G. D'Alessandro, T. Tagariello, G. Piana

Department of Dental Science, Dental School, Bologna University

e-mail: dr.dalessandro@gmail.com

Craniofacial changes and treatment of the stomatognathic system in subjects with Cleidocranial Dysplasia

ABSTRACT

Aim *Cleidocranial dysplasia (CCD) is a rare disorder that is inherited as an autosomal genetic trait. It is characterised by defective ossification, delayed bone and tooth development, stomatognathic and craniofacial abnormalities and it is caused by mutations in the RUNX2 gene that is responsible for osteoblast differentiation. CCD is a dental disease that needs complex rehabilitation and the assistance of several specialists. In most cases, this disease precipitates towards the end of childhood with the progressive morbidity of the deciduous dentition, thus leading to edentulism at a young age and giving patients an older appearance. Several therapeutic approaches have been proposed within literature. The aim of this paper is to revise the literature on the proposed therapeutic approaches for the functional and aesthetical rehabilitation of the typical defects caused by CCD in the cephalic region, and to identify the most effective therapy currently available.* ***Conclusions*** *The most effective therapeutic approach for the early treatment of the orthodontic and orthopaedic diseases in CCD patients would start with an orthopaedic treatment of the upper jaw followed by orthodontic and surgical treatments. When growth is completed a reintervention for maxillofacial surgery and the orthodontic treatment may be required. Finally, if some teeth are missing. function and aesthetics can be achieved replacing them with prosthesis.*

Key words: *Cleidocranial dysplasia; Orofacial features; RUNX2; Supernumerary teeth; Delayed tooth eruption; therapy.*

Introduction

Cleidocranial dysplasia (CCD) is a rare disorder that is inherited as an autosomal genetic trait. It is characterised by defective ossification and delayed bone and tooth development, and it is caused by mutations in the RUNX2 gene, which induces osteoblast differentiation.

The most significant manifestations in the cephalic region are: brachycephaly and flat occiput, prominent forehead, frontal and parietal bossing, persistent wormian cranial bones, small sphenoid; thickened cranial theca, delayed or incomplete development of the paranasal sinuses and mastoid cells, reduced height of the mid-face and small facial bones, of the upper maxillary hypoplasia, Class III malocclusion, ogival/cleft palate, retrognathia and micrognathia, grooved receding chin, broad base of the nose, poorly defined lips and small upper lip, delayed ossification of the mandibular symphysis, large cranial fontanels with delayed closure (sometimes open until adulthood), delayed closure of the sutures (including the metopic suture), and closure of some sutures with interposition of wormian bone (Fig. 1). The most significant dental manifestations are: dental anomalies of number (formation of multiple supernumerary teeth in the permanent dentition), of form (delayed resorption and shedding of primary teeth), of eruption (delayed or absent eruption of permanent teeth combined with ectopic position of both normal and supernumerary permanent teeth), and of structure (enamel hypoplasia, lack of cellular cement) [Jensen and Kreiborg, 1992] (Fig. 2). Therefore, CCD is a dental disease that needs complex rehabilitation and the assistance of several specialists. In most cases, the disease takes shape at the end of childhood with the progressive morbidity of a deciduous dentition, which leads to edentulism at a young age, thus making patients look older. The aim of this paper is to revise the literature on the therapeutic approaches proposed for the functional and aesthetic rehabilitation of the typical defects caused by CCD in the cephalic region.

Several therapeutic approaches have been proposed in the literature.

Surgical removal of overlying bone and extraction of supernumerary and primary teeth

Jensen and Kreiborg [1992] reported that a diagnosis should be made early so that formation of supernumerary teeth can be diagnosed and early intervention undertaken. It should be possible to detect supernumerary incisors at about 5-7 years of age and supernumerary canines and premolars a few years later. When root length of the normal permanent teeth has reached about one third of its final length, the overlying supernumerary teeth should be removed, together with the overlying bone and primary teeth. In regions where no supernumerary teeth are formed, eruption may also be helped by removal of primary teeth and surgical exposure of the underlying permanent teeth. Conventional orthodontic treatment and autotransplantation of teeth may still be necessary in the future but it can be anticipated that the new strategy, with much earlier intervention, will reduce the extent of surgical and orthodontic interventions, which have previously been of extremely long duration, tedious to the patients and often of limited success.

