Case Report

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# The Spectrum Of Disorder : Cleidocranial Dysplasia

**Abstract:**
Cleidocranial dysplasia (CCD) is a complex congenital defect characterized by dysplastic bone formation. It is caused by mutations in 6p21 gene encoding transcription factor Core Binding Factor Subunit Alpha 1 ( CBFA1) or Runt related transcription factor 2 (RUNX2) ,which is involved in osteoblasts differentiation and bone formation. This paper reports a case of 20 year old female patient with cleidocranial dysplasia and the characteristic routine radiographs aided diagnostic conclusion to the case.

**Key-words:** Cleidocranial dysplasia, CBFA1, RUNX2

## Introduction:

Cleidocranial dysplasia is a complex congenital defect, an autosomal dominant inheritance of skeletal disorder with characteristic clinical and radiological features [1]. Thepathogenic variant induced by a de novo RUNX2 gene has been reported highest[2]. Variable mutations of RUNX2 gene such as deletion, missense, nonsense and frameshift mutations are the only genetic cause associated with the syndrome. RUNX2 gene since is key in osteoblastic differentiation, cartilage formation, aberration in its function affects both intramembranous and cartilaginous bone formation. It was first described by Martin in 1765 and was termed in 1879 as cleidocranial dysostosis by Marie and Sainton considering the disease only influence the skull, clavicle and spongy bones which endure intramembranous ossification; the term was later changed to cleidocranial dysplasia as development of bone by endochondral ossification along with abnormalities in the skeletal system has been reported [3, 4]. This rare entity has prevalence of 1/1000000 with no gender predilection. It can affect the population of any age however the cranial deformities are associated with birth. The characteristic presentation of the condition includes clavicular aplasia, delayed cranial bone ossification, skeletal deformities including oral features like delayed exfoliation of deciduous dentition, multiple supernumerary and impacted teeth. However, generalized bone involvement are rare.[1,3]

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## Case Report:

A 20-year-old female patient reported to the outpatient Department of Oral Medicine and Radiology, with the complaint of difficulty on eating food. She related the difficulty with irregularly arranged teeth of both upper and lower jaw. Her mother stated she was dull and left schooling after sixth standard.

Genealogical examination revealed that the patient was the second child born from normal vaginal delivery of non-consanguineous healthy parents. Clinical examination revealed ectomorphic physique 68.78 pounds weight, euryprosopic face form , brachycephalic head , short stature 4 feet 9 inches tall, waddling gait, slopey shoulders with absence of clavicle on palpation but unable to approximate shoulders in middle of the chest. Extraorally, ( Figure 1) depressed

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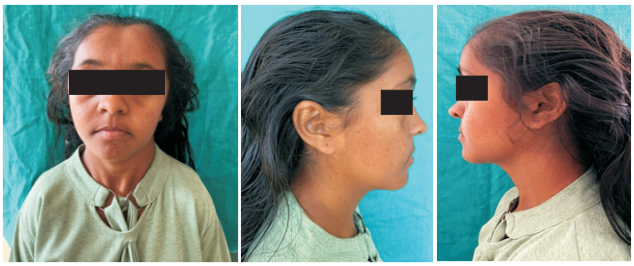
fontanelle, frontal bossing prominent towards left side, flat short face with depressed left infraorbital region, sunken nasal bridge, increased nasal width and ocular hypertelorism was present. On palpation the fontanelle was soft and tender. Both the feet (Figure 3) had short broad toes , broad halluces with hypoplastic phalanges and koilonychia.



(A) (B) ©

**Figure 1: (a) Frontal view**-Depressed fontanelle, frontal bossing prominent towards left side, flat short face with depressed left infraorbital region, sunken nasal bridge, increased nasal width, ocular hypertelorism**:(b), (c)Lateral views**- Concave profile

Figure 2 : Upper extremities and halluces

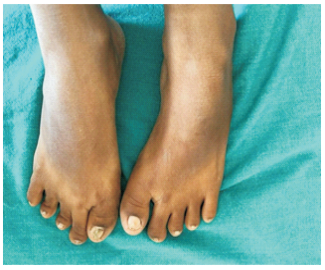
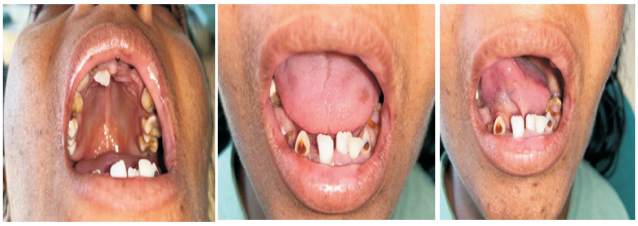


Figure 3 : Short broad toes

Intraoral examination revealed (Figure 4)retained multiple carious deciduous teeth with first and second maxillarypermanent molars ; partially erupted permanent right maxillary central incisor, mandibular central incisors and right mandibular first premolar. High arched palate (Figure 4 (a)), fissuring on the dorsal surface of anterior two-third part of tongue (Figure 4 (b)) and tongue tie (Figure 4 (c)) was observed.



