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Case Report

Cleidocranial dysplasia: clinico-radiological illustration of a rare case

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Abstract: Cleidocranial dysplasia is an autosomal dominant condition caused by mutation of RUNX2, characterized by generalized dysplasia of the bones and teeth. Affected individuals have short stature, atypical facial features, and skeletal anomalies affecting mainly the skull and clavicle. The dental manifestations are mainly delayed exfoliation of the primary teeth and delayed eruption of the permanent teeth, with multiple impacted supernumeraries, and absence of cellular cementum. The frequency of this disorder is 1 per million individuals. Here we report a rare case of CCD in a 9-year-old male patient having most of the characteristic features of this syndrome. Interestingly, disorganized dentinal tubules were found in the roots of an extracted deciduous first molar, which seems to be a unique feature not reported previously. (J Oral Sci 52, 161-166, 2010)

Keywords: cleidocranial dysplasia; autosomal dominant; skeletal dysplasia; clavicle; delayed eruption; impacted supernumeraries; disorganized dentinal tubules.

Introduction

Cleidocranial dysplasia (CCD) is a dominant, inherited autosomal bone disorder with a wide range of expressivity, primarily affecting bones undergoing intramembranous ossification and characterized by clavicular aplasia or hypoplasia, retarded cranial ossification, supernumerary teeth, short stature and a variety of other skeletal abnormalities (1). This condition is usually caused by a mutation of the RUNX2 gene, which encodes a protein necessary for the correct functioning of osteoblasts (2). However 40% of CCD cases appear spontaneously with no apparent genetic cause (3).

The main features of this syndrome are persistent open skull sutures with a bulging calvaria, hypoplasia or aplasia of the clavicle permitting an abnormal ability to appose the shoulders, open fontanelles, wormian bones, a wide pubic symphysis, short middle phalanges of the fifth fingers, and various vertebral and dental abnormalities. Dental abnormalities include retained deciduous dentition, delayed eruption or retention of the permanent dentition, multiple supernumerary teeth, crown and root abnormalities, crypt formation around impacted teeth, and a high palate (1,2,4-7). There is complete absence of cellular cementum and an increase in the amount of acellular cementum of the roots of the affected teeth (8,9).

The aim of this article is to illustrate the clinical features, radiological features and dental abnormalities in a rare case of cleidocranial dysplasia.

Case Report

A 9-year-old male patient reported with his parents to our department with a chief complaint of prolonged retention of deciduous teeth. Medical history revealed exertional dyspnea, repeated ear infections and sinusitis. The family history was unremarkable.

General physical examination demonstrated a thin build, short stature, slurred speech, narrow thorax and shrugged shoulders which were easily apposable (Fig. 1). He also had macrocephaly and a prominent forehead, with hypertelorism, a depressed nasal bridge, and mid-facial hypoplasia. Frontal, parietal and occipital bossing was present, giving the skull a large globular shape (Arnold

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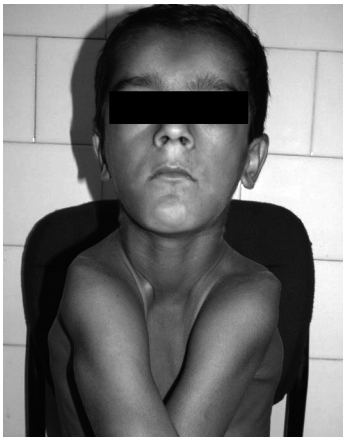


Fig. 1 The patient, showing evident thin build, short stature, prominent forehead, hypertelorism, globular skull and shrugged shoulders, which can easily appose each other.

