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CLEIDOCRANIAL DYSPLASIA:- A CASE REPORT

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ABSTRACT: Cleidocranial dysplasia is a rare autosomal dominant disorder of bone development characterized by abnormalities in the skull, jaw, shoulder girdle as well as of the dentition. It may be caused by a mutation in CBFA1 gene. This case is reported because of rarity.
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KEYWORDS: ***Cleidocranial dysplasia, autosomal dominant, hypoplasia of clavicles, supernumerary teeth, Fontanella.***

INTRODUCTION

Cleidocranial dysplasia (CCD) is a rare congenital disorder with an autosomal dominant inheritance pattern, primarily affects bones of intramembraneous origin and characterized by clavicular aplasia or hypoplasia, retarded cranial ossification, multiple supernumerary teeth, short stature and a variety of other skeletal abnormalities.[1,2]

Cranial abnormalities may include wide open skull sutures, patent or late closure of fontanells and presence of wormian bones.[3] Affected individuals present a characteristic facial appearance with frontal and parietal bossing, hypertelorism, midfacial hypoplasia with flat and narrow nasal bridge.[4]

Frontal bossing, brachycephaly and hypertelorism are seen as a result of delayed closure of anterior fontanella, metopic sutures and reduced growth of dysplastic skull bone.[5]

The clavicles being the first bone to ossify are commonly affected by this disorder either by hypoplasia or aplasia. Complete clavicular agenesis or aplasia is also seen in only 10% of cases.[6] Clavicular deformity along with dysplastic muscle attachments give rise to elongated neck, narrow drooping and hypermobility shoulder with tendency to approximate them anteriorly at midline.[7] Among the bones of maxillofacial complex, maxilla is underdeveloped along with hypoplasia of paranasal sinuses[8]. Narrow and high arched palate is also observed. Mandible appears to be apparently prognathic.[9]

Dental problems present the most significant manifestation of CCD which include the presence of several impacted permanent and supernumerary teeth often in premolar region, prolonged retention of deciduous teeth and delay in eruption of permanent teeth.[10]

Thorax is narrow with short oblique ribs.[11] Other features seen in CCD are the deformities of pelvis, pubic bone and finger. Abnormalities may include short, tapered finger with anomalies of phalanges, tarsal, metatarsal, carpal and metacarpal bones.

We report one CCD case of a 25-year old female patient, unaware of her condition attending the Oral Medicine and Radiology Department of S.C.B Dental College and Hospital, Cuttack, Odisha.

Case Report

A 25-year old female patient reported to the department of Oral Medicine and Radiology Department, S.C.B. Dental College and Hospital in July 2016 with a chief complaint of malaligned upper frontal teeth. Medical history revealed exertional dyspnea, a known case of sickle cell anaemia. Family history was unremarkable. General physical examination revealed that the patient was well oriented and of normal intelligence. She had a thin built, short stature, narrow thorax and shrugged shoulder. She also had macrocephaly, a depressed nasal bridge, midfacial hypoplasia, frontal and parietal bossing **(Fig. 1)**.

Intra oral finding showed a narrow, highly arched palate, the dentition of which mainly consist of deciduous teeth with few permanent teeth in either arch **[Fig. 2 (a), (b), (c)]**, with upper right primary lateral incisor and canine are in cross-bite. Intra oral examination showed presence

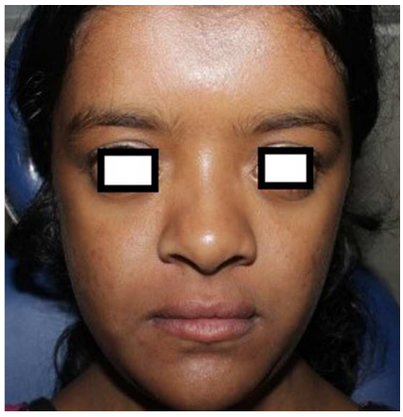


Fig. 1: Frontal bossing and widely spaced eyes with mid facial hypoplasia

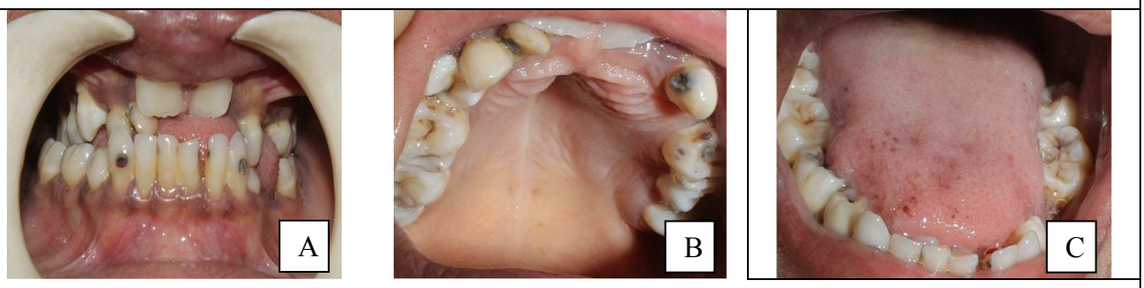


Fig. 2: Intra oral view of patient (a) Occlusal view; (b) Maxillary arch; (c) Mandibular arch

