Cleidocranial Dysplasia With Dens Invaginatus: A Report Of Two Cases

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Abstract: Background: Cleidocranial dysplasia (CCD) is an autosomal dominant malformation syndrome affecting bones and teeth. It has been demonstrated that mutation of the RUNX2 gene which controls osteoblastic differentiation, appropriate osteogenesis and odontogenesis via participation in odontoblast differentiation, enamel organ formation and dental lamina proliferation is responsible for CCD. The dental abnormalities associated with CCD are often the reason for diagnosis in mildly affected individuals. Here we present two cases of cleidocranial dysplasia with radiographic analysis, both presenting with a rare dental anomaly; dens invaginatus. [Parikh S Natl J Integr Res Med, 2020; 11(4):94-98]

Key Words: Autosomal Dominant, Cleidocranial Dysplasia, Dens Invaginatus

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Introduction: Cleidocranial dysplasia (CCD), also known as Marie and Sainton Disease, Scheuthauer Marie-Sainton Syndrome, and Mutational dysostosis[1,2], is an autosomal dominant malformation syndrome affecting bones and teeth[1-5].

CCD was recognized by Marie and Sainton in 1898.[2] Cleidocranial dysplasia is very rare in occurrence, incidence being 1: 1,000,000 with equal sex predilection[2,3].

It has been demonstrated that mutation of the RUNX2 gene (synonyms: CBFA1, AML3, OSF2, PEBP2A) is responsible for CCD[2-8]. This osteoblast-specific transcription factor, which is mapped to human chromosome 6p21, is involved in regulation of bone metabolism and plays an important role in osteoblast differentiation and osteoclast formation.

It has been shown that RUNX2 specifically regulates the transcription and expression of some genes related to bone and tooth development, including osteocalcin (OCN), alkaline phosphatase (ALP), type I collagen (Col I), osteopontin (OPN), bone sialoprotein (BSP), and ameloblastin (AMBN)[4].

Thus this gene controls osteoblastic differentiation, appropriate osteogenesis and odontogenesis via parcitipation in odontoblast differentiation, enamel organ formation and dental lamina proliferation[5].

Although the disease affects the entire skeleton, CCD primarily affects the skull, clavicles, and dentition. Affected individuals have been shown to be of shorter stature, the face appears small in contrast to the cranium as a result of hypoplasia of the maxilla and a brachycephalic skull, and the presence of frontal and parietal bossing. The paranasal sinuses may be underdeveloped.

There is delayed closure of the cranial sutures and the fontanels may remain patent years beyond the normal time of closure. The bridge of the nose may be broad and depressed, with hypertelorism. Aplasia or hypoplasia of the clavicles allows excessive mobility of the shoulder girdle[1-6].

The dental abnormalities associated with CCD are often the reason for diagnosis in mildly affected individuals. Characteristically, patients with this disease show narrow high arched palate, prolonged retention of the primary dentition, delayed eruption of the permanent dentition and multiple unerupted supernumerary teeth are present. Extraction of primary teeth does not adequately stimulate eruption of underlying permanent teeth[1-6].

Case Report: A 30-year-old male patient reported to the Department of Oral Medicine and Radiology with chief complaint of multiple missing teeth with mobility of lower anterior teeth and a 25-year-old female patient reported with pus discharge in lower left posterior teeth region.

Upon general physical examination, both the patients were found to be of short stature; 4’8” and 4’6” respectively however, their gaits were normal. Head and neck examination revealed that both the patients had a, brachycephalic head, frontal bossing, and broad forehead with depression in the center, and depressed zygoma. There was ocular hypertelorism and a wide nasal bridge. (Figure 1, Figure 2) Palpation of the forehead suggested a non-fused metopic suture in patient 1.

