Review

Orthodontic Care of Cleidocranial Dysplasia Patients

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ABSTRACT
Cleidocranial dysplasia (CCD) is a rare congenital deformity inherited as an autosomal genetic trait with the prevalence of 1:1,000,000. It is characterized by dental defomities such as retained primary teeth, presence of supernumerary teeth, skeletal dicrepancy, malocclusion and retarded/absence of eruption of permanent teeth. The orthodontist take part in the team for patients with CCD to resolve the eruption delay of permanent teeth and correct skeletal discrepancies. The aim of this review is to discuss the history, genetic backgrounds, clinical and dental features, different dental treatment approaches and orthodontic management of CCD. (*Turkish J Orthod* 2015;28:31–37)

KEY WORDS: Cleidocranial dysplasia, Orthodontic care

INTRODUCTION

Cleidocranial dysplasia (CCD), also known as Marie-Sainton syndrome, is a rare congenital deformity with a prevalence of 1:1,000,000.[1] The frequency was found equal between genders.[2] Cleidocranial dysplasia is associated with pathologic conditions in anatomic structures such as long bones, clavicles, skull, jaws, and teeth. A worldwide definitive set of accepted treatment protocols for this patient are not known, despite the fact that the discovery of this disorder is not new.

History of CCD

In early history, possible examples of CCD were mentioned or documented. One of the heroes (Thersites) was described with the ability to oppose the shoulders in front of his body by Homer,[3] and a skeleton of a woman living with absent clavicula was remarked as CCD in ancient Greek.[4] Moreover, the skeleton of a woman who died in 1809 showing characteristic features of CCD is displayed in the Museum of Pathological Anatomy (Vienna, Austria).[5]

The first report of clavicular defects was published in 1765 in French literature.[6] Nevertheless, the term *Cleido-cranial dyasostosis* was coined by Marie and Sainton[7] in 1897, and thus the disorder was also titled with the names of the authors. However, 30 years later in 1926, it was Hesse[8] who described the craniofacial and dental deformities in CCD patients.

Genetic Background of CCD

Cleidocranial dysplasia shows an autosomal dominant trait. Occurrence in other family members is important in the diagnosis of CCD. Of course, as will be discussed later, the absence or hypoplasia of the clavicle is the most important feature in patients suffering from CCD. Nevertheless, this abnormality can also be observed in a nonsyndromic entity or other syndromes, such as in Yunis-Varon syndrome, in which both clavicles are absent.[9]

The genetic evaluation of CCD shows the mutation in gene RUNX2 that is essential for proliferation of osteoblast and dental cells. RUNX2, located on the chromosome 6p21, has been proven as the only gene associated with CCD.[10,11] Therefore, RUNX2 molecular genetic testing can be used in the diagnosis of CCD. As mentioned, this gene is

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responsible in the proliferation of precursor cell and membranous bone formation resulting in the deformities associated with CCD. In a study, the absence and mutation of RUNX2 were evaluated in experimental animals, resulting in failure and arrest of bone and tooth development, respectively.[12] Also, numerous different mutations of RUNX2 have been identified. Suda *et al*.[13] demonstrated the occurrence of several supernumerary teeth in cases with RUNX2 mutations.

Clinical General Features of CCD

Cleidocranial dysplasia may be detected at any age, but it is mostly not diagnosed until the patient comes into contact with specialists, generally because of the lack of complications, which is different from other dysplasias. Nevertheless, some patients with CCD have been reported. In some cases, recurrence of upper airway infections may be experienced, because of the maldevelopment of sinuses. Moreover, these patients have potential hearing loss.[14]

Individuals with CCD have no significant physical, physiologic, or social handicap, and most have normal intelligence. As for skeletal features, bony disorders can be categorized as into 2 parts: (1) statural malformations and (2) head and neck malformations.[15] The most prominent characteristic of this deformation is hypermobility of the shoulders caused by hypoplasia or absence of clavicles. Patients may oppose both shoulders in the frontal midline of their body (Fig. 1). Also, abnormalities of the hands and feet are common, such as a long second metacarpal and epiphysis of metacarpals/tarsals. In general, a moderate short stature is evident. Other statural malformations include osseous malformation in the cranial base and skull, pelvis and pubic bone deformity, vertebral defects, and bossing of frontal, parietal, and occipital bones. On the other hand, delayed closure of fontanels is an example pertaining to head and neck malformations in CCD (Fig. 2). The fontanels may remain open throughout life.[2] In individuals with CCD, the upper forehead is depressed in the midline and bulky bilaterally to the midline, because of the patency of the anterior fontanel. The facial structures appear small compared with the large head. The nasal and zygomatic structures are hypoplastic.

