Cleidocranial Dysplasia

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INTRODUCTION:

The cleidocranial dysplasia, also known as Marie and Sainton Disease, Scheuhauer Marie-Sainton Syndrome and Mutational dysostosis.1 It is a congenital autosomal dominant disorder, characterized by generalized dysplasia of osseous and dental tissue commonly resulting in defects in the skull, clavicle and teeth.2 It is associated with a spontaneous mutation in the gene coding for osteoblast transcription factor for RUNX2, which is essential for osteoblast and dental cell differentiation as well as for bone and tooth formation.3

Along with dental abnormalities, this condition is characterized by delayed ossification, absence of the clavicles, which occurs in 10% of cases or the presence of hypo plastic clavicles which allow the patient the movement of the shoulders up to the medial plane of the body without any discomfort.1

The term dysostosis means defective ossification or defect in the normal ossification of fetal cartilages (Gr. osteon – bone). In dysostoses the distribution follows a defect in ectodermal or mesenchymal tissues. Rarely are all bones involved. As derived from the Greek, dysplasia refers to abnormality of development or “ill formed” (Gr. plassein – to form); in pathology it means alteration in size, shape, and organization of adult cells. Bone dysplasia are those in which the predominant error is an intrinsic one; it affects all growing bones similarly and is generalized in distribution. At Present, this congenital condition is known to be a generalized disorder of bone, and as such was renamed in 1978 cleidocranial dysplasia.4

Diagnosis is made by clinical correlation and radiographic findings. This condition is of clinical significance to the dentist, due to the involvement of facial bones, cleidocranial dysostosis with classic clinical and radiological features supplemented by relevant literature.

CASE REPORT:

A 20 year female patient reported to our department of oral medicine & radiology, with a complaint of missing teeth. History revealed that
there is delayed shedding of primary teeth. No positive family history is elicited. Clinical examination revealed that patient is short statured (fig1) and presented with brachycephalic skull, frontal bossing, depressed frontal and parietal bones, hypoclastic maxilla, zygoma & clavicles. Mandible seems protruded. Shoulder girdle feature present (fig2). Intra orally, patient has number of missing permanent & over retained deciduous teeth. High vault palate is present. Based on clinical examination, an orthopantamograph, PA view of skull, chest X ray was advised.

Orthopantamograph revealed that multiple impacted permanent teeth. Multiple supernumerary teeth (31 in number), in all quadrants in premolar region were present. Condyles are underdeveloped (fig3). PA view of skull showed sutural persistence seen in coronal and lamboid sutures. Both parietal bones show defective fusion in the center with wormian bones formation. Frontal sinus appears small (fig4). Chest radiograph shows both clavicles tapering and defective portion of lateral ends. Right clavicle is seen in 2 pieces (fig 5). Clinical and radiologic findings are suggestive of cleidocranial dysplasia.

DISCUSSION:

Cleidocranial dysplasia (CCD) is an autosomal dominant disorder with complete penetrance and variable expression. This pathology was first described in 1765, whereas only in 1898 Marie & Sain ton had described cases of the disease and associated them with patterns of inheritance. Later, Bauer apud Kallialla (1962) suggested the genetic mutation as an etiological factor of the disease. In 1946 Lasker apud Forlan (1962) had concluded that it was a genetic disease with an autosomal dominant inheritance, and in some cases, external interferences in the foetal period could cause this mutation that is transferred to the progeny. In our case, the patient did not report the existence of direct ancestors or descendents who presented any of the clinical characteristic of cleidocranial dysplasia. She was alerted of the inheritance characteristic of the disease and also about the genetic counseling.

It is a relatively uncommon disorder with the prevalence being 0.5 per 100,000 live births. It is associated with a spontaneous mutation in the gene coding for osteoblast transcription factor for RUNX2. There is a mutation in CBF alpha 1 (core binding factor); the affected molecule is a transcription factor, and the phenotype shows abnormal clavicles, wormian bones and supernumerary teeth. The gene has been mapped to chromosome 6p21 in the region containing CBF alpha1, which controls the differentiation of precursor cells into osteoblasts.

