Case Report

Cleidocranial Dysplasia: A Clinico-Radiological Illustration of a Rare Case
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Abstract
Cleidocranial dysplasia is a rare autosomal dominant condition with generalized dysplasia of bone, characterized by delayed closure of cranial sutures, hypoplastic or aplastic clavicles, short stature, dental abnormalities and a variety of other skeletal abnormalities. In this case report, we describe an otherwise healthy 11 year-old male child with a chief complaint of missing anterior maxillary teeth who was diagnosed with cleidocranial dysplasia.

Keywords: Cleidocranial Dysplasia; Autosomal Dominant; Dental Abnormalities; Hypoplastic Clavicles.

Introduction
Cleidocranial dysplasia is a rare congenital defect of autosomal dominant inheritance, primarily affecting bones that undergo intramembranous ossification, i.e. generally the calvarian but also the clavicular bones.1,2 It is also known as Marie and Sainton disease, Mutational dysostosis and Cleidocranial dysostosis.3 Cleidocranial dysplasia was first reported by Martin in 1765. In 1897 Marie and Sainton coined the descriptive title cleidocranial dysostosis since then, over 1000 cases have been documented in the medical literature.4,5

The disorder was originally thought to involve bones of intramembranous origin only, namely the bones of the skull, clavicles and flat bones, hence the name cleidocranial. It is now known that bones of endochondral ossification are also affected, and that it is a generalised disorder of many skeletal structures. The term cleidocranial dysplasia was therefore substituted for cleidocranial dysostosis to reflect the more generalised nature of the condition.6

This condition is of clinical significance to every dentist due to the involvement of the facial bones, altered eruption patterns and multiple supernumerary teeth. Here is an unusual clinico-radiological illustration of a rare case of cleidocranial dysplasia with an insight regarding its molecular etiopathogenesis.

Case Report
An eleven year old boy reported to department of pedodontics and preventive dentistry with a chief complaint of missing anterior teeth in upper jaw since past six months. Medical and dental history was non-contributory with no relevant habit history. Family history revealed that patients’ mother showed similar clinical manifestations in her childhood. General examination and extra oral examination showed that the patient had a thin built, short stature, prominent forehead, globular skull and shrugged shoulders, which could easily appose each other (Figure 1a). Intraoral examination revealed a narrow high arched palate, multiple grossly carious retained deciduous teeth and missing upper anterior teeth (Figure 1b).

The panoramic radiograph showed multiple unerupted teeth in both the jaws. Skull radiograph (lateral view) demonstrated open skull sutures, delayed closure of fontanels and multiple wormian bones (Figure 1c). Besides this, Chest radiograph (PA View) confirmed the clavicular hypoplasia and bell shaped rib-cage (Figure 1d). It also showed poorly formed paranasal sinuses and zygomatic complex. A diagnosis of Cleidocranial dysplasia was confirmed and the patient is undergoing treatment for prosthetic rehabilitation for his missing teeth.

Discussion
Cleidocranial dysplasia follows an autosomal dominant pattern of inheritance. “Autosomal” means that the gene responsible for the condition is located on one of the numbered chromosomes, not the sex chromosomes. “Dominant” means that only a single gene change is necessary for an individual to show features of the condition. Therefore, people who have Cleidocranial dysplasia...
have one gene of a pair that is unchanged and working properly and one gene that is changed and is not working properly. The gene that is altered “dominates” over the unchanged gene, causing the features of Cleidocranial dysplasia. The gene that causes Cleidocranial dysplasia is denoted by the symbol RUNX2, and it directs the body to make a protein that helps to control the development of osteoblasts, which are cells that are important in the formation of bone. While most individuals with this disorder either inherited their mutated gene from an affected parent or are the first in their families to have a gene change, there are several reports of families in which two siblings with Cleidocranial dysplasia were born to unaffected parents, suggesting that some parents may have a percentage of egg or sperm cells that carry the gene change. This phenomenon is referred to as “gonadal mosaicism.”

The RUNX2 gene provides instructions for making a protein that is involved in bone and cartilage development. RUNX2 protein acts as a “master switch,” regulating a number of other genes involved in the development of cells that build bones. Some mutations change one protein building block (aminoacid) in the RUNX2 protein. Other mutations introduce a premature stop signal that results in an abnormally short protein. These genetic changes reduce or eliminate the activity of the protein produced from one copy of the RUNX2 gene in each cell, decreasing the total amount of functional RUNX2 protein. This shortage of functional RUNX2 protein interferes with normal bone and cartilage development, resulting in the signs and symptoms of cleidocranial dysplasia.

Cleidocranial dysplasia presents with skeletal defects of several bones, the most striking of which are partial or complete absence of clavicles, late closure of the fontanels, presence of open skull sutures and multiple wormian bones. The skull base is dysplastic and reduced in growth resulting in increased skull width leading to brachycephaly and hypertelorism. Delayed closure of anterior fontanel and metopic sutures results in frontal bossing. Thoracic cage is small and bell shaped with short ribs.
Typically, clavicles are underdeveloped to varying degrees and in approximately 10% of cases, are completely absent. This allows excessive mobility of the shoulder girdle. Other bones may also be affected including long bones, the vertebral column, the pelvis and the bones of hands and feet. Characteristically, patients with cleidocranial dysplasia, show prolonged retention of deciduous dentition and delayed eruption of permanent teeth. Adults with cleidocranial dysplasia have mixed dentition in their oral cavities. In addition, patients with this condition, frequently show a large number of unerupted supernumerary teeth. Maxilla is also underdeveloped along with ill formed paranasal sinuses. The clinical findings of cleidocranial dysplasia, although present at birth, are often either missed or diagnosed at a much later time. Some cases are diagnosed through incidental findings by physicians, treating patients for unrelated conditions.

The suggested treatment for dental complications of cleidocranial dysplasia is the fabrication of dentures over the unerupted teeth and the removal of teeth as they erupt, for very little bone structure would be left, if supernumerary, impacted and unerupted teeth were all extracted at once. Cleidocranial dysplasia can be diagnosed by ultrasound examination in the offspring of an affected parent as early as 14 weeks gestation. The most consistent features are abnormal clavicles, which are either short or partially or totally absent. Less specific findings include brachycephalic skull with under mineralization, frontal bossing, and generalized immature ossification. Gene testing is available on both a research and a clinical basis.

Cleidocranial dysplasia may be identified by family history, excessive mobility of shoulders and radiographic pathognomonic findings of the chest, skull and jaws. A team approach to management of dental abnormalities of cleidocranial dysplasia on a long-term basis is necessary. The overall goal is to provide an aesthetic facial appearance and functional occlusion by late adolescence or early adulthood. Proper anticipatory guidance for people with this disorder can eventually lead healthy and productive lives.

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