Case Series

Clinico-Radiographic spectrum of cleidocranial dysplasia: A case series

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ABSTRACT

Cleidocranial dysplasia (CCD) is a rare autosomal dominant disorder that presents with skeletal dysplasia and dental manifestations. The most common features seen in CCD are aplastic or hypoplastic clavicles, late closure of fontanelles, open skull sutures, and dental abnormalities which include mainly delayed exfoliation of primary teeth and delayed eruption of permanent teeth, with multiple impacted supernumeraries. A relatively low number of multiple case studies are reported in the literature, with only eight reporting on more than three affected individuals. Here, we report a case series of five such rare cases showing characteristic clinical and radiographic features of CCD.

Key words: Autosomal dominant, Cleidocranial dysplasia, Impacted permanent teeth, Skeletal dysplasia

Cleidocranial dysplasia (CCD) is a rare genetic syndrome with an autosomal dominant inheritance pattern, recognized by Marie and Sainton in 1898. The prevalence of CCD is one per million, displaying no sex or ethnic group predilection [1]. It is characterized by either absence of clavicles (10% cases) or hypoplastic clavicles that allow a patient to move the shoulders up to the medial plane of the body without any discomfort (clavicular sign). Sutures of the skull close lately or may remain open. The principal affected bones are the cranial vault, clavicles, maxilla, nasal, and lacrimal bones [2]. Dental dysplasia manifests as the presence of multiple supernumerary teeth, the prolonged retention of deciduous teeth, and the delayed or failed eruption of the permanent dentition [1].

Here, we report a case series of five rare cases of CCD to emphasize the importance of detailed clinical and radiographic examination for diagnosis.

CASE SERIES

Case 1

A 35-years-old female patient reported to the department of oral medicine and radiology with the chief complaint of loose teeth and intermittent dull aching pain in the upper right back teeth for 2 months. The patient has not taken any medication/treatment for the same. General physical examination showed a short stature patient with thin and lean built. The skull was brachycephalic. The mid-face was depressed due to the underdeveloped maxilla, so the mandible appeared prognathic. She had drooping shoulders, frontal bossing, hypertelorism, short fingers, polydactyly with both the lower limbs, and positive clavicular sign. Her detailed intraoral examination showed Grade III mobility with 15, 16, 23, 24, and 36, Grade II mobility with 46, Grade I mobility with 25 and 35, the presence of multiple over-retained teeth, and clinically missing multiple permanent teeth in the maxillary and mandibular anterior region. The palate was high arched and narrow. Her intelligence was normal.

Radiological investigations included orthopantomogram (OPG), lateral and posteroanterior (PA) skull views, and chest X-ray. OPG revealed several unerupted permanent teeth in both maxilla and mandible, dense overlying alveolar bone with impacted 37 and 38 regions, and increased pericoronal space with impacted 47 suggestive of the follicular cystic lesion. The coronoid process appeared slender, gonial angles on both sides of the mandible were obtuse, and maxillary sinuses were underdeveloped. Bell-shaped thorax and hypoplastic clavicles were seen on the chest radiograph. Lateral and PA view of the skull revealed open fontanelles, depressed, bulb-shaped skull, and multiple wormian bones. Family history did not reveal similar findings. Thus, a detailed clinical and radiological examination revealed her to be a case of CCD (Fig. 1). A multi-disciplinary treatment approach was advised, which included extractions of mobile teeth, periodontal therapy, and prosthetic rehabilitation.

Access this article online

Received - 5 October 2020
Initial Review - 25 October 2020
Accepted - 22 November 2020