Figure 1: Patient 1; (a) Front Profile, (b) Side Profile

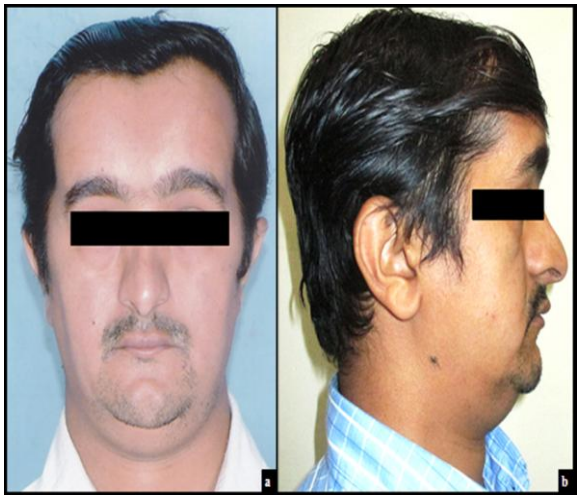
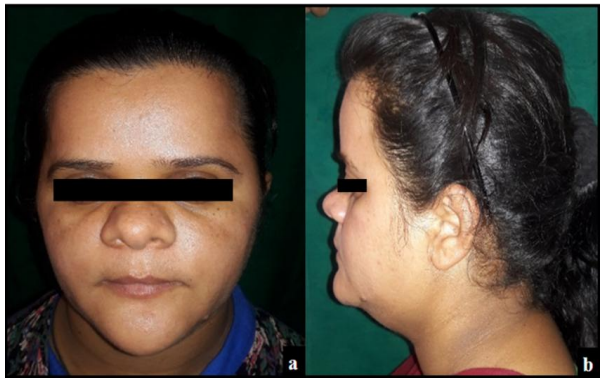


Figure 2: Patient 2; (a) Front Profile, (b) Side Profile



Both the patients had hypermobility of the shoulders and the digits were also relatively shorter (Figure 3a, 3b, Figure 4a, 4b). Upon further probing patient 1 reported similar facial features in her mother and maternal uncle suggestive of an autosomal dominant pattern of inheritance. However patient 2 claimed to not have direct ascendants who presented any physical or craniofacial abnormalities.

Figure 3: Patient 1; (a) Sloping Shoulders With Hypermobility, (b) Short Digits

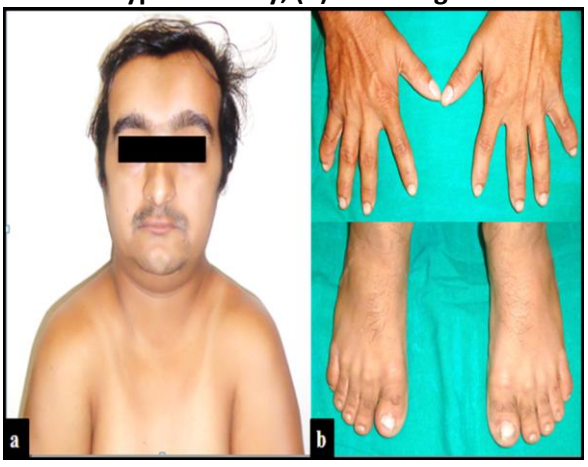
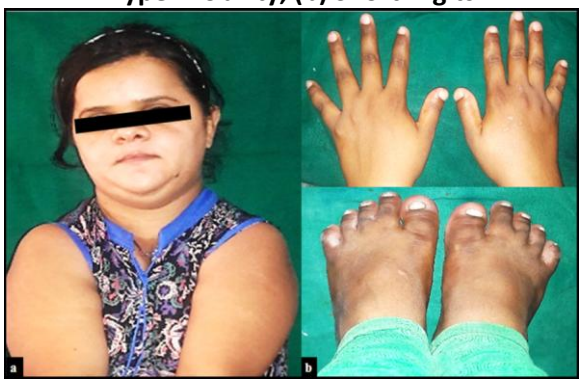


Figure 4: Patient 2; (a) Sloping Shoulders With Hypermobility, (b) Short Digits



Intraoral examination of the patient 1 revealed poor periodontal health of all teeth, malaligned teeth, multiple missing teeth, and retained root piece of 5D, 6D, 46. Periodontal health of patient 2 was also poor with malaligned teeth in maxillary anterior region owing to the presence of supernumeraries. The palate was narrow and high arched in both the patients. (Figure 5a, 5b Postero-anterior (PA) skull radiograph revealed wide sagittal suture, open fontanelles and presence of wormian bones in patient 1 (Figure 6a). Paranasal sinus (PNS) view of the same patient showed hypoplastic sinuses (Figure 6b).

