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Case Report

Maxillofacial 3D Imaging in Cleidocranial Dysplasia: A Case Report and Literature Review

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ABSTRACT

Cleidocranial dysplasia (CCD) is an inherited autosomal dominant disorder affecting the skeletal and craniofacial structures, exhibiting distinct maxillofacial abnormalities. A case of CCD in an adolescent girl who presented with significant maxillofacial abnormalities is reported in this study. She had a total of 58 teeth including the retained deciduous, impacted, and unerupted teeth. The role of radiography in the diagnosis and treatment planning of CCD is inevitable. In our case, the application of cone-beam computed tomography aided in effective treatment planning which included surgical and orthodontic interventions for the management of the maxillofacial abnormalities. Gene testing was done for the patient and the diagnosis of CCD was confirmed. A dental surgeon can be the first person to diagnose the disease because of its striking craniofacial features and associated dental problems. Hence, adequate knowledge about the maxillofacial abnormalities of CCD among dental and maxillofacial surgeons is necessary to aid in an early diagnosis and better aesthetic outcome.

Keywords: Cleidocranial dysplasia, Cone-beam computed tomography, Genetic diseases, Impacted tooth

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Introduction

Cleidocranial dysplasia (CCD) is a relatively uncommon skeletal disorder affecting both the general and craniofacial skeleton. This condition follows an autosomal dominant pattern of inheritance, caused due to chromosomal abnormalities in the Runx2 gene (1). Initially, CCD was known to affect bones undergoing intramembranous ossification, but it was later found that bones undergoing endochondral ossification can also be affected (2). The prominent skeletal features of CCD include the partial or complete absence of clavicles, delayed closure of fontanelles, open sutures of the skull, and the presence of multiple wormian bones. Maxillofacial abnormalities include delayed eruption of primary, permanent, retained deciduous, multiple impacted supernumerary teeth and hypoplastic maxilla and paranasal sinuses (3). These anomalies result in severe malocclusion, which affects the normal functioning of the stomatognathic system. Management of maxillofacial abnormalities of CCD is quite challenging because of the alteration in the eruption pattern of teeth and the presence of multiple supernumerary teeth that can be present at various locations of the jaws and can be in close approximation to the vital structures (4).

The role of radiographic investigations in the diagnosis and management of CCD is inevitable. The advent of cone-beam computed tomography (CBCT) has made it easy to obtain sectional images of the maxillofacial region, promoting efficient diagnosis and treatment planning. In this article, we report a case of a teenage girl referred for evaluation of her unerupted teeth who was later diagnosed with CCD.

Case Report

Our case was a 19-year-old female patient referred to the Department of Oral Medicine and Radiology by a general dental practitioner for evaluation of unerupted teeth. The patient's history revealed that she had a delay in the eruption of her primary teeth and has irregularly placed teeth since childhood. The medical history of the patient was non-contributory. Family history revealed that the patient's father also had a history of delayed eruption and irregularly placed teeth. The patient was moderately built with short stature. She was well-oriented and had normal intellect. On extra oral examination, brachycephalic skull, flat face with frontal bossing, hypertelorism, and sunken nasal bridge were noted. The drooping shoulder was prominent and the clavicles were found to be absent on palpation. The patient was able to approximate both shoulders towards the midline of the chest (Figure 1). Intraoral examination revealed a high-arched palate and multiple retained deciduous teeth in the maxillary and mandibular arches with few missing permanent teeth. There were no significant abnormalities in the intraoral soft tissues.

Figure 1. Hypoplastic clavicles resulting in the ability to approximate the shoulders along the midline.