Quick Response code

DOI: 10.32677/IJCR.2020.v06.i11.001

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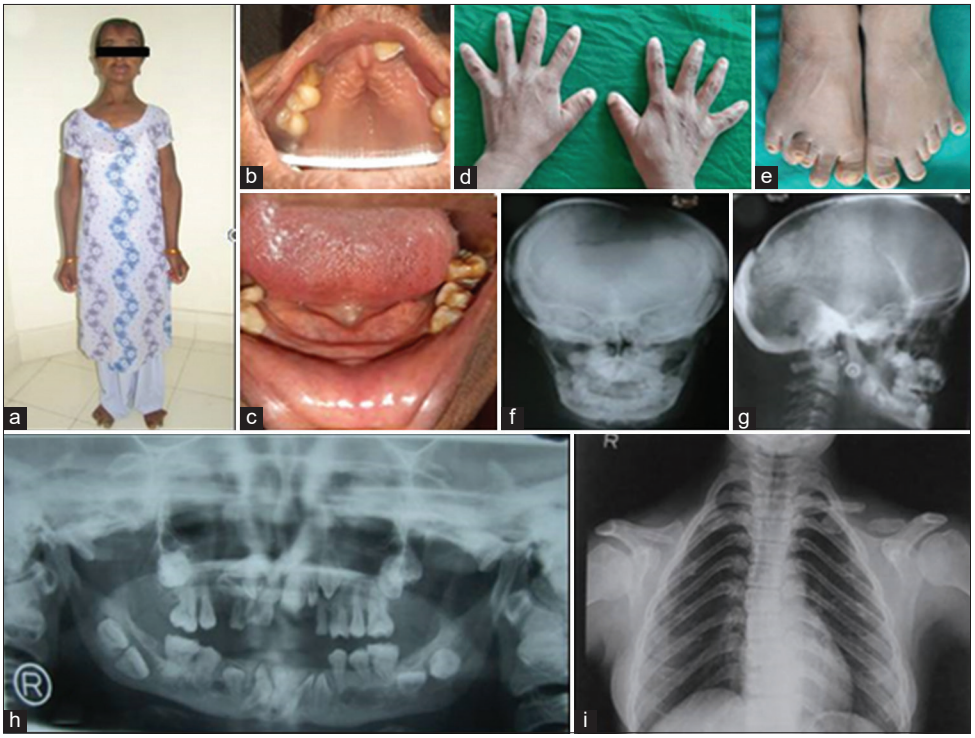

Figure 1: (a-i) Clinical and radiographic photographs of case 1

Case 2

A 30-years-old male patient reported a complaint of food lodgment in the upper right posterior region of the jaw for 1 month. On general examination, the patient had short stature, drooping shoulders, and a brachiocephalic head. The facial features included hypertelorism, depressed nasal bridge, frontal bossing, and hypoplastic maxilla. The other features were positive clavicular sign and short fingers. Intraoral examination showed root stump of over-retained 55, which was mobile, spacing with upper and lower anteriors, clinically missing few permanent teeth, and the presence of multiple retained primary teeth. The patient also reported delayed eruption of various permanent teeth. There was also evidence of a high-arched and narrow palate.

OPG revealed sloping of the zygomatic arch; multiple un-erupted permanent, and supernumerary teeth in the upper and lower jaws, and missing gonial angles. The mandible was characterized by a narrow ascending ramus with nearly parallel anterior and posterior borders. Overlying alveolar bone was dense with impacted 34 regions. There was also evidence of bulb-shaped head, open fontanelles, and multiple wormian bones in lateral and PA skull views. Family history revealed similar findings in his father, presented here as Case 3 (Fig. 2). The patient was treated by performing extraction of root piece with 55 and other over-retained deciduous teeth. The patient was not willing for any other treatment.

Case 3

A 72-years-old male patient reported the complaint of pain and swelling in the lower right posterior region of the jaw for 4 days. The patient was of short stature with a moderate built,