Prosthetic rehabilitation with removable total prosthesis

Several authors proposed the rehabilitation of the stomatognatic system with removable prosthesis [Fardy,

FIG. 1, 2 - *FA 13 years old, female CCD patient.*

FIG. 3 - *Lateral teleradiograph with mineralisation defect and mosaic skull.*

1984; Kelly and Nakamoto, 1974; Magnus and Sands, 1974; Maw, 1978; Weintraub and Yalisove, 1978; Winther and Khan, 1978]. Most reports concern patients in childhood. Some authors achieved rehabilitation by leaving supernumerary unerupted teeth covered by bone; some patients developed complications, such as mucosal ulceration caused by the eruption of embedded teeth, odontogenous cysts and osteomyelitic processes, which required surgery and subsequent readjustments of the prosthesis [Trimble et al., 1982]. According to some reports, edentulous saddles were rehabilitated with overdentures on unerupted teeth which underwent surgery.

Prosthetic rehabilitation with fixed prosthesis

Other authors proposed rehabilitation of edentulous saddles with fixed prosthesis, using spontaneously erupted permanent teeth as pillars. The choice between traditional and adhesive prosthesis (like Maryland-type prosthesis) is based on the number and condition of the pillar teeth [Probster et al., 1991].

Implant prosthodontic rehabilitation

Lombardas and Toothaker [1997] proposed prosthetic rehabilitation with osseointegrated implants, after the surgical extraction of deciduous and unerupted supernumerary teeth at the implant site. This approach involved a double onlay bone graft from the iliac crest. The first bone graft had to be done at the time of extraction of the teeth, while the second had to be done three months later. This study does not report the age of the patient, the assessment of the maxillofacial growth and development, the type and the extent of a possible post-surgery intermaxillary discrepancy nor a long-term prognosis.

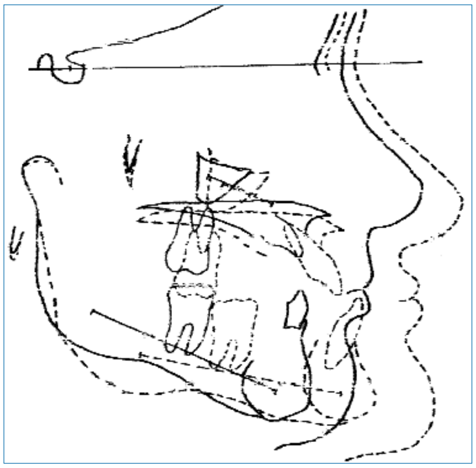

FIG. 4 - *Simulation of splanchnocranial development from childhood to adulthood in a subject with CCD (4).*

Autotransplantation of permanent teeth

Autotransplantation of unerupted permanent teeth, after the surgical extraction of supernumerary teeth, is a frequent approach to rehabilitation [Jensen and Kreiborg, 1992; Becker et al., 1997; Nordenram, 1971]. The preparation of the alveolar cavity is done immediately after the extraction, so that the tooth to transplant is exposed to the extraoral conditions for less than 5 minutes. The re-implant is followed by the application of a 3-week dental splint with braided thread and a 4-week splint with light thread.