(a) (b) ©

Figure 4 : Intraoral view - **(a)** High arched palate **(b)** Retained carious deciduous teeth, Partially erupted permanent dentition, Fissure on anterior 2/3rd part of tongue **(c)** Tongue tie

Based on all the above mentioned clinical finding , the patient was provisionally clinically diagnosed as **Cleidocranial dysplasia** and subjected to routine hematological examination and radiographs.

Hematological examination revealed patient was anemic with Hemoglobin 7.3 gm% and all other parameters were within normal range.

The panoramic radiograph (Figure 5) revealed multiple impacted permanent teeth in both jaw and retained deciduous teeth. The root apices of mandibular teeth were seen to approximate to the inferior border of mandible bilaterally in the parasymphysis region, on left mandibular body and ramus area suggestive of reduction in bone height of mandible. The left coronoid process appeared pointed.

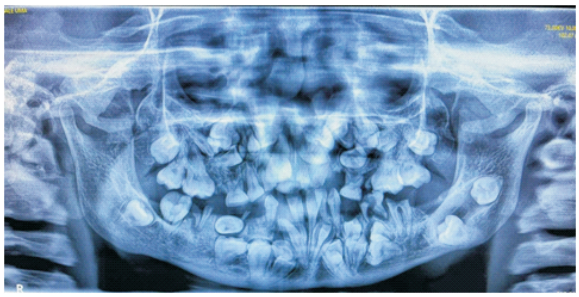


Figure 5 :Panoramic radiograph

Multiple impacted permanent teeth and retained deciduous teeth of both maxillary and mandibular arch, Supernumerary teeth in maxillary arch, Root apices of mandibular teeth approximate to inferior border of mandible bilaterally in the parasymphysis region and on left mandibular body area, Narrow mandibular ramus and body.

Lateral cephalogram (Figure 6)revealed persistence of metopoic suture and other fetal sutures with widening of the sututres, hypoplastic maxilla, multiple impacted teeth.

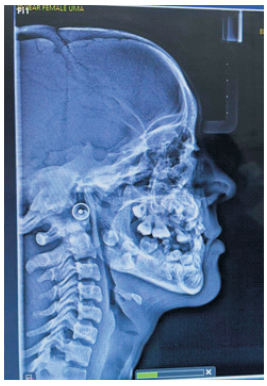


Figure 6 : Lateral cephalogram

Persistence of metopoic and fetal suture**,** Widened sutures**,** Hypoplastic maxilla, Multiple impacted teeth

Antero-posterior skull radiograph(Figure 7)showed open fontanelles, open suture, wormian bones, hypoplastic maxilla with poorly developed sinus.

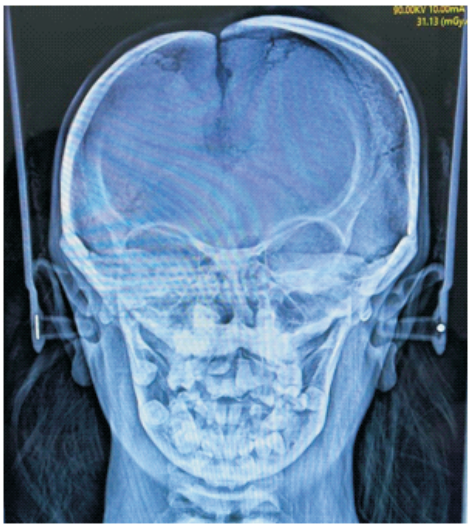


Figure 7 : Antero-Posterior view

Open fontanelles, Open suture, Wormian bones, Hypoplastic maxilla with poorly developed sinus

The posteroanterior view of chest radiograph (Figure 8)showed bilateral agenesis of middle and medial part of clavicle and cone shaped thorax.