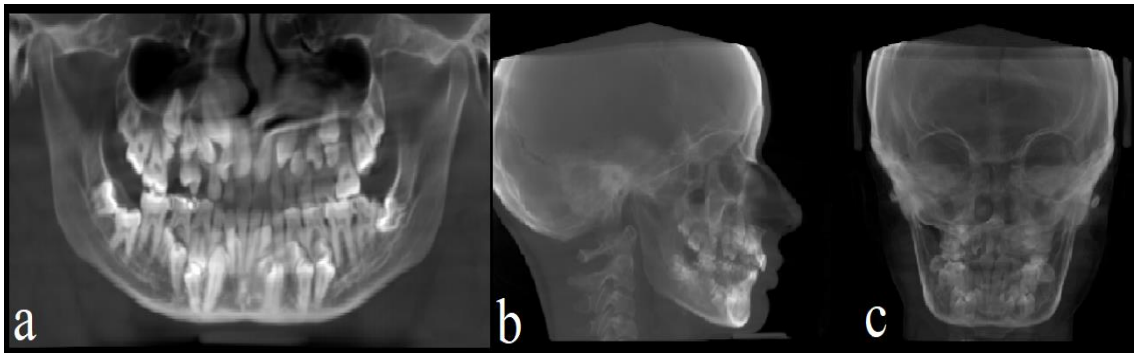

Figure 2. a. Panoramic radiograph showing mixed dentition with multiple impacted permanent and supernumerary teeth. b. Reconstructed lateral cephalogram showing multiple wormian bones. c. Reconstructed postero-anterior cephalogram showing light bulb appearance.

A radiographic assessment was carried out for the patient. Panoramic radiograph revealed multiple retained deciduous teeth (tooth numbers: 51,52,53,61,63,64,72,73,74,75,83,84, and 85) and multiple impacted permanent and supernumerary teeth. Approximately there was a count of 58 teeth, including both erupted and impacted teeth, visible in the radiograph. Hence, cone-beam computed tomography (CBCT) imaging was done for further evaluation. Reconstructed virtual lateral cephalogram obtained from CBCT showed multiple wormian bones and thickened temporal bone. The reconstructed virtual postero-anterior cephalogram showed the light bulb shape of the skull (Figure 2). CBCT imaging aided in the localization of the impacted permanent and supernumerary teeth that were present at different locations in varying depths within the alveolar bone. Thickened calvaria, hypoplasia of right and left zygomatic arches, and absence of sphenoid and frontal sinuses were also evident (Figure 3). Although there were other differential diagnoses (Table 1), with the correlation of the clinical and radiographic findings, finally the patient was diagnosed with cleidocranial dysplasia. The patient was referred to a tertiary care center for gene testing, which confirmed the diagnosis of cleidocranial dysplasia.

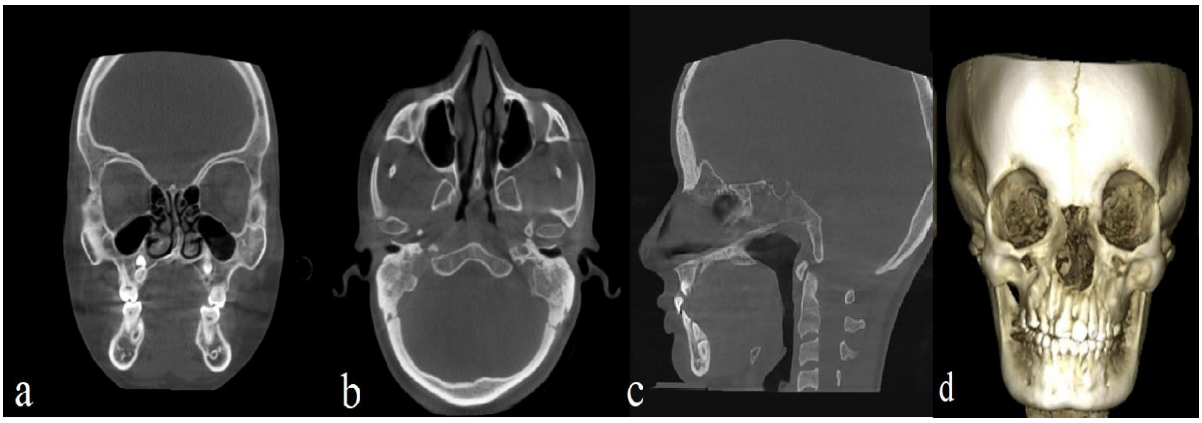

Figure 3. a. Coronal section showing hypoplastic maxillary sinuses with midface hypoplasia. b. Axial section showing thin zygomatic arches with discontinuity in the frontozygomatic region. c. Sagittal section showing absence of sphenoidal and frontal sinuses. d. 3-D skeletal reconstructions demonstrating increased intra-orbital hypertelorism and mid-face hypoplasia.