Clinical Dental Features of CCD

The dentoalveolar characteristics of patients with CCD are as follows:

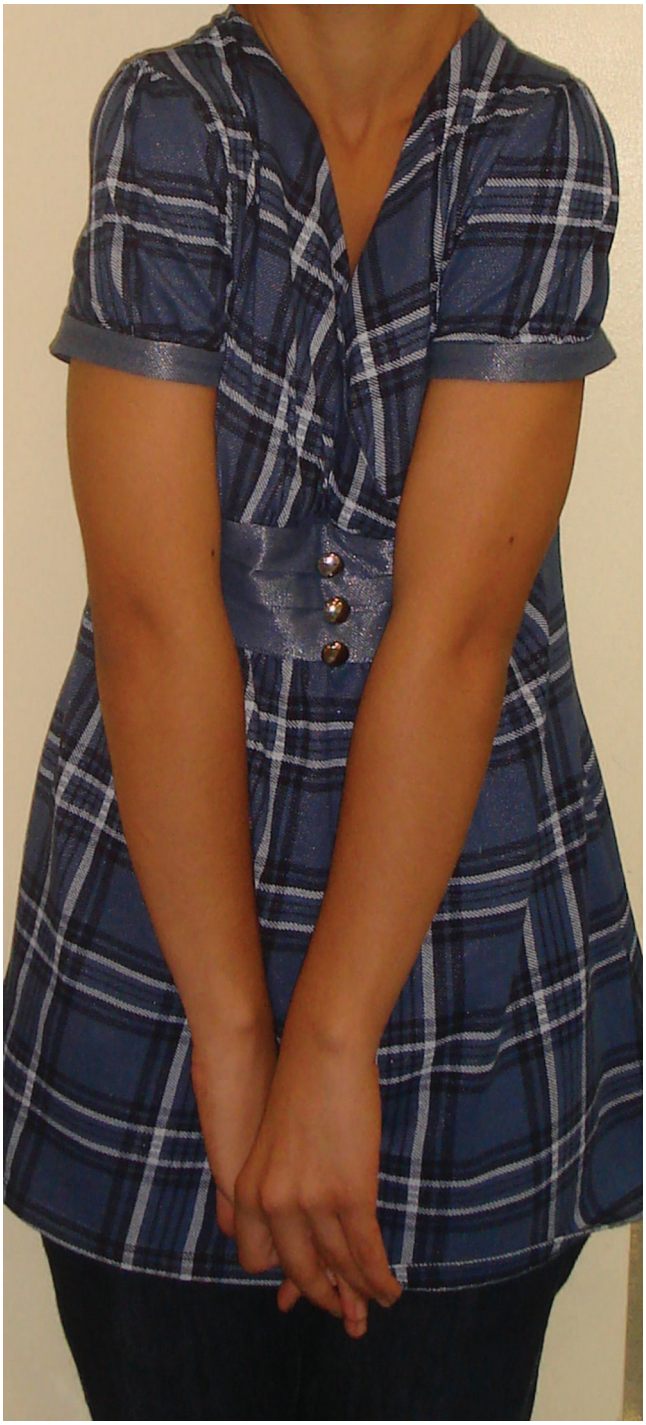

Figure 1. An example patient with cleidocranial dysplasia. A female patient with hypoplasia of bilateral clavicles, who can oppose both shoulders in frontal midline of her body.