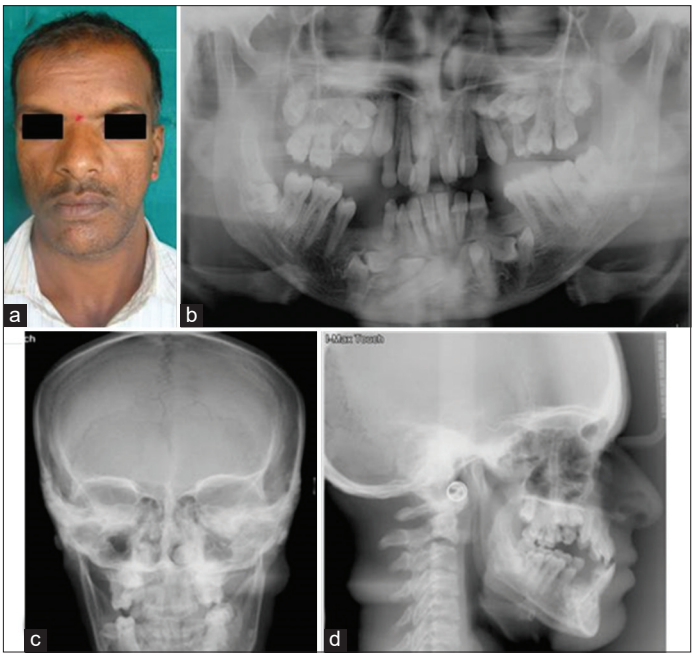

Figure 2: (a-d) Clinical and radiographic photographs of case 2

brachycephalic head with scanty hairs, frontal bossing, broad and depressed nasal bridge, hypertelorism, and prognathic mandible. Intraoral examination revealed missing 43 and 44. A slight bulge was present with the same region which was firm in consistency and tender on palpation. Pus discharge through the intraoral sinus on the buccal aspect was evident. Other intraoral findings were poor periodontal condition and multiple missing teeth, for which the patient gave a history of exfoliation due to mobility.

OPG showed multiple impacted permanent teeth with both maxillary and mandibular arch, multiple impacted supernumerary teeth in the mandibular anterior region, and dense alveolar bone

above the impacted 44 and 34 regions. Bone resorption was seen with impacted 43 and 44 regions. Zygomatic arch sloping and obtuse gonial angles were also evident. Open fontanelles, depressed skull, and multiple wormian bones were evident on lateral cephalogram and PA skull (Fig. 3). The patient was advised for extraction with impacted 43 and 44 under antibiotic cover. The patient was lost for the follow-up.

Case 4

A 56-years-old male patient reported the complaint of a loose tooth in the upper front region of the jaw for 3 months. Physical examination demonstrated similar facial features, as seen in Case 3. Intraoral examination showed Grade II mobility with 11; multiple missing teeth in both the arches, one supernumerary tooth was seen buccal to 11 and partially erupted 43 and 45. The patient also gave a similar history of missing teeth, short height, and small face in his son and daughter. His son's case is presented here as Case 5.

Characteristic radiographic findings of CCD similar to Case 3 are noted (Fig. 4). Extraction with 11 was done followed by a removable partial denture.

Case 5

A 27-years-old male patient reported the complaint of sensitivity in the upper left back teeth for 3 months. General physical examination showed similar facial features in addition to polydactyly with both the upper limbs. On intraoral examination, deep distoproximal caries was present with 65 which was non-tender. Multiple over-retained teeth and clinically missing multiple permanent teeth in both the arches were noted.

Panoramic radiograph showed multiple impacted permanent teeth in both the arches, increased bone density with impacted 36 and 37 regions, and increased follicular space seen below 37. Besides this, cone-beam computed tomography of the maxilla and mandible, lateral cephalogram demonstrated bulb-shaped head, open fontanelles, multiple wormian bones, and aplastic maxillary sinuses (Fig. 5). Extraction with carious 65 and other over-retained primary teeth was done. He refused surgical exposure and orthodontic alignment for other impacted teeth.

Characteristic clinical and radiological features of all five cases are summarized in Table 1.

DISCUSSION

CCD is caused by a mutation in the gene on 6p21 encoding transcription factor core-binding factor alpha 1, that is, runt-related transcription factor 2 [3]. This gene normally guides osteoblastic differentiation, chondrocyte maturation, and appropriate bone formation [4]. It also plays an important role in the epithelial-mesenchymal interactions that control progressive tooth morphogenesis and the histodifferentiation of the epithelial enamel