Figure 5: Intraoral Picture; (a) Patient 1 (b) Patient 2

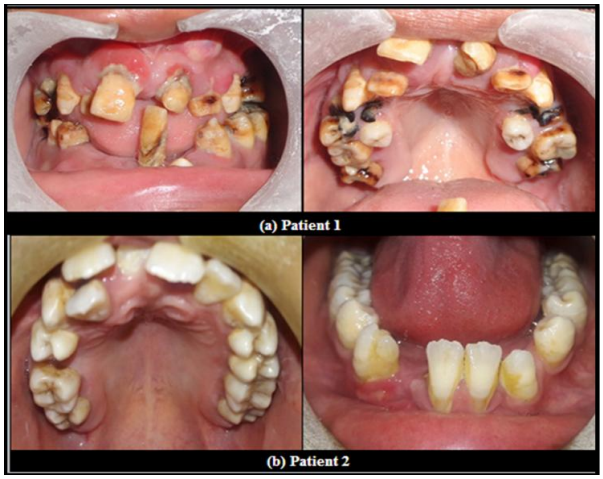
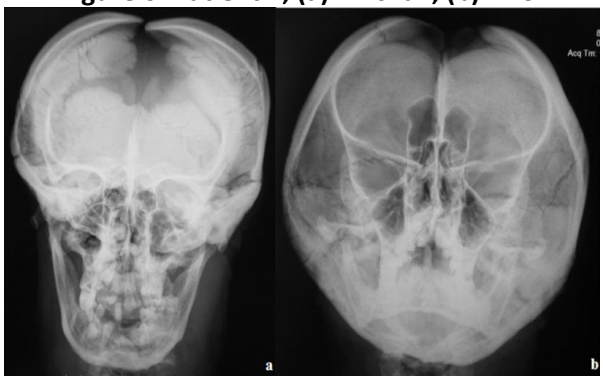


Figure 6: Patient 1; (a) PA skull, (b) PNS



PA skull of patient 2 also showed open sagittal suture (Figure 7a) and her lateral cephalogram showed underdeveloped zygoma (Figure 7b). PA thorax of both the patients showed narrow bell shaped thorax with hypoplastic clavicle (Figure 8a, 8b). Hand and wrist radiograph and feet radiograph of both the patients showed short carpals, metacarpals, tarsals and metatarsals (Figure 9a, 9b).

Figure 7: Patient 2; (a) PA skull, (b) Lateral Cephalogram

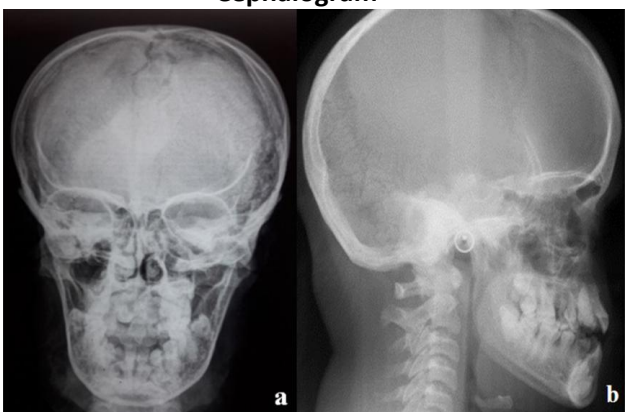


Figure 8: PA Thorax; (a) Patient 1, (b) Patient 2

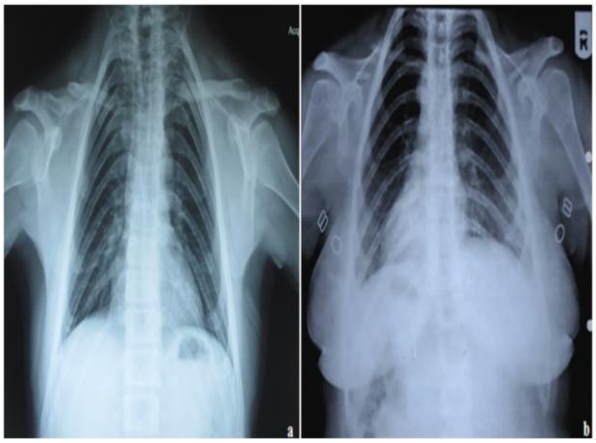
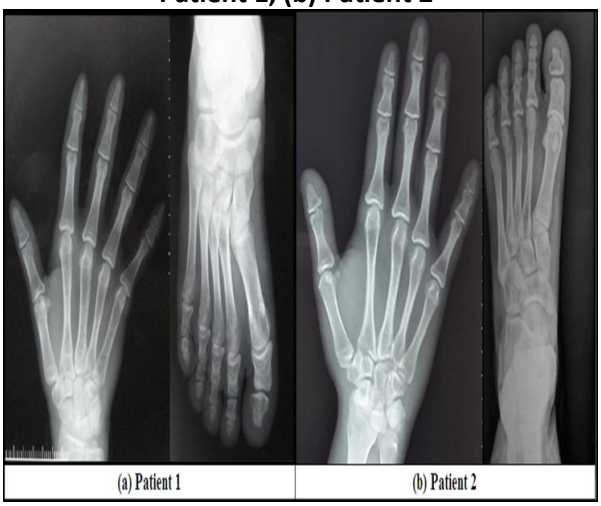