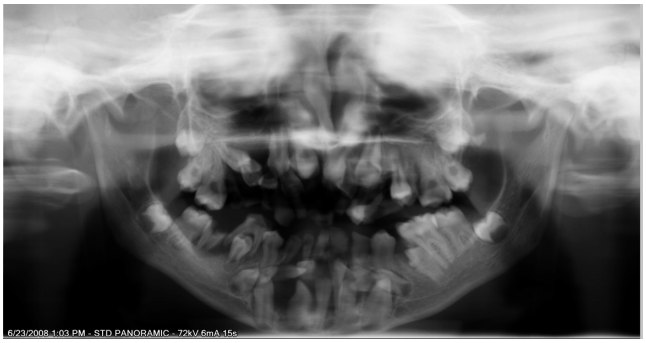


Fig. 2 Orthopantomogram showing 56 teeth including multiple unerupted and supernumerary teeth along with other features.

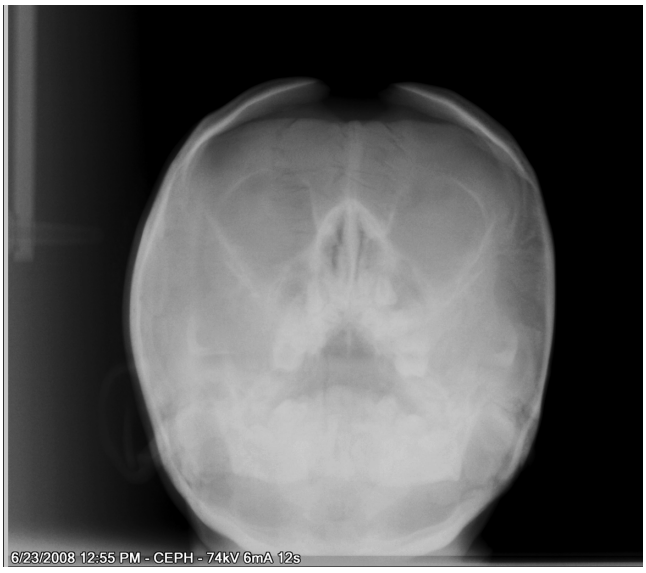
head) (Fig. 1).

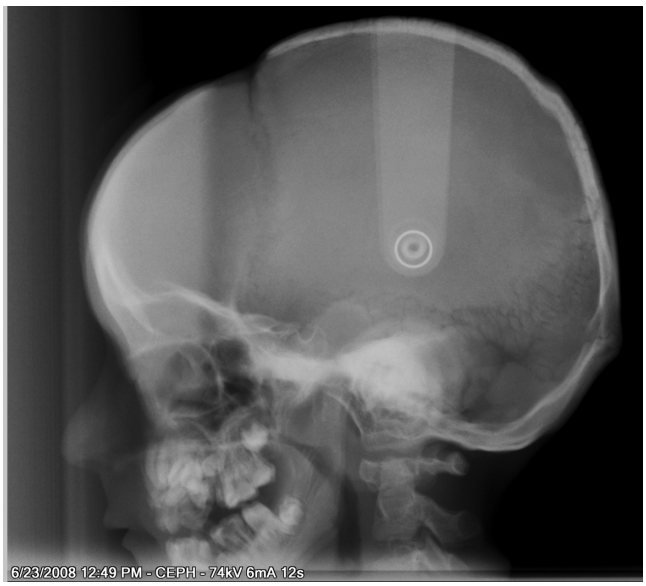
Intraoral examination revealed a narrow high arched palate, multiple grossly carious retained deciduous teeth, and a fissured tongue.

On the basis of clinical examination, the patient was diagnosed as having cleidocranial dysplasia for which the differential diagnoses included hypohidrotic ectodermal dysplasia, focal dermal hypoplasia, Apert syndrome and mandibulofacial dysplasia.