1. Overretained primary teeth
2. No resorption of the roots of primary teeth
3. Multiple supernumerary teeth. Indeed, hyperdontia is the most prominent dental characteristic of CCD. Yamamoto *et al*.[16] reported an

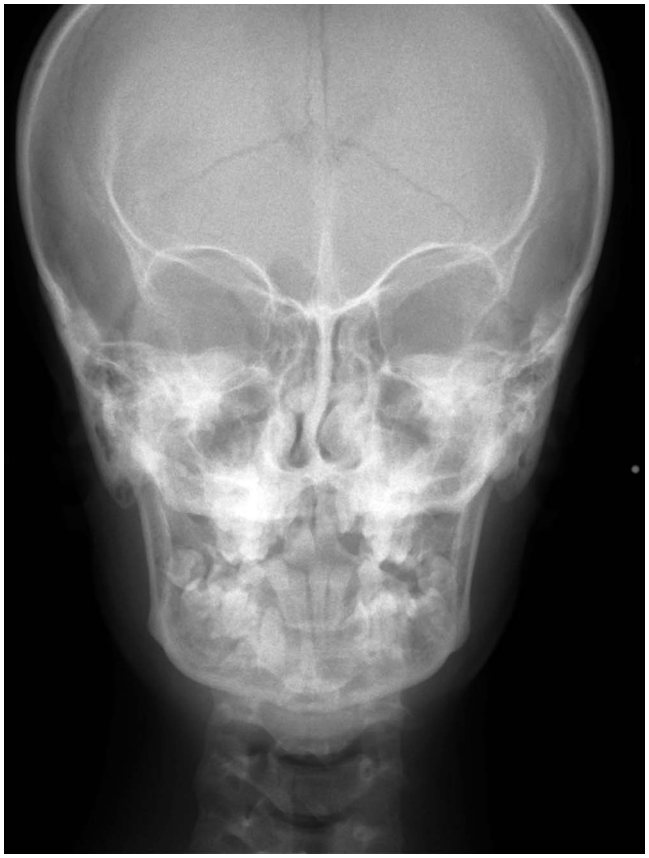

Figure 2. An example patient with cleidocranial dysplasia. The metopic suture is still visible on the posteroanterior radiography.

individual with CCD who had 63 supernumerary teeth present. It was hypothesized that the supernumerary teeth are due to the incomplete or delayed resorption of dental lamina.[17] These teeth may be located uniformly, in a double row, or chaotically in either the maxillary or mandibular dental arch.[18]

4. Retarded eruption and lessened eruption potential of permanent teeth (Fig. 3). Different claims are proposed about this topic. Some researchers have observed in their histological studies that the cementum layer of the unerupted as well as the erupted tooth roots of CCD patients was absent.[19,20] On the contrary, Counts *et al*.[21] compared the cementum of 2 to 10 teeth of individuals with and without CCD, respectively. They suggested that no differences were present between them and concluded that the amount of cementum is not the critical factor in occurrence of multiple unerupted teeth in CCD.
5. Reduced height of the lower third of the face
6. Skeletal Class III tendency

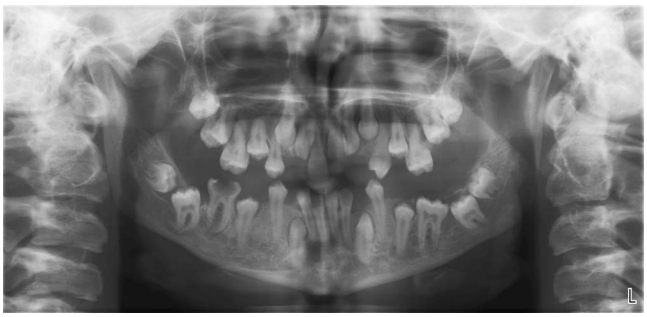

Figure 3. An example patient with cleidocranial dysplasia. Multiple unerupted permanent teeth present on panoramic radiography.

7. Underdeveloped maxilla in all 3 dimensions (Fig. 4)
8. Upward and forward rotated mandible
9. Shallow buccal as well as lingual sulcus of alveolar bones
10. Insufficient vertical development of alveolar bones
11. An approximately 3-year delay of root development of permanent teeth[17,22]
12. Abnormally high palate (Fig. 4)
13. Cleft palate[2]
14. Open bite
15. Dental crowding and malalignment

Dental Treatment

The purpose of dental treatment is to provide a functional masticatory mechanism and an acceptable appearance. To achieve these goals, different approaches have been defined in the literature. However, the main dental treatment steps can be summarized into the following groups[22]:

1. Prosthodontic approach: Removal or extraction of persistent primary, supernumerary, and unerupted permanent teeth and prosthetic replacement
2. Surgical approach: Removal of persistent primary and supernumerary teeth and surgical autotransplantation of unerupted permanent teeth
3. Orthodontic approach: Removal of persistent primary and supernumerary teeth and orthodontic active traction and alignment of unerupted permanent teeth