Figure 9: Hand, Wrist And Feet Radiograph; (a) Patient 1, (b) Patient 2



Furthermore, Orthopantomograms (Figure 10a, 10b) of both the patients outlined the presence of multiple impacted permanent and supernumerary teeth, a few erupted supernumerary teeth with malformed structure, generalized horizontal bone loss and condylar hypoplasia. Retained root pieces of deciduous teeth were also present in patient 1. Pulp stones were appreciated in mandibular first molars in patient 2. Intraoral periapical (IOPA) radiograph of maxillary anterior teeth (Figure 11a) revealed dens invaginatus in supernumerary teeth in patient 1. The tooth was conical in shape with reduced crown root ratio. IOPA of mandibular anterior teeth (Figure 11b) of patient 2 revealed dens invaginatus in supernumerary tooth in fourth quadrant which resembled first premolar in anatomy.

Figure 10: Orthopantomogram; (a) Patient 1, (b) Patient 2

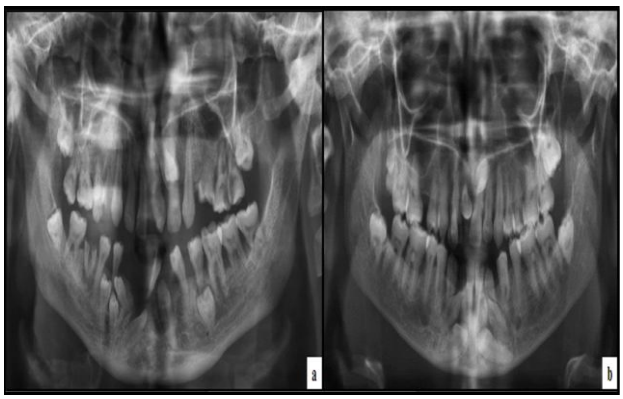
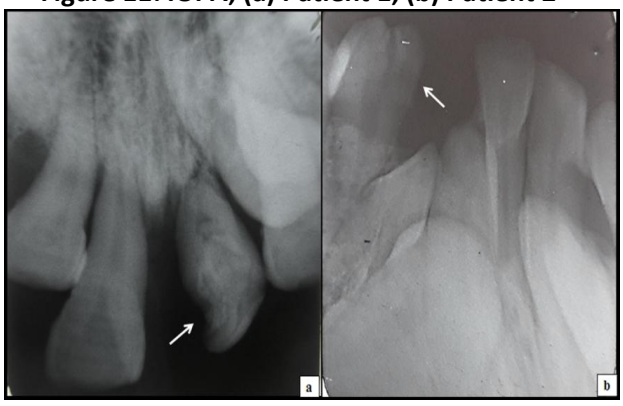


Figure 11: IOPA; (a) Patient 1, (b) Patient 2



Owing to the poor periodontal health and severe bone loss, conservative treatment was sort in both the patients. In patient 1 extraction of periodontally compromised teeth with poor prognosis was carried out that included supernumerary tooth diagnosed of dens invaginatus whose ground section was prepared confirming the diagnosis (Figure 12). Impacted permanent and supernumerary teeth were not

extracted owing to deficient bone thickness and removable partial denture was constructed following scaling and root planning. Similar treatment was planned for patient 2; however patient did not turn up on follow up.

Figure 12: Dens Invaginatus In Supernumerary Tooth Of Patient 1 With Ground Section

Discussion: Cleidocranial dysplasia primarily affects the bones undergoing intramembraneous ossification, especially skull, clavicles, and flat bones hence termed cleidocranial[1]. CCD may be identified by the family history, excessive mobility of the shoulders, clinical examination of the skull, and pathognomonic radiographic findings of prolonged retention of the primary teeth with multiple unerupted supernumerary teeth. Other conditions associated with multiple unerupted and supernumerary teeth, such as Gardner's syndrome and pycnodysostosis must be considered in the differential diagnosis[3].