Radiological investigations included an orthopantomogram, lateral cephalogram, postero-anterior view of the skull, chest radiograph, hand-wrist radiograph, antero-posterior and lateral views of the spine, antero-posterior views of the pelvis and both hips, and 3D computed tomography of the skull. The orthopantomogram revealed multiple impacted permanent and supernumerary teeth in the incisor and bicuspid regions of the maxilla and mandible (total number of teeth present, 56). The follicular spaces of some impacted teeth were enlarged in the mandibular incisor and right parasymphysis region, suggesting cystic transformation. The ascending ramus of the mandible appeared narrow, with nearly parallel borders and coarse trabeculation. The coronoid process appeared slender and pointed. The zygomatic arch was thin with a downward tilt, and there was increased density of the alveolar crest bone overlying the unerupted teeth (Fig. 2).

The antero-posterior view, paranasal sinus view (Fig. 3) and lateral cephalogram (Fig. 4) showed open sutures of the skull, large fontanelles, small maxillary sinuses and multiple wormian bones. Chest X-ray revealed a narrow thorax with oblique ribs and hypoplastic clavicles (Fig. 5).





Figs. 3 and 4 PNS view and lateral cephalogram showing open sutures, large fontanelles and multiple wormian bones.

X-ray of the spine showed normal vertebral bodies and posterior elements. Pelvic radiography showed widening of the pubic symphyseal space along with a "chef's hat" appearance of the femoral head (Fig. 6). Hand-wrist radiographs showed normal joints with smooth articular surfaces. 3D computed tomography clearly demonstrated open fontanelles and wormian bones (Fig. 7).

A ground section and a decalcified section of an extracted deciduous first molar demonstrated complete absence of cellular cementum, paucity of acellular cementum (Fig. 8), and disorganized dentinal tubules (Fig. 9). Biochemical analysis revealed a decreased serum alkaline phosphatase level with a normal phosphate level.

After completing all the necessary investigations, the patient was confirmed as having cleidocranial dysplasia. He is currently being treated by a team comprising oral physicians, pedodontists, orthodontists and pediatricians, giving prime consideration to growth and development of the facial structures, along with psychological support. His grossly decayed retained deciduous teeth have been extracted. The cysts in the mandibular incisor and premolar region have been enucleated along with the involved teeth. Histopathological examination of the enucleated cystic epithelium confirmed the diagnosis of dentigerous cyst formation. The patient is attending for regular follow-up and care.

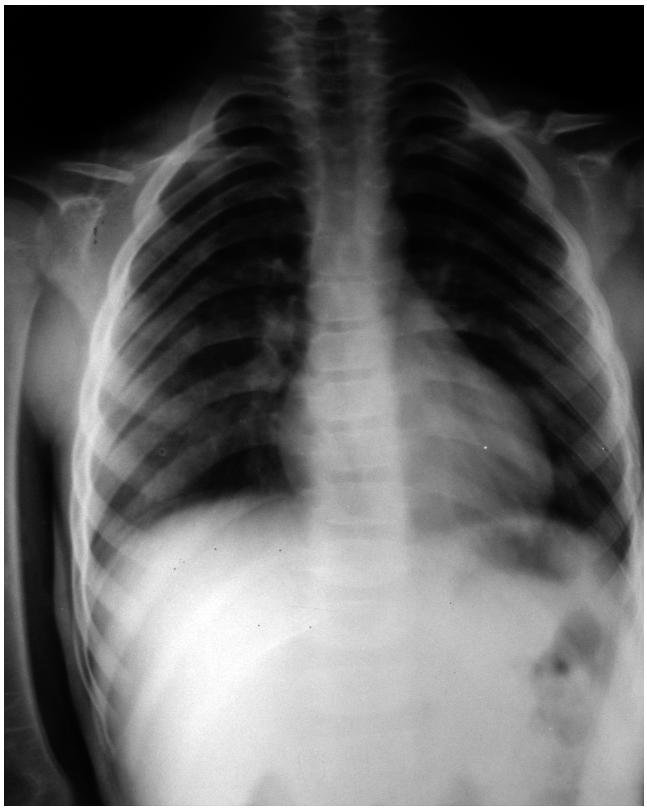


Fig. 5 Chest radiograph showing a narrow thorax, oblique ribs and hypoplastic clavicle.