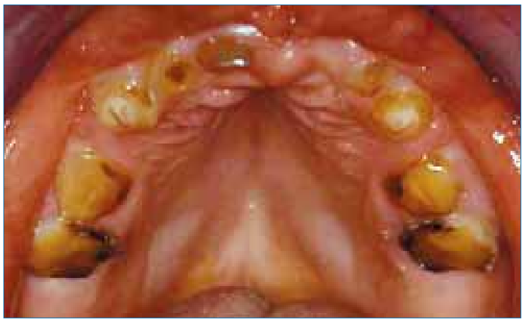

FIG. 5 - *Intraoral picture showing ogival palate and weared and decayed deciduous teeth.*

FIG. 6 - *Orthopantomography showing supernumerary permanent teeth.*

Endodontic treatment begins two months after autotransplantation. The cleaning and the moulding of the endodontic spaces is followed by the application of an intracanal calcium hydroxide dressing and a hermetic coronal filling, and the final filling is applied 4 months later [Hazalonetis and Hazalonetis, 1995]. Some authors highlighted the possibility to maintain pulp vitality in teeth with incomplete apexogenesis [Nordenram, 1971]. Hazalonetis and Hazalonetis [1995] presented a case report with a positive 5-year follow-up: absence of ankylosis and root resorption, normal periodontal tissues (<4 mm probing depth), correct functionality, and satisfying aesthetic result for the patient. These authors consider autotransplantation in patients with CCD as the best choice.

Surgical-orthodontic approach

The surgical-orthodontic approach involves the surgical extraction of deciduous and supernumerary unerupted teeth, the exposure of permanent unerupted teeth, their orthodontically-induced eruption and their subsequent alignment [Angle and Rebellato, 2005; Balaton et al., 2007; Becker et al., 1997a; Becker et al., 1997b; Hemalatha and Balasubramaniam, 2008; Vertrynge et al., 2006], using also a titanium screw anchorage [Kuroda et al., 2007]. In medical literature three different approaches are proposed: Toronto-Melbourne, Belfast-Hamburg, and Jerusalem.

1. Toronto-Melbourne approach. This approach implies two surgeries under general anaesthesia. Such surgeries allow the extraction of deciduous and unerupted supernumerary teeth and the surgical exposure of the teeth to extrude. The first surgery is performed in 5-6 year old children, after the spontaneous eruption of the first molars and their bandage. Permanent incisors are bonded with brackets after healing. Later on, at the age of 9-10, premolars and canines are operated on and bonded with brackets after healing. The authors do not give specific information about the orthodontic techniques that were used for the extrusion of unerupted teeth and for their subsequent alignment [Hall and Hyland, 1978; Smilski et al., 1974].
2. Belfast-Hamburg approach. The main goal of this approach [Richardson and Swinson, 1987] is to perform all surgical therapies in one surgery under general anaesthesia, which involves the extraction of all deciduous and supernumerary unerupted teeth and the exposure of the permanent unerupted teeth to extrude. After surgery, a compression bandage is applied in order to ensure correct healing of tissues by second intention. Such compression bandage is to be changed frequently until healing allows the application of brackets. The authors highlighted that some teeth erupted spontaneously, although not to such an extent that this allowed the avoidance of active extrusion. Completely erupted teeth are bonded with orthodontic devices, whereas unerupted teeth are tractioned with intraoral elastic bands. These authors do not focus their attention on the root formation of exposed permanent teeth and do not give any specific information about the orthodontic techniques that were used.
3. Jerusalem approach. This involves two surgeries under general anaesthesia. Prior to these operations, root development of unerupted teeth has to be assessed and must be at least two-thirds of final length [Becker et al., 1997a]. The first surgery is performed at the chronological age of 10-12, with a dental age of 7-8 years, which assumes the presence of a sufficient number of anchorage teeth in the arch – usually the first permanent molars and, in many cases, one or two permanent incisors. During the operation, deciduous incisors and supernumerary unerupted teeth are extracted, permanent incisors which did not erupt are exposed, attachments are bonded to permanent incisors and first molars, and the surgical flap is closed. In the second operation, at the chronological age of > 13 years, with a dental age of 10-11 years, deciduous canines and molars are extracted, permanent canines and premolars are exposed, attachments are bonded and the surgical flap is closed. Both procedures are performed in both arches at the same time. The extraction of supernumerary unerupted teeth and the exposure of permanent unerupted teeth are performed with a conservative approach in order to maintain the integrity of vestibular and lingual/palatal bone plates: ostectomy is only aimed at the exposure of the coronal area needed for the bonding of attachments. In order to encourage healing by first intention, the flap is repositioned so as to completely cover the wound, without compresses. Surgical procedures are followed by the application of low extrusion forces using a rigid arch, which is meant to oppose the possible distortions caused by the excess of space in the arch. The shape of the arch must allow the application of vertical extrusive forces and it must adapt to the transition from mixed to permanent dentition. The therapeutic goals that the authors found the most difficult to achieve, were the correction of severe tooth rotations and the labiolingual positioning of front teeth. In order to correct them, they resorted to a strong extroversion of superior incisors (with the positioning of the incisal edge below the level of the upper lip) and to the application of a fixed compress from one canine to the other in both arches (with a retainer). Moreover, as the authors consider cephalometric standard parameters inappropriate for the assessment of the labiolingual inclination of the incisors, they suggest that the results are clinically tested and, although they make a cautious prognosis, they underscore that there is no recurrence after orthodontic treatment.