In addition to this categorization, skeletal treatment can also be formulated as (1) an orthodontic approach (orthopedic treatment and realignment of

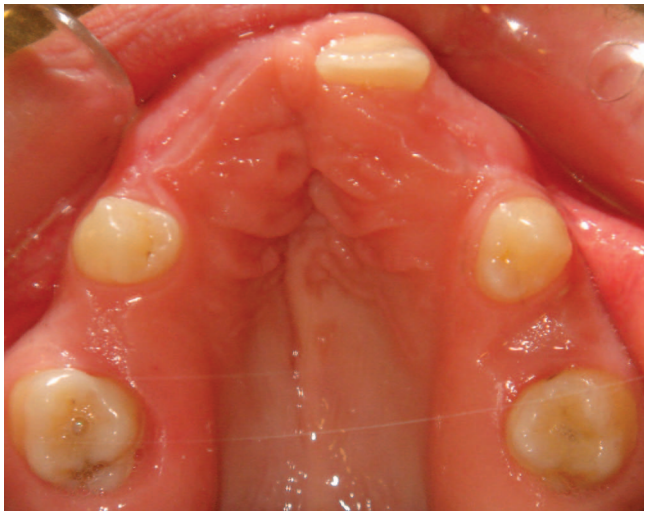

Figure 4. An example patient with cleidocranial dysplasia. A constricted maxilla with abnormal high palate.

jaws) or (2) a surgical approach (orthognathic surgery).

The orthodontic treatment goals in patients with CCD could be summarized as[23]

1. Diagnosis and treatment planning
2. Correction of transversal deficiency in the maxillary arch[24]
3. Monitoring Class III skeletal growth tendency
4. Extraction of persistent primary teeth
5. Surgical removal of supernumerary teeth and cyctic pathologies
6. Anteroposterior space regaining in the alveolar arch
7. Planning of the anchorage units for orthodontic traction
8. Uncover and bond unerupted permanent teeth
9. Guiding the permanent teeth into occlusion
10. Alignment of teeth, finishing and retention

Every patient should be considered unique, and according to the requirements as well as the age of the patients, several of the above-mentioned treatment steps might be skipped or added.

If the orthodontic approach is planned, other subgroup approaches are present according to the timing of removal of primary teeth and active eruption of unerupted teeth[18]:

1. The Toronto- Melbourne approach: A series of surgical procedures are performed at different intervals. At age 5 to 6 years, deciduous anterior teeth and at age 9 to 10 years, deciduous posterior teeth are removed. Also, at each intervention, the supernumerary teeth and pathological conditions in the corresponding region are removed. After eruption of permanent first molars, permanent incisors are exposed. At age 9 to 12 years, the premolars are exposed.[25]
2. The Belfast-Hamburg approach: One episode of surgery. All deciduous teeth and supernumerary teeth are removed, and all unerupted permanent teeth are exposed at 1 appointment. The age is not specified.[26]
3. The Jerusalem approach: Two episodes of surgery. During the first stage (at age 10–12 years) and second stage (at 13 years and older), the anterior teeth and posterior teeth are guided into occlusion, respectively.[22,27]
4. The Bronx Approach: Two or at most 3 episodes of surgery. The age is not specified. First, all primary and supernumerary teeth are removed. Afterward, unerupted teeth are exposed and guided orthodontically into occlusion. Finally, orthognathic surgery and placement of dental implants are performed.[28]

Orthodontic Approach in CCD

Dental abnormalities are typical in 93.5% of the cases suffering from CCD.[29] The treatment duration may last longer depending on the number of dental abnormalities present. Rocha *et al*.[30] reported an orthodontic treatment duration of 13 years and argued that this long period is a reasonable time in a CCD patient. Therefore, to provide long-term care for these patients, special attention should be given during the diagnosis, and an interdisciplinary approach should be performed throughout the treatment.