Discussion

CCD is an autosomal dominant condition characterized by generalized dysplasia of the bones and teeth. The more obvious features of the defect in the clavicle and cranium prompted Marie and Sainton to coin the term cleidocranial dysostosis for this condition. However, the more generalized dysplasia of bones and teeth has led to the abandonment of "dysostosis" in favour of "dysplasia". The frequency of this disorder is one per million individuals. The CCD gene is located on either the long or short arm of chromosome 6p21 (1,4). Zheng et al. reported that humans with CCD have altered endochondrial ossification due to

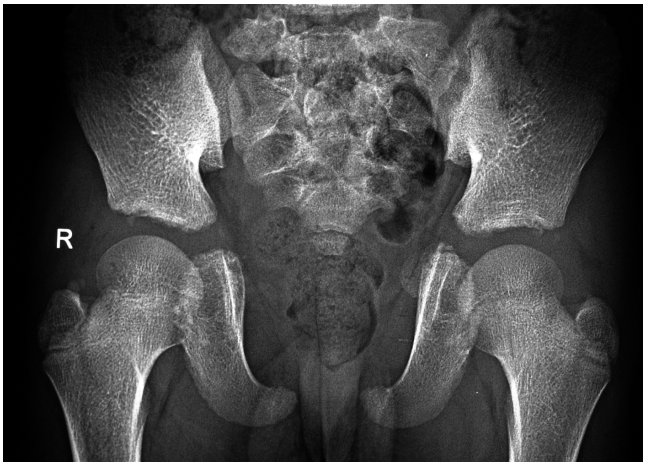


Fig. 6 AP view of pelvis revealing a wide pubic symphyseal space and a "chef's hat" appearance of the femoral head.

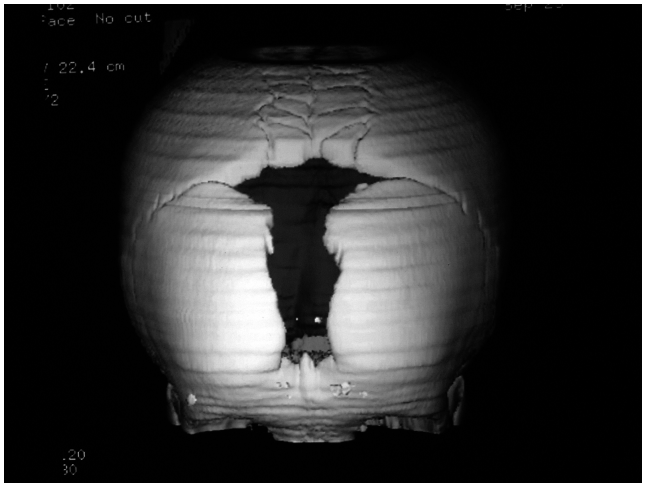


Fig. 7 3D CT scan of skull, clearly delineating the open frontanelle and multiple wormian bones.

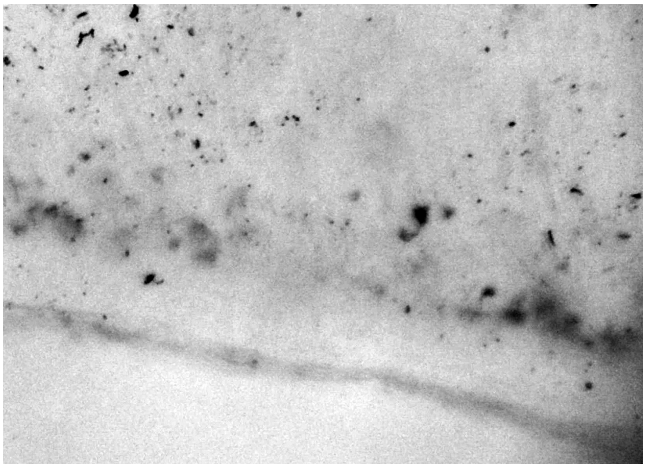


Fig. 8 Ground section prepared from one of the extracted deciduous first molars showing complete absence of cellular cementum, and paucity of acellular cementum.