The clinical and radiological images were documented after obtaining consent from the patient. A comprehensive treatment plan was formulated in consultation with orthodontists and oral surgeons. Extraction of retained primary teeth followed by orthodontically and surgically assisted eruption of permanent teeth with orthodontic correction was planned for the patient.

Table 1. List of differential diagnoses with the differentiating features.

Differential diagnosis	Clinical / Radiographic features	
	Similar features of CCD	**Differentiating features**
Crane-Heise Syndrome	• Brachycephaly • Poorly mineralized calvarium • Palatal Cleft • Low-set and dysplastic ears • Hypoplasia or Aplasia of clavicles • Vertebral anomalies	• Lethal condition • Multiple joint contractures • Absent cervical vertebrae • Anteverted nares
Mandibuloacral dysplasia	• Short stature • Delayed closure of cranial sutures • Hypoplastic Mandible • Dysplastic clavicles • Delayed in the ossification of carpal bones • Micrognathia and Malocclusion	• Acro-osteo-dysplasia of fingers and toes • Hyperpigmentation • Lipodystrophy • Alopecia • Progressive stiffness of joints
Pyknodysostosis	• Short stature • Acro osteolysis and short terminal phalanges • Delay in the closure of cranial sutures and persistence of open fontanelles • Clavicular dysplasia • Delay in the eruption of permanent teeth	• Increased bone radiodensity along with bone fragility. • Absence of supernumerary teeth
Yunis Varon Syndrome	• Pre and Post-natal growth deficiency • Wide-open fontanelles & sutures • Agenesis or Hypoplastic clavicles • Hypoplastic or absent thumbs & great toes • Pelvic bone dysplasia	• Absence/hypoplasia of thumb, halluces, and distal phalanges • Hypoplasia of proximal phalanx and agenesis of distal phalanx of toe • Structural brain abnormalities
CDAGS Syndrome	• Delayed closure of fontanelles and cranial defects • Clavicular hypoplasia	• Craniosynostosis • Anal anomalies • Porokeratosis
Crane-Heise Syndrome	• Brachycephaly • Poorly mineralized calvarium • Palatal Cleft • Low-set and dysplastic ears • Hypoplasia or Aplasia of clavicles • Vertebral anomalies	• Lethal condition • Multiple joint contractures • Absent cervical vertebrae • Anteverted nares

Discussion

Cleidocranial dysplasia is a rare autosomal dominant inherited disorder with an estimated incidence rate of one per million. Meckel was the first to report CCD. Though the exact etiology of the disorder is unknown, mutation in the runt-related transcription factor 2 (RUNX2) present on the 6p21 chromosome is known to be the responsible factor. The genetic mutation affects the core-binding factor subunit alpha-1 (CBFA1) or RUNX2, which is a major regulator of osteoblastic differentiation and dental epithelial cells (5). Hence, it affects skeletal growth and maturation.