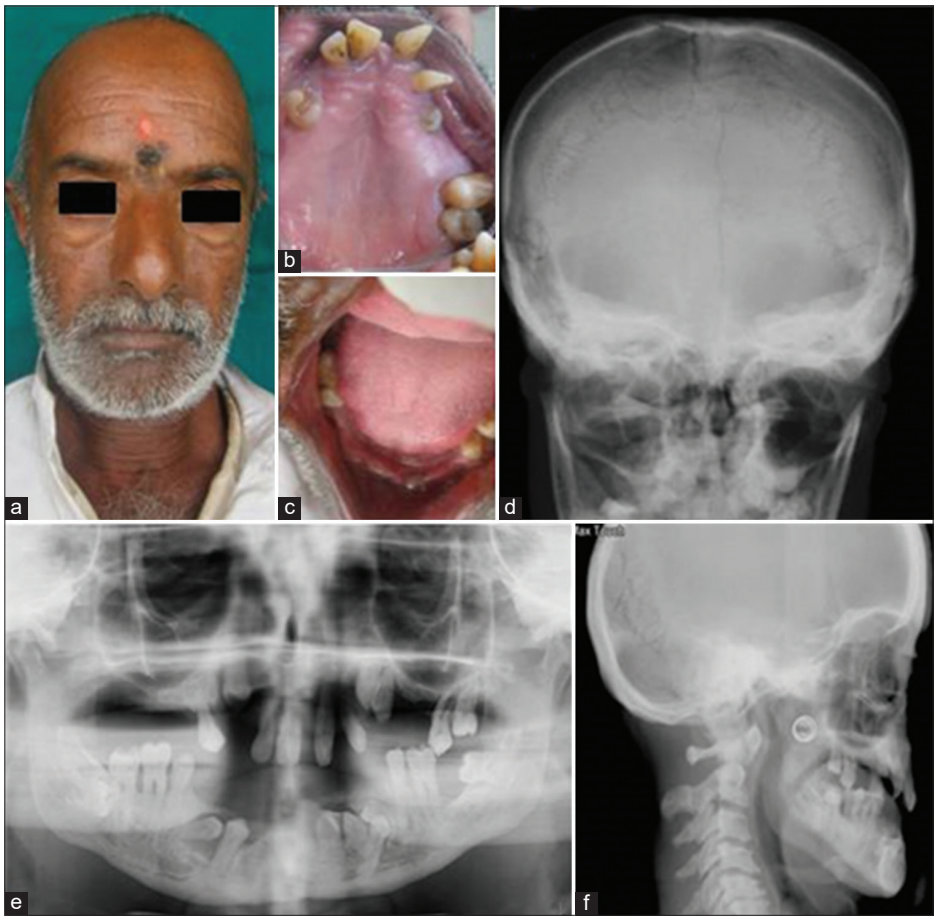

Figure 3: (a-f) Clinical and radiographic photographs of Case 3

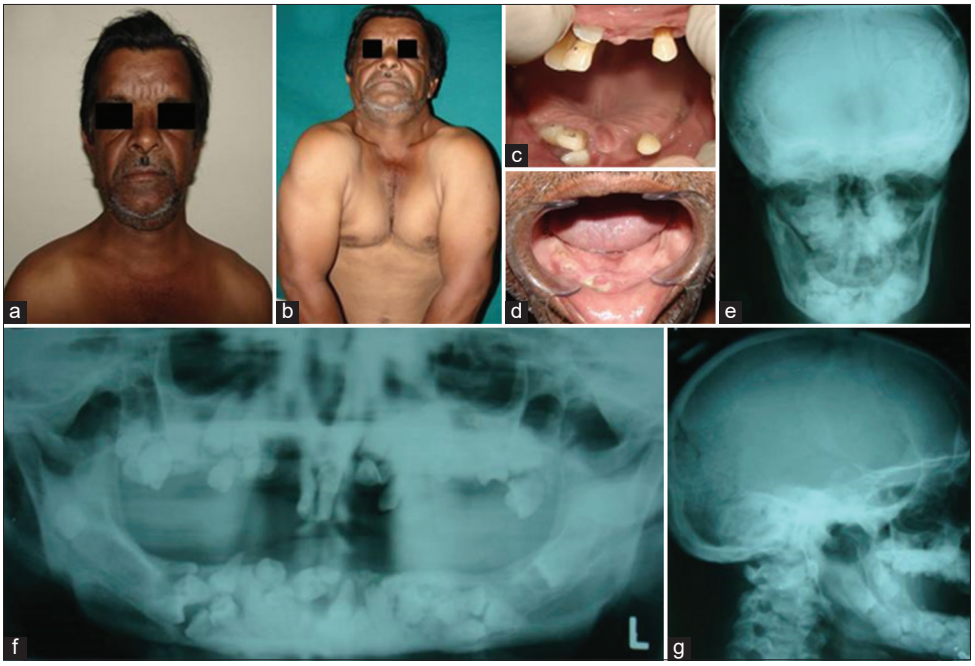

Figure 4: (a-g) Clinical and radiographic photographs of case 4

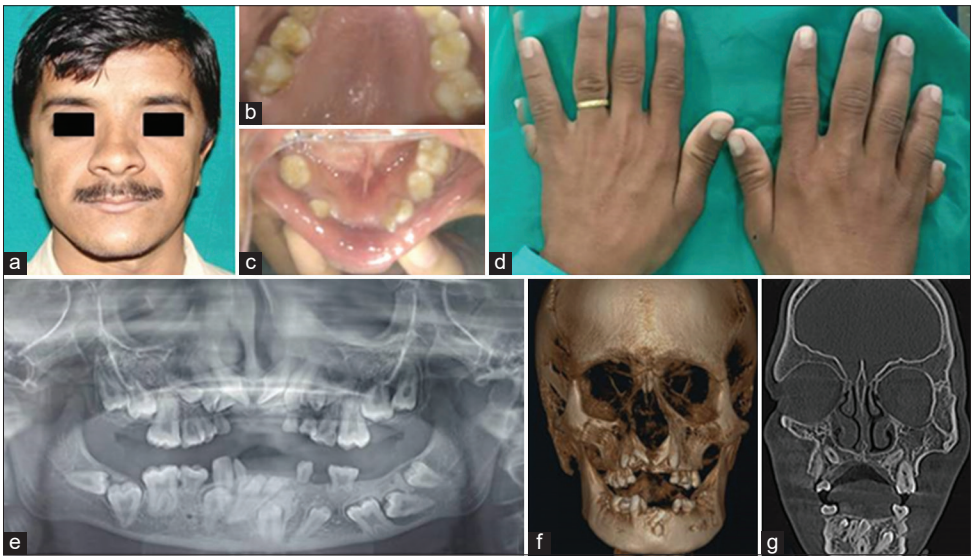

Figure 5: (a-g) Clinical and radiographic photographs of Case 5

organ [5]. The gnathic and dental features of CCD are distinctive and may lead to an initial diagnosis in most CCD cases [6].

Recent detailed clinical investigations have shown that CCD is a generalized skeletal dysplasia affecting not only the clavicles and the skull but the entire skeleton. CCD is, therefore, considered to be a dysplasia rather than dysostosis [7]. CCD may present with a triad of features: Multiple supernumerary teeth and delayed eruption of permanent teeth, partial or complete absence of the clavicles, and open sagittal sutures and fontanelles. This triad is pathognomonic for the diagnosis of CCD [3].

This condition may be inherited, transmitted as dominant characteristics in either of the sex or sometimes may appear spontaneously. In the present case series, both fathers and sons presented with similar skeletal and dental abnormalities (Cases 2–5). This supports the fact that CCD is transmitted by an autosomal-dominant mode of inheritance with high penetrance and variable expressivity. The sporadic occurrence has been reported in about 40% of cases [8], and autosomal recessive inheritance has also been reported [4]. In the cases reported here, it appears that CCD occurred sporadically