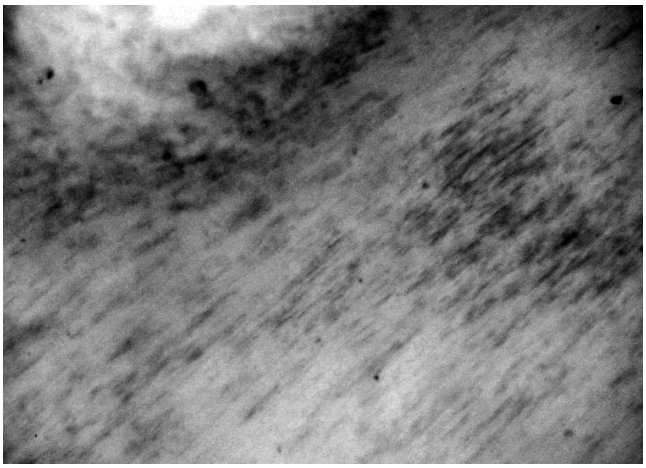


Fig. 9 Ground section prepared from one of the extracted deciduous first molars showing disorganized dentinal tubules.

perturbed RUNX2 regulation of hypertrophic chondrocytes (7). This gene is essential for osteoblast and dental cell differentiation, and thus for normal bone and tooth formation (1,4,7,10).

Recent studies have indicated that RUNX2 serves as a master gene regulating osteoblast-specific gene expression. The gene is expressed in the cells of osteoblast lineage only, and its expression is regulated by calciotropic agents. In odontogenesis, RUNX2 regulates key epithelial mesenchymal interactions that control the progress of morphogenesis and histodifferentiation of the epithelial enamel organ (10).

In CCD, there is early developmental disorder of mesenchyme or connective tissue, causing retarded ossification of bone precursors, especially at junctions, which can lead to defective ossification or even failure of ossification of some portions of skeletal structures. The syndesmoses between cranial bones and the symphysis of other bones are basically connective tissue junctions. The medial and lateral centers of ossification of the clavicles are separated by a fibrocellular structure (1,5).

CCD affects both males and females equally. The important clinical features include persistently open skull sutures, macrocephaly, brachycephaly, prominent forehead, hypertelorism, a depressed nasal bridge, midfacial hypoplasia, a narrow high arched palate, delayed tooth eruption, enamel hypoplasia, a long neck, narrow sloping shoulders, a narrow thorax, absence of the clavicle, hands with finger length asymmetry due to extraepiphysis in metacarpals II and V and multiple cone-shaped epiphyses, conductive deafness, scoliosis (which is usually diagnosed at an early age and continues to progress after skeletal maturation), a normal intelligence quotient, respiratory distress, growth retardation, recurrent sinus abnormalities and occurrence of syringomyelia (1,2,4-6). Our patient presented with most of these features, but lacked syringomyelia, asymmetric phalange length, scoliosis and vertebral abnormalities.

The radiological appearance of CCD is almost sufficient for diagnosis. Various features that are evident on panoramic radiographs are multiple unerupted abnormal teeth, a narrow ascending ramus, a slender and pointed coronoid process, a thin zygomatic arch with a severe downward tilt, small or absent maxillary sinuses, coarse trabeculation of the mandible, cyst formation with supernumerary teeth mainly in the premolar region, and increased density of the alveolar crestal bone over unerupted teeth (11). Skull radiographs show brachycephaly, a persistently open anterior fontanelle, multiple wormian bones, open skull sutures, small sphenoid bones, and calvarial thickening especially over the occiput and wormian bones. Chest radiography shows a narrow thorax, oblique ribs and absence of the clavicle (3).