Conventional records such as photographs and cephalometric and panoramic radiographs are taken in patients with CCD. Also, recent advances in imaging technology yielded better outcomes with 3-dimensional records such as cone beam computed tomography. The most recognizable dental feature in patients is the eruption delay and impaction of permanent teeth and the presence of multiple supernumerary teeth. Thus, 3-dimensional evaluation of the dentition will be beneficial, not only to detect the precise location of supernumerary teeth and the contiguity to roots of erupted permanent teeth, unerupted teeth buds, and anatomical structures but also to distinguish between supernumerary and permanent teeth.[31]

Providing space for the unerupted teeth may maximize the potential for eruption and also the root formation.[32] Space in the vertical, sagittal, and transversal dimensions can be obtained by extraction of the supernumerary and primary teeth, as well as anteroposterior and transversal expansion of the alveolar arch.[23,31,33] Farrar and Van Sickels[34] argued that the mechanical interference of supernumerary teeth is the reason for lack of eruption of permanent teeth. On the other hand, Hitchin and Fairley[35] suggested that the failure of resorption of alveolar bone is the reason for unerupted permanent teeth. Therefore, while spontaneous eruption of unerupted teeth after removal of primary teeth and providing space is expected, this is generally not common in CCD patients after root formation is finished.[17] However, in patients of young age, allowing natural eruption after removal of primary and supernumerary teeth is the current protocol.[30]

Regardless of the cause of unerupted teeth, it is necessary to stimulate the eruption process. Consequently, the next treatment step is the orthodontic traction of the unerupted teeth.[27,32,36] A number of erupted teeth is required as anchorage to enable this traction. In many cases, the first molars in each jaw are erupted, and usually either an anchorage appliance containing the molar is fabricated. If these teeth are missing, alternatives to dental anchorage units should be arranged.[27] Becker and Shochat[32] suggested that the palatal arch is a better alternative than erupted teeth for anchorage; hence, the traction period would be too long and the supporting tissues of the teeth could be damaged. If an anchorage appliance is the choice, it has to be rigid to withstand oral functions as well as long spans of archwires.[32]

Nowadays, dental implants,[37] miniscrews,[38,39] and miniplates[40] are preferred as orthodontic anchorage units, which provide skeletal anchorage. Dental implants can be placed in the retromolar or palatal region to tract unerupted teeth in the mandibular and maxillary posterior region, respectively.[37,41] In cases with several impacted permanent teeth in the alveolar bone area, dental implants are indicated instead of screws. The implants are combined with orthodontic appliances such as lingual arches to serve as indirect anchorage units. If only several teeth are unerupted in one-quarter of dental arches and the other teeth are well aligned, screws can also be preferred (Fig. 5). Screws are suitable for direct as well as indirect anchorage. In this method, incisions or mucogingival flap reflection is not necessary, and therefore it is noninvasive and more comfortable for the patient. In addition, Kuroda *et al*.[42] advised the placement of screws in the contralateral jaw and afterward to tract the unerupted teeth using intermaxillary elastics. However, this method requires patient cooperation, and in cases with multiple unerupted teeth, such as CCD cases, usage could be problematic. After traction of the permanent teeth, alignment is performed. If malposition of the jaws are present, orthodontic preparation for orthognatic surgery may also be needed.

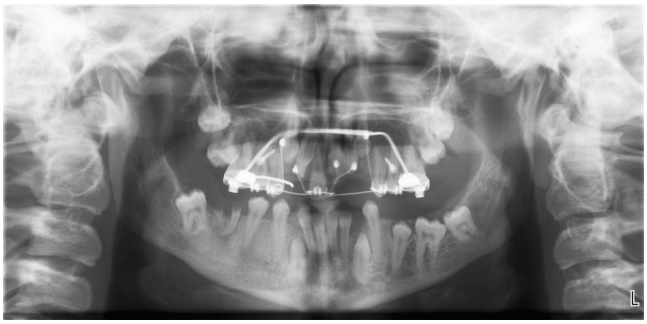

Figure 5. An example patient with cleidocranial dysplasia (CCD). The panoramic radiography of a 16-year-old patient with CCD. The case was prepared for orthodontic traction by placement of orthodontic attachments on each tooth and miniscrews bilaterally.

Surgical and orthodontic treatment of CCD patients is difficult, and unexpected complications in 1 or more treatment steps may occur. Tooth buds may be damaged during tooth exposure while they are in an insufficient developmental state.[43] Furthermore, the operator may be confused when distinguishing supernumerary from unerupted permanent teeth and may remove the permanent teeth.

CONCLUSION

The orthodontic management of patients with CCD is challenging. The duration is long and is frequently not finished until growth is seized. Therefore, a careful and comprehensive treatment plan should be determined and followed by an interdisciplinary team. The operator has to take preferences of the patient into account, since different treatment options exist and thereby differ in cost and treatment duration. Overall, the dialog for motivation and chief complaints with the patient is one of the most important parts in the treatment protocol of patient with CCD.