in fathers, which was then transmitted by the autosomal dominant mode of inheritance to their sons. Molecular genetic testing such as sequence analysis or deletion analysis can be applied in CCD for genotypic evaluation. Mutations have been detected in 60–70% of individuals with a clinical diagnosis of CCD [9].

Important clinical features include persistently open skull sutures, macrocephaly, brachycephalic skull, prominent forehead, hypertelorism, a depressed nasal bridge, mid-facial hypoplasia, a narrow high arched palate, delayed tooth eruption, narrow sloping shoulders, a narrow thorax, absence or hypoplasia of

Table 1: Characteristic clinical and radiological features of all the five cases

Serial No.	Clinical and radiological features	Case – 1	Case – 2	Case – 3	Case – 4	Case – 5
1	Age (In years)	35	30	72	56	27
2	Gender (M/F)	F	M	M	M	M
3	Family history	N	Y	Y	Y	Y
4	Short stature	Y	Y	Y	Y	Y
5	Multiple retained deciduous teeth	Y	Y	N	N	Y
6	Multiple impacted permanent teeth	Y	Y	Y	Y	Y
7	Multiple supernumerary teeth	N	Y	Y	Y	N
8	Hypertelorism	Y	Y	Y	Y	Y
9	Polydactyly	Y	N	N	N	Y
10	Prognathic mandible	N	N	Y	Y	N
11	High arched palate	Y	Y	Y	Y	N
12	Hypoplastic maxilla and mandible	Y	Y	Y	Y	Y
13	Mid face hypoplasia	Y	Y	Y	Y	Y
14	Multiple wormian bones	Y	Y	Y	Y	Y
15	Open fontanelles	Y	Y	Y	Y	Y
16	Depressed skull	Y	N	Y	N	N
17	Bulb-shaped head	Y	Y	Y	Y	Y
18	Hypoplastic/aplastic maxillary sinus	Y	N	N	N	Y
19	Slender coronoid process	Y	N	N	N	N
20	Obtuse/missing gonial angle	Y	Y	Y	Y	N
21	Zygomatic sloping	N	Y	Y	Y	N
22	Clavicular sign	Y	N	N	Y	N