According to the literature, about 70% of individuals affected with CCD are known to have point mutation, and 13 % have a deletion involving Runx2 (3). Both dominant and recessive forms of the disease are known to exist. Romeo *et al.* reported an autosomal recessive form of CCD in children born to unaffected parents (6). There is no specific gender predilection for CCD; both genders are equally affected (7). The cranial and clavicular defects are the most prominent features of CCD. The clinical features of CCD vary based on the extent of skeletal involvement ranging from mild dental abnormalities to extreme skeletal deformities (7-9). The patients affected will have short stature. The common craniofacial features of CCD are brachycephalic skull with frontal and parietal bossing, open/delayed closure of fontanelles, presence of multiple wormian bones, mid-face hypoplasia, and hypertelorism with a depressed nasal bridge (9). All these findings were present in our case, except for open fontanelles. The

clavicles are one of the bones known to ossify in the early stages, so defective ossification of clavicles may exhibit as aplastic or hypoplastic clavicles; therefore, the patient has the ability to approximate the shoulders towards the midline. Among CCD cases, 10% of affected individuals exhibit a complete absence of the clavicles (4). Other skeletal deformities include cervical or thoracic vertebral defects, kyphosis, scoliosis, supernumerary ribs, pelvic bony anomalies, hypoplasia or aplasia of fibula, radius, and phalanges (10).

McNamara *et al.* reported that dental anomalies were more prominent in about 93.5% of CCD cases based on their analysis of multiple radiographs (11). The outstanding dental abnormalities include failure or delay in the eruption of the secondary teeth and multiple impacted supernumerary teeth that are commonly seen in the premolar region (4, 10). Lotlikar PP *et al.* described a case of severe CCD with a total of 58 teeth (12). In our case, there were similar findings of multiple retained primary and impacted permanent teeth with supernumerary teeth, making a total count of 58 teeth. Lack of cellular cementum, deficiency in the expression of cytokines, inadequate inflammatory response, and increased altered bone density, along with the underlying bone defects, are the factors that can be attributed to the delayed tooth eruption in the affected individuals (13). According to Kreiborg *et al.*, reactivation of the remnants of the permanent tooth buds' dental lamina results in the formation of supernumerary teeth in CCD patients. The abnormalities in the structure of supernumerary teeth may be due to the space deficiency in the jaws during their development (14). Histological profile of teeth in CCD patients includes distortion in dentinal tubules with marked interglobular dentine and acellular cementum with conspicuous lack of cellular cementum (2, 15).

Underdeveloped paranasal sinuses with the lack of pneumatization of mastoid air cells are common in CCD (12, 16). Similar findings were observed in our case. A study by Kulczyk *et al.* showed that the maxillary sinus volume in children with CCD is smaller compared to that of healthy individuals. They also reported that the volume of the maxillary sinus in a 14-year-old child with CCD is about half of that in a normal healthy child of the same age (16). Similarly, in our case, there was a considerable reduction in the maxillary sinus volume, which was approximately 17 cm^3 on the right and 19 cm^3 on the left maxillary sinus. Hypoplastic zygoma with flat, thin zygomatic arch and discontinuity at the zygomaticotemporal suture, as noticed in our case, are common in CCD (11, 12).

Recurrent sinus and ear infections, which can lead to conductive hearing loss, are among the complications of CCD spectrum disorder. Young patients with open fontanelles are more prone to skull traumatic injuries; therefore, skull protection using helmets is recommended (17). Affected patients have shown to have low vitamin D and serum alkaline phosphatase (ALP) levels. Hence, active monitoring for osteoporosis in the adolescence stage of CCD patients is advised (18).

There are various dental treatment approaches for CCD available in the literature. But the approach given by Becker *et al.* (19) is one of the most successful treatment plans. It states that early removal of primary teeth to aid in the eruption of permanent teeth, application of necessary traction forces at the appropriate time, extraneous force to aid in eruption and promoting vertical alveolar development, and priority in bringing anterior teeth into the correct position should be carried out to promote psychological wellbeing of the patient (9). Orthognathic surgery for the correction of midface hypoplasia and cranioplasty for the repair of metopic depressions is also advocated (20).

Conclusion

Maxillofacial abnormalities in cleidocranial dysplasia may lead to esthetic concerns in the affected individual. Management of cleidocranial dysplasia requires a multidisciplinary approach involving orthodontists, maxillofacial surgeons, and radiologists. The ultimate goal of dental treatment in such patients is to provide a functionally efficient masticatory system with esthetically pleasing dentition that may improve their quality of life.

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