				
Unerupted/impacted permanent teeth	22	12	8	3
Total teeth present	No	No	No	No

The coronoid process, zygomatic arch and bone can all be extremely slender and occasionally irregular.

Maxillary sinus may be hypoplastic with pneumatization or absent [18].

A perpetually open anterior fontanelle, open skull sutures, several wormian bones, short sphenoid bones, brachycephaly, and calvarial thickening, particularly over the occiput, are all visible on PA radiographs [2,15].

Table 1 and Table 2 show the summary of clinical and radiological findings of all cases that reported to the outpatient department for dental or aesthetic concerns and had varying findings.

CCD needs to be differentiated from mandibuloacral dysplasia, dental anomalies, congenital clavicle pseudoarthrosis, Yunis-Varon syndrome, Crane-Heise syndrome, picnodisostosis, hypophosphatasia, congenital hypothyroidism, among other conditions sharing common clinical feature [6,19].

These illnesses are all autosomal recessive syndromes with unique features, albeit they may have some similarities to CCD.

Gene mutations affecting RUNX2's ability to function on its downstream targets may be the cause of some of these disorders [6].

Difficulty in speech, mastication, swallowing and breathing are caused due to craniofacial and dental anomalies.

Also, there might be significant psychological effects from the typical premature aging appearance [5].

An interdisciplinary team must carefully plan and coordinate the long-term, difficult process of managing orofacial and dental manifestations of CCD.

Depending on the patients age, the treatment plans may vary [4].

Supernumerary teeth and deciduous teeth should be removed to improve the possibility of orthodontic guided eruption [20,21].

The duration of orthodontic treatment can be shortened by using mini-implant screws for traction of impacted teeth [22].

In adults with fully developed jaws requiring multiple extractions of teeth, dental implants and fixed prostheses are the preferred therapeutic measures [4].

A management protocol as advised by Roberts et al. is summarized in Table 3 [23, 24].

Table 3. Dental management options for CCD.

Anomaly	Management option	Rationale
Retained deciduous teeth	Removal	Assist eruption of permanent teeth
Supernumerary teeth	Removal	Assist eruption of permanent teeth
Permanent teeth abnormalities	Removal	Construction of removable full/partial dentures (not indicated in childhood)
	Retention	Abutments for fixed appliances (not indicated in childhood)
Unerupted teeth	Surgical exposure Orthodontic eruption Implants Surgical translocation and/or auto transplantation	Support for overdenture Function and aesthetics and alignment Support overdenture Guide impacted teeth into occlusion Function and aesthetics
Malocclusion	Fixed or removable orthodontic appliances	Function and aesthetics
Palatal vault narrow-high arched	Expansion with removable orthopaedic appliance	Reduce crowding

10.12865/CHSJ.51.02.14

Vitamin D and calcium supplements should be taken into consideration as a form of treatment if bone density is below normal.

Osteoporosis prevention measures should begin early because the second and third decades are when bone mineral density increases.

Therefore, early detection of CCD is advantageous for timely intervention, which will have a significant impact on the better restoration of craniofacial function and aesthetics [6].

Cranioplasty have been used to successfully restore abnormalities of calvarium in the open anterior fontanelle, sagittal and metopic suture by using bone cement.

Orthognathic surgery can be used to repair a midface deficiency once growth is complete [22].

In young children with CCD the fontanels may be so enormous that a helmet should be worn to protect the brain.

From the time of birth, hearing exams should be conducted on a regular basis (at least once a year) [6].

Recurrent sinus infections, upper airway problems, recurrent otitis, hearing loss, dental cavities, dentigerous cysts, osteomyelitis of the jaws, respiratory distress in the early stages of infancy, shoulder and hip dislocations, pes planus, and genu valgum are among the most prevalent complications of CCD.

Nevertheless, these people have regular life spans despite these potential challenges [23].

Conclusion

In conclusion, cleidocranial dysplasia is a rare genetic disorder characterized by skeletal abnormalities.

This case series highlights the importance of early diagnosis and a coordinated multidisciplinary approach in improving functional and aesthetic outcomes.

Further studies are essential to understand the full spectrum of the condition, advance diagnostic accuracy and optimize individualized management protocols.

Such efforts are vital to advancing standards of care and improving long-term outcomes for affected individuals.

Author Contributions

Conceptualization- F.M.D., K.A.; Design- F.M.D., K.A.; Literature search- F.M.D., B.B., R.P., S.M.; Data acquisition- F.M.D., B.B., Dr. R.P., S.M.; Manuscript preparation- F.M.D., K.A., B.B., R.P., S.M.; Manuscript review editing- F.M.D., K.A.; Supervision- F.M.D., K.A.

All authors have read and approved the final manuscript.

Funding

No funding received

Conflicts of Interest

The authors declare no competing interests

Institutional Review Board

Not applicable

Consent Statement

Written informed consent for publication of anonymized data was obtained from all patients.

Data Availability

All data presented in the manuscript are available from the authors upon request.