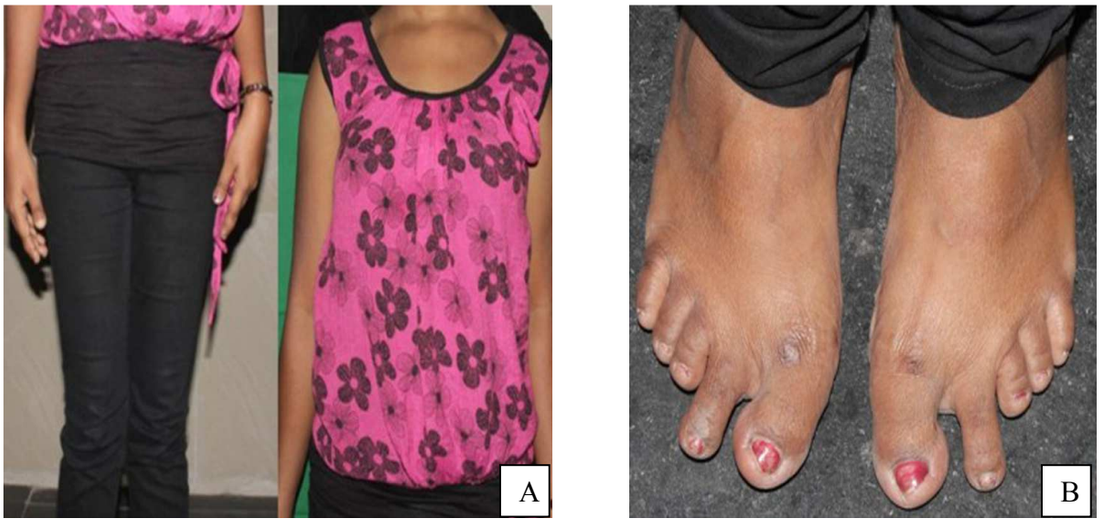


Fig. 3: (a) Bowing of long bones; (b) Bowing of digits

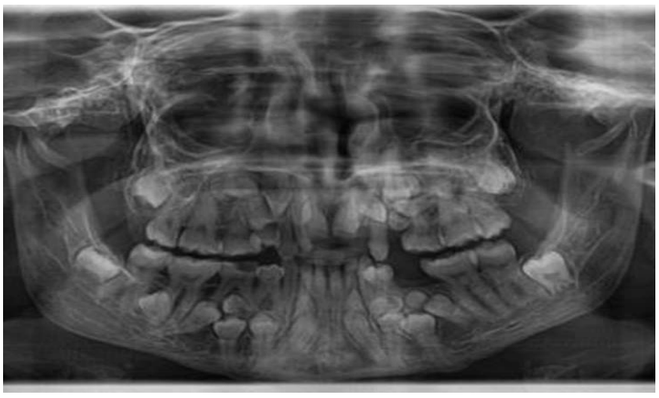


Fig.4. OPG showing multiple supernumerary teeth and impacted permanent teeth in maxilla and mandible