REFERENCES

1. Park TKN, Vargervik K, Oberoi S. Orthodontic and surgical management of cleidocranial dysplasia. *Korean J Orthod*. 2013;43:248–260.
2. Farronato G, Maspero C, Farronato D, Gioventu S. Orthodontic treatment in a patient with cleidocranial dysostosis. *Angle Orthod*. 2009;79:178–185.
3. Bartsocas CS. Cleidocranial dysostosis in Homer. *Archeia Ellin Pediátr Etair*. 1973;36:107.
4. Bartsocas CS. Cleidocranial dysostosis in Homer. *Archeia Ellin Pediátr Etair*. 1973;36:107.
5. Beighton P, Sujansky E, Patzak B, Portele KA. Genetic skeletal dysplasias in the Museum of Pathological Anatomy, Vienna. *Am J Med Genet*. 1993;47:843–847.
6. Martin S. On natural displacement of the clavicle [in French]. *J Méd Chir Pharmacol*. 1765;23:456–460.
7. Marie P, Sainton P. Observation of hereditary hydrocephalus (father and son) by vice development of the skull and brain [in French]. *Bull Soc Méd Hôp Paris*. 1897;14:706–712.
8. Hesse G. Other findings on dental system individual dysostosis [in German]. *St Z Stomat*. 1926;24:205.
9. Corona-Rivera JR, Romo-Huerta CO, López-Marure E, Ramos FJ, Estrada-Padilla SA, Zepeda-Romero LC. New ocular findings in two sisters with Yunis-Varon syndrome and literature review. *Eur J Med Genet*. 2011;54:76–81.
10. Mundlos S, Mulliken JB, Abramson DL, Warman ML, Knoll JHM, Olsen BR. Genetic mapping of cleidocranial dysplasia and evidence of a microdeletion in one family. *Hum Mol Genet*. 1995;4:71–75.
11. Mundlos S, Otto F, Mundlos C, *et al*. Mutations involving the transcription factor CBFA1 cause cleidocranial dysplasia. *Cell*. 1997;89:773–779.
12. Åberg T, Cavender A, Gaikwad JS, Bronckers AL, Wang X, *et al*. Phenotypic changes in dentition of RUNX2 homozygote-null mutant mice. *J Histochem Cytochem*. 2004;52: 131–139.
13. Suda N, Hattori M, Kosaki K, Banshodani A, Kozai K, Tanimoto K, *et al*. Correlation between genotype and supernumerary tooth formation in cleidocranial dysplasia. *Orthod Craniofac Res*. 2010;13:197–202.
14. Segal N, Puterman M. Cleidocranial dysplasia—review with an emphasis on otological and audiological manifestations. *Int J Pediatr Otorhinolaryngol*. 2007;71:523–526.
15. Chalala C, Noujeim ZEF, Chebel NA, Saade A. Multidisciplinary management of cleidocranial dysplasia. *World J Orthod*. 2014;4:31–39.
16. Yamamoto H, Sakae T, Davies JE. Cleidocranial dysplasia: a light microscope, electron microscope, and crystallographicstudy. *Oral Surg Oral Med Oral Pathol*. 1989;68:195–200.
17. Jensen BL, Kreiborg S. Dental treatment strategies in cleidocranial dysplasia. *Br Dent J*. 1992;172:243–247.
18. Roberts T, Stephen L, Beighton P. Cleidocranial dysplasıa: a review of the dental, historical, and practical implications with an overview of the South African experience. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2013;115:46–55.
19. Rushton MA. An anomaly of cementum in cleidocranial dysostosis. *Br Dent J*. 1956;100:81–83.
20. Smith NH, Sydney NS. A histologic study of cementum in a case of cleidocranial dysostosis. *Oral Surg*. 1968;25:470–478.
21. Counts AL, Rohrer MD, Prasad H, Bolen P. An assessment of root cementum in cleidocranial dysplasia. *Angle Orthod*. 2001;71:293–298.
22. Becker A, Lustmann J, Shteyer A. Cleidocranial dysplasia: part 1—general principles of the orthodontic and surgical treatment modality. *Am J Orthod Dentofac Orthop*. 1997; 111:28–33.
23. Angle AA, Rebellato J. Dental team management for a patient with cleidocranial dysostosis. *Am J Orthod Dentofacial Orthop*. 2005;128:110–117.
24. Kalliala E, Taskinen PJ. Cleidocranial dysotosis: report of 6 typical cases and 1 atypical case. *J Oral Surg*. 1962;15: 808–822.
25. Hall RK, Hyland AL. Combined surgical and orthodontic management of the oral abnormalities in children with cleidocranial dysplasia. *Int J Oral Surg*. 1978;7:267–273.
26. Richardson A, Swinson T. Combined orthodontic and surgical approach to cleido-cranial dysostosis [abstract]. *Trans Eur Orthod Soc*. 1987;63:23.
27. Becker A, Shteyer A, Bimstein E, Lustmann J. Cleidocranial dysplasia: part 2—treatment protocol for the orthodontic and surgical modality. *Am J Orthod Dentofacial Orthop*. 1997; 111:173–183.
28. Berg RW, Kurtz KS, Watanabe I, Lambrakos I. Interim prosthetic phase of multidisciplinary managementof cleidocranial dysplasia: “the Bronx approach.” *J Prosthodont*. 2011; 20:S20–S25.
29. McNamamra CM, O’Riordan BC, Blake M, Sandy JR. Cleidocranial dysplasia: radiological appearances on dental panoramic radiography. *J Dento Maxillo Facial Radiol*. 1999; 28;87–89.
30. Rocha R, Zasso MB, Floriano G, Derech C, Ribeiro GU, Locks A, *et al*. Orthodontic traction in a patient with cleidocranial dysplasia: 3 years of follow up. *Am J Orthod Dentofacial Orthop*. 2014;146:108–118.
31. Liu DG, Zhang WL, Zhang ZY, Wu YT, Ma XC. Three-dimensional evaluations of supernumerary teeth using cone-beam computed tomography for 487 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2007;103:403–411.
32. Becker A, Shochat S. Submergence of a deciduous tooth, its ramifications on the dentition and treatment of the resulting malocclusion. *Am J Orthod*. 1982;81:240–244.
33. Elomaa E, Elomaa M. Orthodontic treatment of a case of Cleidocranial dysostosis. *Suom Hammaslaak Toim*. 1967; 67:139–151.
34. Farrar EL, Van Sickels JE. Early surgical management of cleidocranial dysplasia: a preliminary report. *J Oral Maxillofac Surg*. 1983;41:527–529.
35. Hitchin AD, Fairley JM. Dental management in cleido-cranial dysostosis. *Br J Oral Surg*. 1974;12:46–55.
36. Davies TM, Lewis DH, Gillbe GV. The surgical and