the clavicles, and a normal intelligence quotient. Our patients presented with most of these features. Multiple cone-shaped epiphyses, enamel hypoplasia, a long neck, conductive deafness, scoliosis, respiratory distress, growth retardation, recurrent sinus abnormalities, and occurrence of syringomyelia are also reported in CCD [1,10].

Dental manifestations are prolonged retention of deciduous teeth, impacted permanent successors, and supernumerary elements, occasionally follicular and eruptive pseudocysts also present [11]. The causes of delayed eruption of permanent teeth are still under debate, but potential options include the presence of supernumerary teeth in the eruption pathway [12], the presence of a dense alveolar crest [6], the lack of cellular cementum of the permanent teeth [13], and the reduced ability of periodontal ligament cells to induce osteoclastic differentiation [14].

The radiographic findings of CCD are pathognomic, hence are the most important and reliable means to confirm the diagnosis. These include broad open skull sutures, large fontanels persisting into adulthood, numerous wormian bones, aplasia or hypoplasia of clavicles, and numerous unerupted permanent and supernumerary teeth. All these features were present in all of the five cases except hypoplasia of the clavicle which was present in two cases. The zygomatic arch has a characteristic downward bend [7] and was evident in three cases. In few cases, the mandible is characterized by a narrow ascending ramus with nearly parallel anterior and posterior borders and by an abnormally slender and pointed coronoid process with an abnormally distal curvature [15] which was seen in Cases 2 and 1, respectively. In all five cases, there was evidence of multiple unerupted permanent succedaneous and supernumerary teeth, while multiple over-retained deciduous teeth were present in three cases.

The diagnosis of CCD can be difficult when typical features are not clearly expressed. Due to the rareness of the disorder, dental, or medical consultation is often associated with the "one-patient-one-doctor" phenomenon, where the clinician has consulted one case with CCD. This might explain the relatively low number of multiple case studies (18), with only eight reporting on more than three affected individuals [1].

The differential diagnoses of CCD include Crane-Heise syndrome, mandibuloacral dysplasia, pycnodysostosis, Yunis-Varon syndrome, CDAGS syndrome, and hypophosphatasia. These conditions may share some characteristics with CCD; however, all these are autosomal recessive disorders and have other specific features [9].

Common complications of CCD reported are pesplanus, genu valgum, shoulder and hip dislocation, recurrent sinus infections, upper airway complications, recurrent ear infection, hearing loss, dental caries, osteomyelitis of the jawbones, and respiratory distress in early infancy which may be experienced because of narrow upper thoracic diameter [16].

Treatment is often directed at orthopedic correction which includes correcting multiple dislocated shoulders, radial head, or hips. If bone density is below normal, treatment with calcium and Vitamin D supplementation should be considered [17]. The successful dental management of these patients is dependent on a multidisciplinary assessment and comprehensive staged treatment plan. The timing of intervention is critical to accommodate for alveolar growth and development and eruption of the

permanent dentition. The principles of treatment are focused on surgical intervention, orthodontic alignment, and prosthodontic rehabilitation [18]. Each child of an individual with CCD has a chance of inheriting the mutation. Hence, it would be appropriate to offer genetic counseling to young adults who are affected [9].

CONCLUSION

The present case reports highlight the need for awareness among clinicians with CCD syndrome. A well-functioning permanent dentition, as well as an aesthetically satisfying facial appearance, motivation, and psychological support for the patients and their family members, may be achieved by interdisciplinary treatment when CCD is diagnosed in the early stages of childhood development.

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Funding: None; Conflicts of Interest: None Stated.

How to cite this article: Nayak P, Munde A, Deshpande A, Sawade R. Case series of cleidocranial dysplasia: Clinicoradiographic spectrum of five rare cases. Indian J Case Reports. 2020;6(11):606-611.