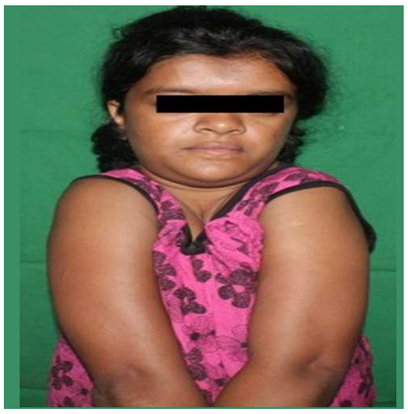


Fig.5.Patient demonstrating hyper-mobility of shoulder girdle

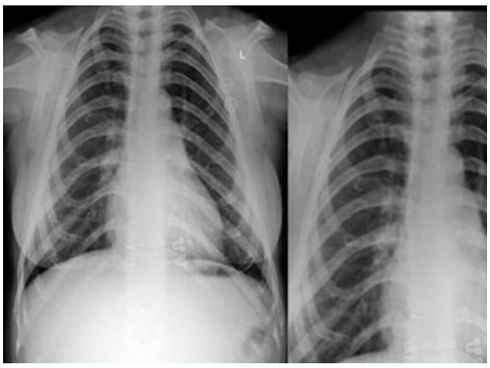
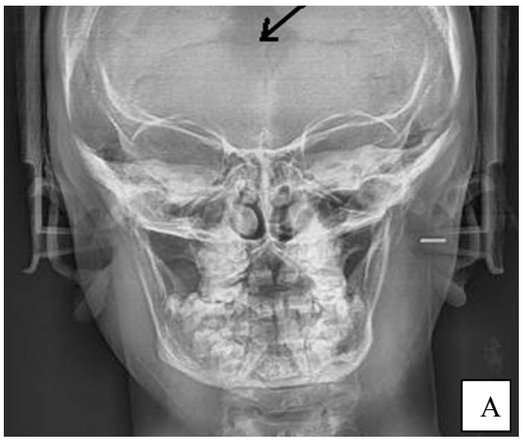


Fig. 6. PA view of chest showing hypoplasia of clavicles and bell-shaped rib cage



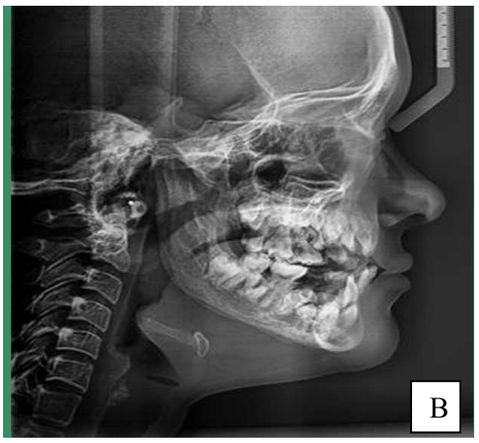


Fig. 7.(a) PA view of skull showing open sagital sutures (arrow); (b) Lateral cephalogram showing large fontanells and multiple wormian bones

of 52, 53, 55, 62, 63, 64, 65, 73, 83, 84 and 85. 12, 13, 15, 22, 23, 24, 25, 33, 34, 35, 43, 44, 45 were missing, but the oral hygiene was good. The long bones and the digits showed bowing**[Fig. 3(a), (b)]**. Panoramic radiographs showed multiple supernumerary and impacted permanent teeth **(Fig. 4).** The patient was asked to approximate her shoulders at midline of chest to check for incomplete clavicle formation which demonstrated more than normal mobility of shoulder girdle **(Fig. 5).** On the basis of clinical, radiographic examination and history, a provisional diagnosis of CCD was made. Differential diagnosis of congenital pseudoarthrosis of clavicle, pyknodysostosis, Mandibuloacral dysplasia, Yunis Varon syndrome were considered.

Chest radiograph (PA view), Lateral cephalogram, radiograph of pelvic bones, hand and feet were taken. Chest radiograph (PA view) confirmed clavicular hypoplasia and bell-shaped rib cage. (Fig. 6) Beside this skull radiograph (PA view and Lateral cephalogram) demonstrated open skull sutures and delayed closure of fontanella[Fig. 7 (a), (b)]. It also showed poorly formed paranasal sinuses and zygomatic complex. Gonial angles on both sides of mandible were missing and maxillary sinuses were underdeveloped.

A diagnosis of CCD was confirmed. Patient was referred to the Department of Orthodontics for treatment of her chief complaint.

Discussion

Cleidocranial dysplasia (CCD) is also known as Marie and Sainton disease, Mutational dysostosis and Cleidocranial dysostosis.[5] The first case of Clavicular aplasia was reported by Martin in 1765.[13] In 1898 Pierre Marie and Paul Sainton coined the term Cleidocranial dysostosis.[5,6,14] CCD was originally thought to involve only bones of intramembraneous origin mainly skull and clavicle. At present this congenital disorder is known to be a generalized disorder of bone practically involving entire skeleton, so renamed in 1978 as Cleidocranial dysplasia.[15] The prevalence has been estimated as one per million live births, with no predilection to gender or races.[16]

The condition is usually caused by a mutation of the Core Binding Factor Alpha 1 (CBFA1), located at chromosome 6p21.[17] CBFA1 is also known as RUNX2 (Runt related transcription factor 2).[18] The CBFA1 (RUNX2) gene controls normal development and growth of human skeleton through progression of intramembraneous and endochondral ossification and may be related to delayed ossification of skull, teeth, pelvis and clavicle.[12,18] RUNX2 is also necessary for odontoblast differentiation and regulates expression of many genes related to development of teeth and bone.[19,20]

There is a notably phenotypic variation of CCD even within one and the same family. However 20%-40% of the CCD presents sporadic mutations.[2,4] Individual with this disorder presents with some or all of very characteristic feature, as in this case.