Rehabilitation with multidisciplinary approach

Suba et al. [2005] suggest, after the surgical extraction of deciduous and supernumerary unerupted teeth, the transverse expansion of the superior maxillary bone with a removable orthopaedic appliance, and the traction of the superior maxillary bone with a Delaire mask. For the rehabilitation of the gaps left by the extraction of unerupted teeth, the authors suggest removable prosthesis, prior to rehabilitation with prosthetic implantation in adulthood.

Maxillofacial surgery using Le Fort I approach

Dann et al. [1980] presented the case of a patient with CCD who had skeletal Class III malocclusion due to superior maxillary hypoplasia and was treated with maxillofacial surgery. After a presurgical orthodontic phase, the patient was reassessed with clinical analysis, analysis of the study models on articulators, cephalometric analysis, skeletal and pelvic X-ray, focusing the attention on the study of the middle and inferior third of the face, forehead and nasal complex. Particularly, radiographies of the zygomatic area are taken in order to assess the level of ossification – which affects the type of maxillomandibular stabilisation – and the type of bone and root anatomy, which may imply a deviation from classic osteotomy techniques, especially in cases of roots that penetrate into the zygomatic bone or into the maxillary sinus, that extend into the pyriform fossa or near the infraorbital foramen. The surgical technique they proposed consists of cutting maxillary bone structures according to Le Fort I model, insertion of alloplastic material between osteotomy lines, and covering of osteotomy sites with an onlay of autologous bone marrow taken from the iliac crest, considering that bone grafts in the alar base must not be excessive so as not to emphasize its flaring. Intermaxillary fixation is applied for about 3 weeks. Subsequently, stabilisation is achieved by traction with light elastic bands, which are positioned between upper and lower brackets and kept for about 12 hours a day. The clinical stability of the maxillary bone is achieved around the 15th postoperative week. There is little documented information about long-term stability, even though it was reported that the anterior vertical dimension of the middle third of the face tended to decrease in the first three postoperative months. According to the authors, recurrence in this interval, which can vary in both extent and incidence, is most likely associated with the quality of graft fixation. A 3-year follow-up shows remarkable stability of results [Dann et al., 1980].

Maxillary distraction osteogenesis

Iida et al. [2007] showed a technique of distraction osteogenesis in adult patient with severe midfacial retrusion using the intraoral cylindrical distraction device with a full-covered maxillary splint, which contributes to determining the 3-dimensional direction of maxillary advancement during the operation, and which can be also used as the anchor of the maxillary segment for distraction osteogenesis. This technique requires two phases under general anaesthesia: the first for placing the intraoral distractors and Le Fort I osteotomy, the second to remove the distractors with the maxillary splint.