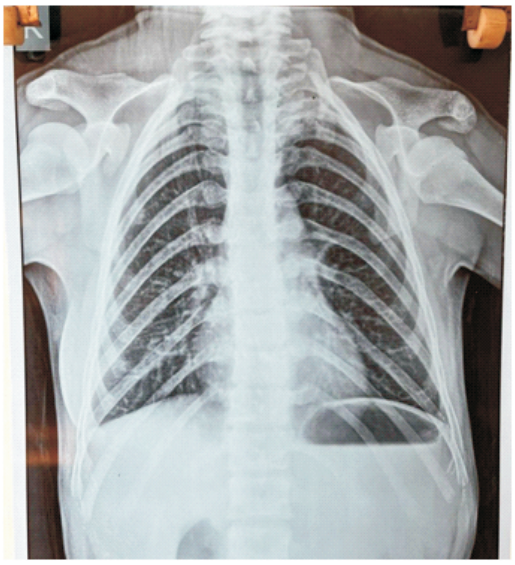


Figure 8 : Postero-Anterio view of Chest

Agenesis of middle and medial part of clavicle with presence of lateral ossification , Cone shaped thorax.

The hand wrist radiograph (Figure 9) shows elongated second metacarpal with sharp pointed all five distal phalanges.

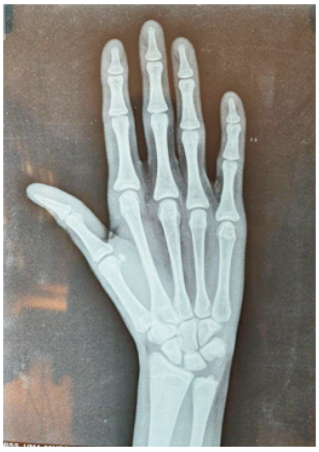


Figure 9 : Hand- wrist radiograph

Hence, based on the typical clinical and radiographic feature, a diagnosis of **CLEIDOCRANIAL DYSPLASIA**was made for the patient.

The patient was motivated for oral hygiene maintenance, advised for physician consultation as she was anemic followed by psychiatrist consultation and Multidisciplinary team ( Oral and Maxillofacial Surgeon,Orthodontics, Prosthodontics) had planned for full-mouth rehabilitation.

## Discussion:

Cleidocranial dysplasia is a complex autosomal dominant inheritance of disorder. Its prevalence is one per million individuals worldwide [2]. The patient detected with this disorder is 18.3 years of age on an average [3]. This disorder represents a clinical spectrum ranging from definitive cleidocranial dysplasia that is delayed closure of skull sutures, aplastic or hypoplastic clavicles and dental deformity followed by mild form to isolated dental abnormalities[2].

The oral manifestation is found on 94% of persons with cleidocranial dysplasia including failure or ectopic eruption of permanent teeth, retained primary teeth , numerous supernumerary teeth, cyst formation due to impacted teeth. The roots of teeth are often thin ,short and deformed.The hard palate is high and narrow [2,4].

The affected individuals typically present short stature, long neck, slopping shoulders , narrow thorax allowing the proximity of the shoulders in front of the chest. Few casesof mental retardation has been reported. Conduction hearing impediment, delayed closure of the pubic symphysis , coxa vara have been observed [5]. The cranial abnormalities involved brachycephaly, open skull sutures, open anterior

fontanel, prominent forehead , wormian bones [5-7]. Complication of upper airway and periodic sinus infections are significant. Also, this disorder can have low Insulin-like Growth Factor-1 level, decrease in level of vitamin D with no reported persistent relation with osteoporosis [2].

The radiographic finding of wide open sutures , presence of wormian bones , poor pneumatization of sinuses on skull radiographs; retained primary teeth, unerupted succedaneous teeth, presence of supernumerary teeth in panoramic radiographs; chest radiographs and hand wrist radiographs can confirm the diagnosis of cleidocranial dysplasia [2,8,9]. The significance of panoramic radiograph for the diagnosis of cleidocranial dysplasia has been emphasized on various articles with reported deformity of the coronoid process, mandibular ramus and the morphological abnormalities of both the jaws[10, 11]. The different molecular testing approaches, full skeletal survey, audiologic evaluation can be early diagnosis [2, 8 ,9].

The management of such patients includes oral rehabilitation with a prosthesis (fixed or partial denture) to improve function and appearance. Nevertheless , the complications of impaction like cyst formation, jaw fracture and delayed healing should be considered. Also, intentional replantationof permanent impacted teeth with surgical exposure and orthodontic traction guided tooth eruption can be the treatment modality[3, 5, 12].

## Conclusion:

The oral physician has great role in diagnosis of cleidocranial dysplasia as 94% of cases has dentofacial deformities and characteristic radiographic findings. Hence, the early diagnosis and multidisciplinary approach of treatment leads to better life of patients aesthetically, functionally and psychologically.

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