orthodontic management of unerupted teeth in cleidocranial dysostosis. *Br J Orthod*. 1987;14:43–47.

37. Roberts WE, Helm FR, Marshall KJ, Gongloff RK. Rigid endosseous implants for orthodontic and orthopedic anchorage. *Angle Orthod*. 1989;59:247–256.
38. Kuroda S, Katayama A, Takano-Yamamoto T. Severe anterior open-bite case treated using titanium screw anchorage. *Angle Orthod*. 2004;74:558–567.
39. Kuroda S, Sugawara Y, Yamashita K, Mano T, Takano-Yamamoto T. Skeletal Class III oligodontia treated with titanium screw anchorage and orthognathic surgery. *Am J Orthod Dentofacial Orthop*. 2005;127:730–738.
40. Umemori M, Sugawara J, Mitani H, Nagasaka H, Kawamura H. Skeletal anchorage system for open-bite correction. *Am J Orthod Dentofacial Orthop*. 1999;115:166–174.
41. Wehrbein H, Feifel H, Diedrich P. Palatal implant anchorage reinforcement of posterior teeth: a prospective study. *Am J Orthod Dentofacial Orthop*. 1999;116:678–686.
42. Kuroda S, Yanagita T, Kyung HM, Takano-Yamamoto T. Titanium screw anchorage for traction of many impacted teeth in a patient with cleidocranial dysplasia. *Am J Orthod Dentofacial Orthop*. 2007;131:666–669.
43. Ben Bassat Y, Brin I, Fuks A, Zilberman Y. Effect of trauma to the primary incisors on permanent successors in different developmental stages. *Pediatr Dent*. 1985;7:37–40.