Other radiographic findings include scoliosis, vertebral anomalies, spina bifida occulta (3), a wide pubic symphyseal space with a “chef’s hat” appearance of the femoral head (12), long second metacarpals and short tapering distal phalanges on both hands (3). 3D computed tomography of the cranium in patients with CCD is beneficial because it clearly delineates the open fontanelle, unlike the anteroposterior view in which the opened fontanelle is superimposed on the occipital bone (3). In the present case, the vertebral and hand wrist radiographs revealed no pathologic features.

Some reported cases of CCD have shown biochemical signs of hypophosphatasia including decreased levels of serum alkaline phosphatase (6). Our patient showed decreased alkaline phosphatase with no hypophosphatasia. A surprising and unexplained feature is absence of cellular cementum on erupted teeth in both dentitions with no increased thickening of the primary acellular cementum, as was seen in the present case (8,9). Our patient also showed an additional histological feature of irregularly arranged dentinal tubules, which is the first reported example of its kind in the English literature. The generalized or localized nature of this feature has yet to be confirmed. The mode of anchorage of periodontal fibers and maintainance of periodontal ligament width are also not understood.

Differential diagnosis of this syndrome includes hypohidrotic ectodermal dysplasia (which includes hypohidrosis, anomalous dentition, onychodysplasia, and hypotrichosis), focal dermal hypoplasia (characterized by relative focal absence of the dermis, skin atrophy, streaky pigmentation, multiple mucosal papillomas, and deformity of the extremities), Apert syndrome (characterized by craniosynostosis, craniofacial abnormalities and symmetrical syndactly of the hands and feet), pycnodysostosis (mainly including a short-limbed stature, acro-osteolysis, osteosclerosis and bone fragility) and cranio-facial dysostosis (characterized mainly by premature craniosynostosis with other abnormalities) (1,4,5).

The increased density of the jaw bones with a coarse trabecular pattern, decreased resorption and multiple reversal lines accounts for delayed eruption of teeth that are not mechanically obstructed. Complications reported in these patients include genua valga, pes planus, sinus infections, recurrent otitis media and hearing loss (2,6).

The planning of treatment for patients with CCD is complicated by a number of factors, and largely depends on both the chronological and dental ages of the patient. The timing of diagnosis is not only important for choosing an appropriate treatment plan but also for obtaining successful treatment results. A team approach to management of dental abnormalities on a long-term basis is necessary. The overall goal is to provide an esthetic facial appearance and functional occlusion by late adolescence or early adulthood (12).

An anomaly in the eruption of anterior teeth can interfere with facial esthetics and lead to other clinical problems. If the impacted teeth are extracted, loss of alveolar bone can be anticipated. Following the healing period, the alveolar ridge becomes thin and deficient. Therefore orthodontic treatment should be chosen to facilitate eruption of natural teeth. Expansion of the maxillary arch should be carried out to gain additional space for tooth alignment. Long-term monitoring of the stability and periodontal health of impacted teeth is necessary after orthodontic traction (2,13).

Orthodontic occlusal movement of the teeth will restore the alveolar ridge to a height compatible with normal dental and skeletal growth. A normal gingival margin and periodontal attachments can be achieved, thus eliminating the need for additional periodontal therapy. Removal of deciduous teeth does not seem to hasten the eruption of permanent teeth. Permanent teeth may be difficult to extract because of malformed roots (2,13).

In conclusion, despite the variable expressivity of CCD, early diagnosis through oral findings is possible. In addition to oral features, diagnosis of this rare syndrome requires a reliable skeletal evaluation. This disorder not only causes physical discomfort to the patient but also leads to psychological problems. Therefore, along with achieving a well functioning permanent dentition and an esthetically satisfying facial appearance, proper motivation and psychological support for the patients and their parents are also important. The presence of disorganized dentinal tubules will need to be confirmed by further studies.

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