Clavicle is the first bone to ossify (fifth to sixth week of fetal life) and exhibits many deformities ranging from various degrees of hypoplasia and hypocalcification. When the clavicles are completely absent, which occurs in 10% of the cases, the neck appears long, and the shoulders are drooping and hypermobile[1]. In the presented cases patients' shoulders were drooping and hypermobile and radiographs confirmed hypoplastic clavicle.

Because of delayed mineralization, there may be abnormal dentition with late eruption and impaction of the deciduous and permanent teeth. The resorption of their root is delayed. Many of the deciduous teeth are retained throughout life and lie among the permanent teeth. The permanent teeth generally lose their eruption stimulus and stay embedded, while the deciduous teeth are retained. Extraction of deciduous teeth does not stimulate the eruption of the permanent teeth[1]. Patient 1 had multiple retained root pieces of deciduous teeth that radiographically did not show signs of resorption. Multiple permanent teeth had failed to erupt in both the patients. Suggested factors of over retained deciduous teeth are lack of eruption potential and lack of cellular cementum on roots of permanent teeth[1,3], delayed mineralization of teeth, physical barrier – abnormal density of bone overlying the succedaneous teeth, and failure of bony crypt to resorb[1].

The most accepted theory to explain the development of multiple supernumerary teeth is the 'dental lamina hyperactivity theory' which states that lingual extension and proliferation of dental lamina gives rise to supernumerary teeth[5]. The presence of multiple supernumerary teeth mainly in the mandibular premolar and anterior maxilla is common which appear similar to premolars[1]. In both the presented cases also supernumeraries were found in maxillary anterior and mandibular premolar region. Also the supernumerary in the anterior maxilla of patient 1 and mandibular premolar region in patient 2 showed dens invaginatus deformity radiographically. Dens invaginatus in patient 1 was confirmed by ground section.

Dens invaginatus is a developmental change that may affect permanent, deciduous, and supernumerary teeth, the maxillary lateral incisor being the most common site of occurrence. It involves an invagination of the crown surface that penetrates the pulp cavity of dental elements, sometimes reaching the apical region.

This anomaly is caused by the folding of the dental papilla, which allows the invagination of the internal epithelium of the enamel organ during dental development before these tissues calcify. Amongst the various etiologies, genetic factor is also considered[9]. RUNX2 gene which specifically regulates the transcription and expression of some genes related to tooth development is mutated in CCD, which may have led to development of abnormal primary dental cells explaining the anomaly in both the patients presented here[4]. The management of the dentofacial manifestations of CCD can be challenging.

A method combining surgical, orthodontic, and prosthetic treatment is promising, and pediatric dentists play an important role in monitoring the correct eruption and alignment of the permanent teeth. Park et al. designed a multidisciplinary treatment protocol for the dentofacial manifestations of CCD, involving the following steps: (1) the appropriately timed removal of the retained primary teeth and supernumerary teeth, (2) surgical exposure of the impacted permanent teeth, (3) orthodontic extrusion and alignment, (4) Le Fort I advancement to correct malocclusion, (5) implant placement and prosthetic rehabilitation[6].

Due to the relatively advanced age of these patients and periodontally compromised dentition, the management of these patients was challenging. The impacted permanent teeth had completed root formation and lost their potential to erupt. The complex location and direction of the supernumerary teeth, the impacted permanent teeth, and the limited thickness of the maxilla and mandible made it difficult to carry out surgical extraction of the teeth. An increased risk of jaw fracture, infection, and possible neurological damage was present.

Orthodontic treatment, orthognathic surgery, or implantation could have proven challenging for the same reasons. Due to the relatively late diagnosis, the patients missed the best timing for obtaining optimal dental management. A conservative treatment plan was designed with the aim of restoring the function and aesthetics of the dentition. In patient 1; the periodontally compromised teeth, grossly carious and root stumps of deciduous teeth were extracted however impacted teeth were not extracted. Removable partial denture was constructed following scaling and root planning.

Although CCD has typical craniofacial deformities, many cases occur spontaneously, with approximately one out of three patients having unaffected parents. The clinical variability ranges from nearly unrecognizable to full-blown cases. The most striking CCD marker, the abnormal shoulder mobility, is often not even expressed. As the majority of the craniofacial findings are age related and become obvious only during adolescence, the most favourable treatment time, which is limited by root development and bone quantity, is frequently missed[8]. Early intervention in CCD patients is very important, and dentists must monitor children with delayed or failed exfoliation of the primary teeth and multiple supernumerary teeth in order to establish an early diagnosis.

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