The main defect lies in faulty ossification of selected endochondral and intra membranous bones, and although any bone may be affected, a classical triad of cranial, clavicular, and pelvic anomalies comprise the most striking changes. This is an early developmental disorder of mesenchyme or connective tissue, producing retarded ossification of the membranous and cartilaginous precursors of bone, especially at the junction of various bones. This may lead to delayed or even failure of ossification of portions of the skeletal structure. The syndesmoses between cranial bones and symphyses of other bones are basically connective tissue junctions. The medial and lateral centers of ossification of the clavicle are also separated by a fibro cellular structure. The distribution follows a pattern in which syndesmoses or suture lines of connective tissue and bones in which cartilage nuclei grow by direct apposition of a fibro cellular layer into proliferative cartilage.

Clinical and radiological features include a large brachycephalic head, small and angular face, prominent frontal and parietal bones and drooping shoulders with excessive mobility. The characteristic skull abnormalities are sometimes referred to as Arnold head named after the descendants of Chinese who settled in south Africa and changed his name to Arnold. Depending on the amount of clavicular involvement, the patient may be able to approximate the two acromial regions below the chin. Height is reduced in both sexes, but dwarfism is not a common finding.

Because of delayed mineralization, there may be abnormal dentition with late eruption and impaction of the deciduous and permanent teeth. The teeth
may appear small, irregularly spaced, and crowded. Furthermore, the teeth often display aplasia, malformed roots, enamel hypoplasia, enhanced caries, and supernumerary teeth. Hand anomalies may include asymmetric length of fingers. Other skeletal abnormalities include delayed mineralization of public bone, wide symphysis pubis, narrow pelvis and spondylolysis. There may be syringomyelia or spina bifida occulta. The thoracic cage is small and bell shaped with short ribs.

The failure in the eruption can be related with the absence or less amount of cellular cementum in the permanent teeth roots (Rushton). This was also claimed by Smith, who had observed the absence of cellular cementum in the deciduous and permanent dentition.

The diagnosis is mainly based upon clinical and radiographic characteristics. Serum alkaline phosphatase activity has been observed to be consistently reduced in patients suffering from CCD. A routine 2D ultrasound examination carried out at a local hospital at gestational age 12 weeks showed no signs of CCD. A 3D ultrasound examination in week 15+4 showed a foetus with typical CCD features including large fontanelles, lack of nasal bones, clavicles without the typical S-form, as well as severe delay in calvarial ossification, especially in the midline. Serial 3D ultrasound examinations during pregnancy confirmed the diagnosis, and over time the manifestations became even more distinct. Herman et al suggested that typical craniofacial CCD traits, including wide unmineralized areas in the calvarial midline and missing nasal bones, are easily recognizable using 3D ultrasound as early as in week 15.

Treatment is mainly supportive with no treatment of the underlying disorder. Multidisciplinary approach should be planned by paediatrics, orthopedics and genetic counselling team. Dental treatment requires an interdisciplinary approach involving orthodontists, maxillofacial surgeons and prosthodontists. Retained deciduous teeth should be restored if they become carious, since their extraction doesn't necessarily induce eruption of permanent teeth. Multiple surgical exposures of unerupted teeth and orthodontic treatment to establish an intact and aligned dental arch can be done. Prosthodontic rehabilitation with dental implants has been used in some cases. Patients should be monitored for development of distal molars & cysts until late adolescence.

In conclusion, a case of CCD is presented, where the clinical appearance & oral examination of the patient should have immediately made the clinicians aware of the condition before performing radiographic examination.

REFERENCES:
**Figure 1:** 20 year old female with brachycephalic skull and frontal bossing, hypoplastic maxilla

**Figure 2:** Hypermobility of the shoulders

**Figure 3:** Orthopantomograph showing multiple supernumerary teeth, over retained deciduous teeth, multiple unerupted permanent teeth.

**Figure 4:** PA view of the skull showing open coronal and lamboid sutures and defective fusion of parietal bones

**Figure 5:** Chest radiograph showing hypoplastic clavicles