Rehabilitation with maxillofacial plastic surgery (craniofacial surgery)

Habal et al. [1978] suggest the surgical reshaping of the forehead through a polyurethane-coated Dacron mesh, which is formed preoperatively and modified at the time of surgery. This mesh is reinforced with a bone paste. Twelve months after surgery, in the absence of oedema, possible residual facial defects are estimated.

McGuire et al. [2007] suggest craniofacial surgery, with the reduction of frontal eminences and the filling of metopic suture defects with autologous bone tissue grafts consisting of fibrin glue and monocortical fixation using a titanium mesh secured by screws.

Discussion

The analysis of the literature highlights that therapeutic choices for the treatment of typical orofacial defects of CCD are differents. The proposed strategy to remove supernumerary teeth, overlying bone and primary teeth [Jensen and Kreiborg, 1992] confiding on a natural eruption of the impacted permanent teeth does not seem to be effectual. The natural eruption in fact lacks or is anyway altered despite the surgical exposure [Becker et al., 1997a; Becker et al., 1997b]. It appears that both removable and fixed prosthetic rehabilitation is inappropriate in childhood [Trimble et al., 1982]. After the extraction of permanent and supernumerary unerupted teeth, removable prosthetic rehabilitation implies an extensive removal of bone tissue, with the worsening of pre-existing alveolar hypoplasia and the compromising of prosthesis retention. Particularly considering the age, long-term prognosis is not satisfying, as this kind of rehabilitation does not allow harmonious growth of bone bases. If it were used, it would be advisable to insert a three-way screw in the upper prosthetic structure and a two-way screw in the lower one, in order to allow and stimulate the growth of bone bases. Rehabilitation with fixed prosthesis is problematic because of the small number of pillars available, considering that the suggested technique is based on the extraction of all permanent and supernumerary unerupted teeth [Probster et al., 1991]. Particularly considering the age, there is a risk that the prosthetic preparation may damage the pulp of permanent teeth. Such risk is worsened by the delayed and decreased ability of odontoblasts to deposit reactive dentine, which characterises CCD [Probster et al., 1991]. Moreover, fixed prosthetic rehabilitation in childhood increases the change in growth potential of mandibular and maxillary bone bases, which characterises CCD. The implantology approach [Lombardas and Toothaker, 1997] is not suitable for children, especially those with CCD, whose osseointegration prognosis is uncertain because of the changes in the ossification process. On the other hand, the analysis of literature supports the technique of autotransplantation of permanent unerupted teeth [Jensen and Kreiborg, 1992; Becker et al., 1997a; Nordenram, 1971], even though there is a risk of ankylosis and/or internal resorption.

The surgical and orthodontic approaches seem to be the most conservative. The Toronto-Melbourne [Hall and Hyland, 1978; Smilski et al., 1974] and Jerusalem [Becker et al., 1997a] approaches involve multiple surgeries under general anaesthesia, whereas the Belfast-Hamburg approach [Richardson and Swinson, 1987] implies only one surgery with the extraction of all deciduous and supernumerary teeth at once, and the exposure of permanent teeth. It is highlighted that the exposure of back canines turns out to be premature, since the apex is not completely formed yet. The Toronto-Melbourne and the Belfast-Hamburg approaches [Richardson and Swinson, 1987] imply positioning brackets after healing, and after the removal of compresses, with a delayed orthodontic therapy. Particularly, in the Belfast-Hamburg approach, surgical sites are kept patent by the application of compresses, which hinder oral hygiene, cause trouble/pain, perception of a bad taste in the mouth and halitosis, and delay active orthodontic extrusion. In the Jerusalem approach [Becker et al., 1997a], brackets are positioned on unerupted elements right after their exposure, before closing the flap, and despite the technical difficulties caused by the presence of saliva and blood, the bonding is almost always successful. The ligature, with a thin thread that runs vertically through the flap, allows the application of effective extrusive orthodontic forces by the end of surgery. It also reduces the accumulation of dental plaque and ensures healing by first intention. In spite of these observations, the Jerusalem technique is now considered the most effective, efficient and reliable in the literature. The possibility of its application, however, must never be considered without the evaluation of individual patients.