The Triad of, partial or total absence of clavicles, open sagital suture and fontanells, presence of multiple supernumerary teeth, is considered as pathognomonic for diagnosis of CCD.[21,22] However in the absence of the triad, it is necessary to consider the possibility of other disorder in differential diagnosis.

Congenital Pseudoarthrosis of clavicle is probably the most common condition to be considered when there is bilateral clavicular involvement in CCD. It is characterized by the absence of one of the two clavicles (usually the right clavicle). No other bone involvement is seen.[14,23] Pyknodyostosis shares many common features with CCD. However absence of supernumerary teeth and increased bone density on X-ray allow for differentiation from CCD.[19,21,22] Mandibuloacral dysplasia (MAD) a progressive disorder can be differentiated from CCD by progressive stiffening of joints and radiographs reveal acro osteodysplasia of fingers and toes with delayed ossification of carpal bones. MAD is also a recessive autosomal disorder associated with mutation in genes LMNA or ZMPSTE24.[3,6] Yunis Varon syndrome in many ways resemble severe CCD, but can be differentiated by absence of distal phalanx of great toe, poorly delinated lips along with less pronounced dental findings.[14,24]

The other differential diagnosis may be osteogenesis imperfecta (frequent fractures), congenital hypothyroidism (disturbed thyroid metabolism), Gardner Syndrome, Hallerman Streiff Syndrome (narrow face, hypotrichosis, micropthalmia), Orofaciodigital Syndrome Type-I, Crane-Heise Syndrome, CDAGS Syndrome and hypophosphatasia, Parietal foramina with Cleidocranial dysplasia and chromosomal abnormalities.[25] These conditions may share some characteristics with CCD, however all these are autosomal recessive disorder and have other specific features. Some of these conditions may result from mutation in genes that affect the action of RUNX2 on its downstream target.[7,25] The clinical findings of CCD, although present at birth, could be easily missed because of their extremely low frequency, rare manifestation of the typical extraoral symptoms in early childhood and clinical variety of disorder.

General physical appearance of patient in sickle cell anaemia and CCD usually overlaps each other and as far as the problems associated in sickle cell anaemia and burden of care involved in it may be one of the many reasons for overlooking manifestation of CCD which causes delay in seeking medical assistance as in this case. Dental anomalies are the main reason for affected individuals seeking medical attention as was true in the present case.

The dental characteristics in CCD are essentially the retention of deciduous dentition, the presence of many

supernumerary teeth and non eruption of permanent teeth. It is suggested that failure in eruption can be related to absence or inadequate cellular cementum in the permanent teeth roots.[10,26] Lack of resorption of deciduous teeth and sub-adjacent bone and also presence of physical barrier, represented by impacted supernumerary teeth or by a fibrous connective tissue interposed between dental follicles and the mucosa are other possible causative factors.[20,27] Formation of supernumerary teeth occurs as a result of activation of remnants of dental lamina left unresorbed during odontogenesis.[1,10,28]

The purpose of dental management is to achieve an aesthetic facial appearance and functional occlusion by early adulthood, which requires a multi disciplinary approach.[2,12,19] The therapeutic dental approach includes a staged process of treatment over a number of years, removal of supernumerary teeth, exposure of impacted or unerupted teeth by forced orthodontic eruption, orthodontic alignment of the occlusion, prosthetic replacement of missing teeth, aesthetic dentistry for misshaped teeth and other orthognathic surgery for skeletal discrepancies of the jaw when skeletal growth has been completed.[4,10,20]

Other aspects of management of CCD may include wearing of helmets to protect the head from blunt trauma (if cranial vault defect is significant) for high risk activities.[28] If bone density is below normal, treatment with calcium and vitamin-D supplement is considered. Preventive treatment for osteoporosis is often initiated at a young age.[3] This disorder although benign has complications associated with it. These include dental caries and delayed eruption of permanent teeth, which may lead to osteomyelitis of mandible or maxilla, hearing loss, respiratory distress in early infancy due to a narrowed thorax, crowding of brain stem and upper cervical cord due to platybasia and basilar invagination.[15]

CONCLUSION

Planning treatment for a patient with CCD is complicated by a host of factors, expected duration of treatment, age of the patient, patient's attitude towards treatment, staged multiple invasive procedure are important considerations for establishing an appropriate treatment plan. Early diagnosis of such condition is extremely important to minimize oral cavity alterations with a view on a functional adaptation and better quality of life.

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Conflicts of interest:- There are no conflicts of interest

CONSENT

This is to be declared that a written informed consent was obtained from the patient for publication of this case report and accompanying images.

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