

CASE REPORT

Cleidocranial dysplasia: a dilemma in diagnosis?

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Keywords

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Abstract Cleidocranial dysplasia is a developmental anomaly and is characterized by craniofacial and skeletal malformations as well as the presence of numerous supernumerary and unerupted teeth. A 16-year-old patient presented with an unaesthetic facial appearance due to unerupted front teeth. General examination showed the absence of the clavicles, a brachiocephalic skull with frontal bossing and a depressed nasal bridge with concave facial profile. Radiographic examination showed multiple supernumerary teeth, rudimentary clavicles with a bell shaped rib cage and an open sagittal suture. A final diagnosis of cleidocranial dysplasia was made and comprehensive management was planned which involved multi disciplinary approach. The role of dentist is vital in the early diagnosis and management of such cases which require interdisciplinary cooperation for better results.

Introduction

Cleidocranial dysplasia (CCD) is a developmental anomaly of the skeleton and teeth, first reported by Martin in 1765 as cleidocranial dysostosis (Fernandes *et al.*, 2006). It was also known as Marie and Sinton disease or mutational dysostosis because it was initially thought to involve bones of intramembraneous origin and it is now well established that endochondral ossification is also affected. CCD is transmitted by an autosomal dominant mode of inheritance with high penetrance and variable expressivity (Gombra and Jayachandran, 2008; Hemalatha and Balasubramaniam, 2008). One third of cases is sporadic and appears to represent new mutation. A spontaneous mutation reported in 20-40% of cases in the core binding factor α 1 (CDFA-1) gene, located on chromosome 6p21 has been shown to be the cause of CCD (Mundlos, 1999; Shafer *et al.*, 2000). CCD is notable for mid-face hypoplasia; clavicular aplasia/ hypoplasia resulting in narrow, sloping shoulders that can be apposed at the midline; and hand abnormalities such as brachydactyly, tapering fingers, and short, broad thumbs

(Kerr, 1988). The most striking dental abnormalities include failure to shed the primary teeth, delayed eruption of secondary dentition and multiple impacted supernumerary teeth resulting in malocclusion (Silva *et al.*, 1997). With delayed ossification of the cranial sutures and fontanelles, the raised intracranial pressure results in expansion of the cranial vault leading to bossing of the frontal, parietal and occipital bones and bowing of the clivus culminating in a brachycephalic skull. As a result of the abnormal ossification pattern, wormian bones may be seen in the coronal and lambdoid regions. The face may appear small in relation to the cranium with hypoplastic maxillary, lacrimal and zygomatic bones and the paranasal sinuses may also be underdeveloped.

Early diagnosis of CCD allows for timely planning of necessary procedures. The goal of treatment is to improve appearance and to provide a functioning masticatory mechanism. The goals may be achieved with prosthetic replacements, with or without prior extractions; by removal of the supernumerary teeth followed by surgical repositioning of the permanent teeth; and by a combination of surgical and orthodontic measures for actively erupting

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and aligning the impacted permanent teeth. The fontanelles close with time in the majority of individuals and cranial remodeling is usually not necessary; however, if the cranial vault defect is significant, the head should be protected from blunt trauma; helmets may be advised for high-risk activities. In these cases, evaluation by a craniofacial surgeon and rehabilitation services are indicated.

If bone density is below normal, treatment with calcium and vitamin D supplementation should be considered. Preventive treatment for osteoporosis should be initiated at a young age since peak bone mineral density is achieved in the second and third decade. So, early diagnosis of CCD is beneficial for prompt intervention which will greatly influence the better restoration of craniofacial aesthetics and function.

Case report

A 16-year-old girl presented with the complaint of an unaesthetic facial appearance due to the presence of unerupted front teeth. She stated that after the loss of deciduous teeth, only one permanent tooth erupted (right lower central incisor). She had visited many dentists who reassured and advised her to wait. The medical history was non contributory and family history revealed that patient was the younger of the two siblings born to parents with non consanguinal marriage with negative syndromic backgrounds.

General physical examination revealed that the patient was well oriented and of normal intelligence. She had short stature, a brachiocephalic skull with frontal bossing, a depressed nasal bridge, malar

hypoplasia, and an underdeveloped maxilla with a prognathic mandible with concave facial profile. On palpation, a depression over the sagittal suture and absence of the clavicles was demonstrated. The patient could approximate her shoulders in midline.

Intraoral examination revealed that all the permanent anterior teeth were missing except 41 (Figure 1) and a Grade II mobility was noted with retained deciduous molars. The permanent first and second molars were present in both the arches with high arched palate.

On the basis of case history and clinical examination, a provisional diagnosis of cleidocranial dysplasia was made and the differential diagnosis of pyknodystosis, mandibuloacral dysplasia and Yunis Varon syndrome were considered.

Panoramic radiograph showed multiple impacted supernumerary and permanent teeth (Figure 2). PA skull showed open sagittal suture and thickening of the supraorbital area as well as hypoplastic zygomatic bones (Figure 3). A lateral cephalogram showed midfacial deficiency and a concave facial profile. PA chest showed rudimentary clavicles with a bell shaped rib cage (Figure 4). Ultrasonic examination of the abdominal region showed no abnormality and hematological and serological investigations were within normal limits. The patient was referred to the clinical geneticist for molecular genetic testing, which showed mutation in RUNX-2 (CDFA-1) gene. A final diagnosis of cleidocranial dysplasia was made and comprehensive management was planned which involved multiply-disciplinary approach.