The analysis of the relationship between the number of spontaneously erupted teeth and the number of supernumerary teeth has in fact highlighted that patients with little or no supernumerary teeth have higher spontaneous eruption frequency [Jensen and Kreiborg, 1992]. Considering the remarkable clinical variability of CCD, it is fundamental to verify the presence of supernumerary teeth and monitor changes through an orthopantomograph before planning a surgical-orthodontic approach. The maxillofacial surgical approach certainly is a valid therapeutic option and the results reported in literature seem to encourage its application. However, the repositioning of bone bases requires demanding operations, which do not eliminate the need for preparatory orthodontic treatment and post-surgical treatment. In our opinion, this approach must be taken into consideration in non-interceptive cases of CCD, when the treatment plan is developed at the end of physical maturity. Suba et al. [2005] proposed an interesting approach based on the orthopaedic pretreatment of the superior maxillary bone. This treatment could be effective since the CCD is characterised by a residual osteogenic activity and the chondroid cells of these subjects do not show any functional anomalies until the final differentiation stages [Takeda et al., 2001; Pavlin et al., 2001]. Moreover it has been recently reported that some molecules could have an active and complimentary role to that of RUNX2 [Ziros et al., 2008]. However, this study does not report pre-surgical investigations, clinical and radiographic data, times and methods of intervention, and results achieved. More particularly, it involves the application of heavy forces in order to achieve orthopaedic distraction, without considering the different physiology of sutures, typical in CCD.

Conclusion

The most effective therapeutic approach in early treatment of orthodontic and orthopaedic pathologies in CCD patients would provide initially an orthopaedic treatment of the upper jaw followed by orthodontic and surgical treatments according to the Jerusalem approach [Becker et al., 1997b]. When growth is ended a reintervention for maxillo-facial surgery and the orthodontic treatment may be required. Finally, if some teeth are still missing, ti achieve complete function and aesthetics it is possible to replace them with prosthesis. However, there is a need for valid clinical studies in patients with CCD to confirm the effectiveness of orthopaedic pre-treatment for the correction of the upper maxillary bone.

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References

Angle AD, Rebellato J. Dental team management for a patient with cleidocranial dysostosis. Am J Orthod Dentofacial Orthop. 2005;128:110-7.

Balaton G, Tarjàn I, Balaton P, Barabàsi Z, Gyulai Gàl S, Nagy K, Vajò Z. Orthodontic and oral surgery therapy in cleidocranial dysplasia. Fogorv Sz. 2007; 100:17-21.

Becker A, Lustmann J, Shteyer A. Cleidocranial dysplasia: Part 1 - General principles of the orthodontic and surgical treatment modality. Am J Orthod and Dentofac Orthopedics. 1997a;111:28-33.

Becker A, Shteyer A, Bimstein E. Cleidocranial dysplasia: Part 2 - Treatment protocol for the orthodontic and surgical modality. Am J Orthod and Dentofac Orthopedics. 1997b;111:173-83.

Dann JJ, Crump P, Ringerberg QM. Vertical maxillary deficiency with cleidocranial dysplasia. Am J Orthod. 1980;78:564-74.

Fardy MJ. Cleidocranial dysostosis: some problems in the dental management of occlusion. Dent Update. 1984;11:363-8.

Habal MB et al. Repair of major cranio-orbital defects with an elastomer-coated mesh and autogenous bone paste. J Plast Reconstr Surg. 1978;61:394-404.

Halazonetis J, Halazonetis DJ. Autotransplantation in cleidocranial dysplasia: case report with 5-year follow-up. J Oral Maxillofac Surg. 1995;53:1472-5.