References

1. Mundlos S. Cleidocranial dysplasia: clinical and molecular genetics. J Med Genet, 1999, 36(3):177-182.
2. McNamara CM. Cleidocranial dysplasia: Radiological appearances on dental panoramic radiography. J Dento Maxillo Facial Raciol, 2005, 28:87-89.
3. Nebgen D, Wood RS, Shapiro RD. Management of a mandibular fracture in a patient with cleidocranial dysplasia: report of a case and review of the literature. J Oral Maxillofac Surg, 1991, 49(4):405-409
4. Pan CY, Tseng YC, Lan TH, Chang HP. Craniofacial features of cleidocranial dysplasia. J Dent Sci, 2017, 12(4):313-318.
5. Farrow E, Nicot R, Wiss A, Laborde A, Ferri J. Cleidocranial dysplasia: a review of clinical, radiological, genetic implications and a guidelines proposal. J Craniofac Surg, 2018, 29(2):382-389.
6. Toptancı İR, Çolak H, Köseoğlu S. Cleidocranial dysplasia: Etiology, clinicoradiological presentation and management. J Clin Exp Invest, 2012, 3(1):133-136.
7. Martin S. Sur underpacement natural de la clavicle. J Med Chir Pharmacol, 1765, 23(3): 456.
8. Azevedo Almeida LC, Faraj de Lima FB, Matushita H, Valença MM, Ferreira Castro TL, de Mendonça RN. Cleidocranial dysplasia, a rare skeletal disorder with failure of the cranial closure: case-based update. Childs Nerv Syst, 2020, 36:2913-2918.
9. Chelvan HT, Malathi N, Kailasam V, Ponnudurai A. Cleidocranial dysplasia: a family report. J Indian Soc Pedod Prev Dent, 2009, 27(4):249-252.
10. Thaweesapphithak S, Termteerapornpimol K, Wongsirisuwan S, Chantarangsu S, Porntaveetus T. The impact of RUNX2 gene variants on cleidocranial dysplasia phenotype: a systematic review. J Transl Med, 2024, 22(1):1-6.
11. Jarvis JL, Keats TE. Cleidocranial dysostosis. A review of 40 new cases. Am J Roentgenol Radium Ther Nucl Med, 1974, 121(1):5-16.
12. Keats TE. Cleidocranial dysostosis: some atypical roentgen manifestations. Am J Roentgenol Radium Ther Nucl Med, 1967, 100(1):71-74.
13. Dhiman NK, Singh AK, Sharma NK, Jaiswara C. Cleidocranial dysplasia. Natl J Maxillofac Surg, 2014, 5(2):206-208.

14. Dhobley AA, Thombre AV, Ghatage D, Patil RI. Cleidocranial dysplasia: a rare case report. J Pharm Bioallied Sci, 2023, 15(Suppl 2):S1335-1337.
15. Granado-Abasto LA, Llaguno-Rubio JM, Fiori-Chíncaro GA, Medina-Ocampo PE. Imaging studies used as aid in the diagnosis of cleidocranial dysplasia. A review. Rev Cient Odontol, 2021, 21;9(2):e063.
16. Becker A, Bimstein E, Shteyer A. Interdisciplinary treatment of multiple unerupted supernumerary teeth. Report of a case. Am J Orthod, 1982, 81 (5):417-422.
17. Martin S. Sur underpacement natural de la clavicle. J Med Chir Pharmacol, 1765, 23(3):456.
18. Symkhampha K, Ahn GS, Huh KH, Heo MS, Lee SS, Kim JE. Radiographic features of cleidocranial dysplasia on panoramic radiographs. Imaging Sci Dent, 2021, 51(3):27.
19. Medina O, Muñoz N, Moneriz C. Cleidocranial dysplasia: a case report. Rev Chil Pediatr, 2017, 88(4):517-523.
20. Becker A, Lustmann J, Shteyer A. Cleidocranial dysplasia: part 1-general principles of the orthodontic and surgical treatment modality. Am J Orthod Dentofac Orthop, 1997, 111:28-33.
21. Becker A, Shteyer A, Bimstein E, Lustmann J. Cleidocranial dysplasia: Part 2 General principles of the orthodontic and surgical treatment modality. Am J Orthod Dentofac Orthop, 1997, 111:173e83
22. Kuroda S, Yanagita T, Kyung HM, Takano-Yamamoto T. Titanium screw anchorage for traction of many impacted teeth in a patient with cleidocranial dysplasia. Am J Orthod Dentofac Orthop, 2007, 131:666-669.
23. Paul SA, Simon SS, Karthik AK, Chacko RK, Savitha S. A review of clinical and radiological features of cleidocranial dysplasia with a report of two cases and a dental treatment protocol. J Pharm Bioallied Sci, 2015, 7(Suppl 2):S428-432.
24. 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.

***Corresponding Author:** Basudha Bera, Department of Oral Medicine and Radiology, SCB Dental College and Hospital, Cuttack, Odisha, India, email: basudha25081996@gmail.com*

10.12865/CHSJ.51.02.14