Figure 1 Intraoral photograph of the patient.



Figure 2 OPG showing multiple impacted supernumerary teeth.



Figure 3 PA skull showing open sagittal suture.

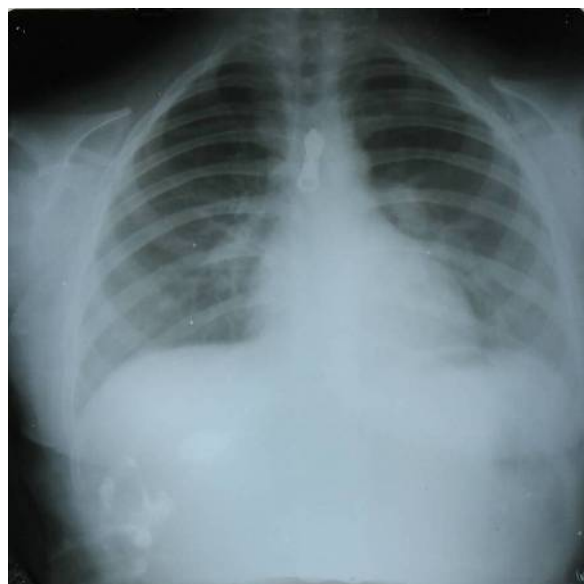


Figure 4 PA chest showing rudimentary clavicles.

Discussion

CCD is a rare autosomal dominant disorder affecting the entire skeletal system. Although there is generalized involvement, the midline osseous structures are primarily involved (Gorlin *et al.*, 2001). The prevalence of CCD has been estimated as 1 per million live births and the disorder is reported to be associated with a spontaneous mutation in the gene coding for osteoblast transcription factor Runx2/Core binding factor and mapped to the chromosome 6p21. This factor is responsible in controlling the differentiation of precursor cells into osteoblasts, which is essential for membranous as well as endochondral ossification (Zhou *et al.*, 1999).

The clavicles are the first bone to ossify and/or commonly affected, being either hypoplastic or aplastic. Complete absence of the clavicles occurs in about 10% of cases and usually only the acromial end is absent (Golan *et al.*, 2004). When there is unilateral absence, it is usually in the right clavicle.

The maxilla, accessory sinuses and mastoid air cells are hypoplastic and together with the hypoplastic development of the facial bone and paranasal sinuses, give the mandible a prognathic appearance. Sometimes, conduction deafness will be a significant finding in CCD (Visosky *et al.*, 2003).

In the chest, patients with CCD have been described as having a "bell-shaped" thoracic cage with short, oblique ribs. Short stature is a significant finding, while birth length is normal. At 4 to 8 years of age

height drops to below 2 standard deviations of the mean.

Intraorally, the most striking feature of CCD is the presence of supernumerary teeth, impacted teeth, often located in the premolar area. Other dental abnormalities include incomplete and delayed eruption of the permanent teeth, as well as retention of deciduous dentition. The causes of unerupted teeth are attributed to the disturbance of bone resorption, the early loss of gubernacular cord or canal, absence of cellular cementum or lack of union between the dental follicle and the mucosa due to interposed fibrous tissue acting as a barrier to eruption (Manjunath *et al.*, 2008). The skull shows typical characteristics, which include open metopic fontanelles and sutures, delayed suture closure and multiple wormian bones. A frontal groove is seen in the midfrontal area, owing to this incomplete ossification (McNamara *et al.*, 1999).

Pyknodysostosis shares many features with CCD; however the absence of supernumerary teeth and increased bone density on X-ray allow for differentiation from CCD (Maroteaux and Lamy, 1962). Mandibuloacral dysplasia (MAD) a progressive disorder can be differentiated from CCD by progressive stiffening of joints and radiographs reveal acroostedysplasia of the fingers and toes, with delayed ossification of the carpal bones (Novelli *et al.*, 2002). MAD is autosomal recessive disorder associated with mutations in the genes LMNA or ZMPSTE24 (Mendoza-Londono and Lee, 2009). Yunis Varon syndrome can be differentiated by absence

of a distal phalanx of great toe, poorly delineated lips along with less pronounced dental findings (Mendoza-Londono and Lee, 2009). Other syndromes and disorders were ruled out by radiographic examination and genetic testing; thus resolving the dilemma regarding the diagnosis of CCD.

Management for the patient with CCD is quite challenging. The earlier the treatment is initiated; the better is the prognosis (Daskalogiannakis et al., 2006; Gulati and Kabra, 2001). Comprehensive dental and craniofacial management involves the team work of radiologists, pedodontists, oral maxillofacial surgeons, prosthodontists and orthodontists to achieve better facial aesthetics (Olszewska et al., 2006; Patel and Athavale, 2004; Ross et al., 1998). For further management of skeletal abnormalities, the patient was referred to an orthopaedic surgeon.

Conclusion

A rare sporadic case of CCD with peculiar skeletal and dental abnormalities was reported. Role of dentist is very crucial in early diagnosis and management of such cases which require interdisciplinary cooperation for better results.

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