Hall RK, Hyland AL. Combined surgical and orthodontic management of the oral abnormalities in children with Cleidocranial dysplasia. Int J Oral Surg 1978;7:267-73.

Hemalatha R, Balasubramaniam MR. Cleidocranial dysplasia: a case report. J Indian Soc Pedod Prevent Dent. 2008;26:40-3.

Iida S, Kogo M, Aikawa T, Masuda T, Yoshimura N, Adachi S. Maxillary distraction osteogenesis using the intraoral distractors and the full-covered tooth-supported maxillary splint. J Oral Maxillofac Surg. 2007;65:813-7.

Jensen BL, Kreiborg S. Dental treatment strategies in cleidocranial dysplasia. Br Dent J. 1992;172:243-247.

Kelly E, Nakamoto RY. Cleidocranial dysostosis - a prosthodontic problem. J Prosthet Dent. 1974;31:518-26.

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 Orth Dentofacial Orthop. 2007;131:666-69.

Lombardas P, Toothaker RW. Bone grafting and osseointegrated implants in the treatment of cleidocranial dysplasia.Compend Contin Educ Dent. 1997;18:509-14.

Magnus WW, Sands NR. Cleidocranial dysostosis - report of a case. Am J Orthod. 1974;65: 638-43.

Maw RB. Cleidocranial dysostosis: report of a case. J Am Dent Assoc. 1978;96:306-9.

McGuire TP, Gomes PP, Lam DK, Sandor GK. Cranioplasty for midline metopic suture defects in adults with cleidocranial dysplasia. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007;103:175-9.

Nordenram A. Autotransplantation of teeth in cleidocranal dysostosis. Odont Revy. 1971;22: 363-370.

Pavlin D, Zadro R, Gluhak-Heinrich J. Temporal pattern of stimulation of osteoblast-associated genes during mechanically-induced osteogenesis in vivo: early responses of osteocalcin and type I collagen. Connect Tissue Res. 2001;42:135-48.

Probster L, Bachmann R, Weber H. Custom-made resin-bonded attachments supporting a removable partial denture using the spark erosion technique: a case report. Quintessence Int. 1991;22:349-54.

Richardson A, Swinson T. Combined orthodontic and surgical approach to Cleidocranial dysostosis. Trans Eur Orthod Soc. 1987;63:23.

Smylski PT, Woodside DG, Harnett BE. Surgical and orthodontic treatment of Cleidocranial dysostosis. Int J Surg. 1974;3:380-5.

Suba Z, Balaton G, Gyulai-Gaal S, Balaton P, Barabas J, Tarjan I. Cleidocranial Dysplasia: diagnostic criteria and combined treatment. J Craniofac Surg. 2005;6:1122-6.

Takeda S, Bonnamy JP, Owen MJ, Ducy P, Karsenty G. Continuous expression of Cbfa1 in nonhypertrophic chondrocytes uncovers its ability to induce hypertrophic chondrocyte differentiation and partially rescues Cbfa1-deficient mice. Genes Dev. 2001;15:467-81.

Trimble LD, West RA, McNeill RW. Cleidocranial dysplasia: comprehensive treatment of the dentofacial abnormalities. JADA. 1982;105:661-6.

Verstrynge A, Carels C, Verdonck A, Mollemans W, Willems G, Schoenaers J. Dentomaxillary and -facial problems in cleidocranial dysplasia. Ned Tijdschr Tandheelkd. 2006;113:69-74.

Weintraub GS, Yalisove IL. Prosthodontic therapy for cleidocranal dysostosis: report of case. J Am Dent Assoc. 1978;96:301-305.

Winther JE, Khan MW. Cleidocranial dysostosis: report of 4 cases. Dent Pract. 1972;22:215-9.

Ziros PG, Basdra EK, Papavassiliou AG. Runx2: of bone and stretch. Int J Biochem Cell Biol. 2008;40:1659-63.