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Review article

Craniofacial features of cleidocranial dysplasia

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Abstract Cleidocranial dysplasia (CCD) is an autosomal-dominant malformation syndrome affecting bones and teeth. The most common skeletal and dental abnormalities in affected individuals are hypoplastic/aplastic clavicles, open fontanelles, short stature, retention of primary teeth, delayed eruption of permanent teeth, supernumerary teeth, and multiple impacted teeth. Treatment of CCD requires a multidisciplinary approach that may include dental corrections, orthognathic surgery and cranioplasty along with management of any complications of CCD. Early diagnosis of this condition enables application of the treatment strategy that provides the best quality of life to such patients. Notably, Runx2 gene mutations have been identified in CCD patients. Therefore, further elucidation of the molecular mechanism of supernumerary teeth formation related to Runx2 mutations may improve understanding of dental development in CCD. The insights into CCD pathogenesis may assist in the development of new treatments for CCD.

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Introduction

The term cleidocranial dysplasia (CCD; OMIM 119600) is derived from the ancient Greek words *cleido* (collar bone), *kranion* (head), and *dysplasia* (abnormal formation). This rare hereditary skeletal disorder, which is also known as Scheuthauer-Marie-Sainton syndrome or cleidocranial dysostosis, is characterized by abnormal skeletal and dental development. The prevalence of CCD is an estimated one per million and does not differ by race or by gender.[1] In most cases, the disorder is an inherited autosomal dominant trait. In 20–40% of reported cases, however, the disorder occurs sporadically.[1] This syndrome is characterized by hypoplastic and/or aplastic clavicles, patent sutures and fontanelles, wormian bones, wide pubic symphysis, supernumerary teeth, short stature, and various other skeletal changes. Although clavicular defects have been reported in the literature as early as 1765,[2] Scheuthauer[3] in 1871 was apparently the first to describe the syndrome accurately. Marie and Sainton[4] in 1898 coined the term "dysostose cléidocrânienne héréditaire" for this condition.

The term "cleidocranial dysostosis" was originally used because CCD was thought to involve only bones of intramembranous origin, i.e., bones of the skull, clavicles and flat bones. Subsequent studies showed that bones of endochondral ossification are also affected and that CCD is a generalized disorder of many skeletal structures. Therefore the term "cleidocranial dysostosis" was changed to "cleidocranial dysplasia" to reflect the more generalized nature of the condition.[5,6]

Clinical features

The clinical appearance of CCD is so distinct that it is pathognomonic. The main clinical features of CCD are recognized during early childhood and include a short stature, delayed closure of fontanelles, prominent forehead, and abnormal dental development. The head of a CCD patient usually shows frontal and parietal bossing and a groove along the metopic suture. The neck appears to be abnormally long, and the shoulders are narrow with marked drooping. Clavicular abnormalities with associated muscle defects allow excessive mobility of the shoulder girdle. For example, many CCD patients can approximate their shoulders in front of the chest for variable levels. The clinical spectrum is extremely variable even within families and ranges from mild cases with only dental abnormalities to severe cases with pronounced skeletal deformities.[7,8]

Radiographic features

The distinctive radiological features of CCD are shortened or absent clavicles, delayed ossification of the skull bones, and delayed ossification of pelvic bones.[1] The chest radiographs for CCD patients in Fig. 1A show that the clavicles may be completely absent (aplasia) or smaller than normal (hypoplasia). The clavicles are typically hypoplastic or discontinuous, either unilaterally of bilaterally; the clavicles are completely absent in 10% of cases. Hypoplastic clavicles include hypoplasia of the acromial end or absence of the sternal end with the acromial end present. The missing segment may cause fibrous pseudoarthrosis or may be replaced by a fibrous tether or cord.[9]

Craniofacial morphological features

Fig. 1B shows that the skull in CCD is characterized by brachycephaly, delayed or failed closure of the fontanels, open skull sutures, and multiple wormian bones in the coronal and lambdoid suture regions. Defective fusion of frontal and parietal bones leading to open coronal and sagittal sutures are also visible. The nasal bones are missing or hypoplastic. Mandibular prognathism may be secondary to nasomaxillary deficiency. Dense alveolar crestal bone can be seen in the anterior mandible.

Other craniofacial morphological features of CCD include abnormally small or nonexistent maxillary sinuses, hypoplastic zygomatic bones, and patency of the mandibular symphysis.[1,10] The zygomatic arch may be thin or even discontinuous at the zygomaticotemporal suture. The zygomatic arch has a characteristic downward bend.[1] The mandible is characterized by a narrow ascending ramus with nearly parallel anterior and posterior borders and by an abnormally slender and pointed coronoid process with an abnormally distal curvature.[10] The trabecular pattern of the mandible is very coarse. Fig. 1C is a panoramic radiograph of these features.

Radiographic features associated with the teeth

Fig. 1C shows that CCD is characterized by prolonged retention and delayed shedding of the primary teeth and multiple unerupted permanent and supernumerary teeth.[10] Dentigerous cysts occasionally arise in association with these unerupted teeth. Although development of the primary teeth is rarely affected, root resorption and exfoliation of the primary teeth may be delayed.

Cone-beam computed tomography (CBCT) imaging

Imaging by CBCT is now routinely used for three-dimensional dentition, which reduces guesswork and enables better anatomical localization of supernumerary and impacted teeth. Other pertinent information provided by CBCT include the precise location of a supernumerary tooth in relation to important structures such as the cortex of the nasal floor, labial cortex of the nasal ridge, nasopalatine duct, and the mandibular canal and adjacent root apices.[11] Because CBCT clearly depicts the position and anatomy of impacted teeth, CBCT is useful for both diagnosis and treatment planning in CCD.

Histopathological features

Tooth formation and eruption occur in a series of complex and highly regulated process. The reasons for failure of permanent tooth eruption and retention of the primary teeth in CCD patients are poorly understood. Absence of cellular cementum at the root apex is presumably one factor in failed or delayed eruption of permanent teeth and

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