

Cleidocranial dysplasia: importance of radiographic images in diagnosis of the condition

Jefferson L. O. Tanaka, Evelise Ono, Edmundo Médici Filho, Julio C. M. Castilho,
Luiz C. Moraes and Mari E. L. Moraes

Department of Oral Diagnosis and Oral Surgery,
Dentistry School of Sao Jose dos Campos, Sao Paulo State University,
São José dos Campos, Brazil

(Received 9 September 2005 and accepted 27 June 2006)

Abstract: Cleidocranial dysplasia (CCD) is a rare syndrome usually caused by an autosomal dominant gene, although 40% of cases of CCD appear spontaneously with no apparent genetic cause. This condition is characterized by several cranial malformations and underdevelopment, absence of the clavicles, and multiple supernumerary and impacted permanent teeth. The diagnosis of this condition is usually based on the presence of the main features (supernumerary teeth, partial or total absence of one or both the clavicles, and bony malformations) and on clinical and familial evidence. The bony and dental features of CCD may be visualized on radiographic images of the face and skull. Here, we present a familial case of CCD and discuss the importance of dental radiographs in diagnosis of the condition. (*J. Oral Sci.* 48, 161-166, 2006)

Keywords: cleidocranial dysplasia; radiography; panoramic; diagnosis.

Introduction

Cleidocranial dysplasia (CCD) is a well-known, rare syndrome usually caused by an autosomal dominant gene (1-3) with high penetrance and variable degree of

expression. This condition is usually caused by a mutation of the Core Binding Factor- $\alpha 1$ gene (4), located at chromosome 6p21 (1). This gene encodes a protein necessary for the correct functioning of osteoblast cells (4). However, 40% of cases of CCD appear spontaneously with no apparent genetic cause (2,3,5). The main features of CCD are partial or complete absence of the clavicles, multiple supernumerary teeth, multiple impacted permanent teeth, retention of the deciduous teeth, and delayed closure of the sagittal fontanelles (1,2,5). Progressive reduction of upper facial height is often observed in older patients, but is rare in younger patients. Reduced sutural maxillary growth can also occur (2,6). Other features include a bell-shaped thorax, enlargement of the frontal and occipital bones, hypoplasia of the pelvis and distal phalanges, and short stature (1,2,5). Less common findings of CCD patients include shortened or absent nasal bones, reduced or absent paranasal sinuses (1,2,5,7), thickening of some segments of the calvaria, underdevelopment of the maxilla, and delayed union of the mandibular symphysis (1). Some reported CCD patients have exhibited hypoplasia of the masseter muscles, which may be caused by discontinuity of the zygomatic arch. As expected, this hypoplasia of the masseter muscles leads to hyperfunction of the temporal muscles. Consequently, in such CCD patients, the anterior border of the mandibular ramus is usually parallel to the posterior border, and the coronoid process is directed upwards and backwards (8).

Many CCD patients have the following triad of lesions: multiple supernumerary teeth; partial or complete absence of the clavicles; and open sagittal sutures and fontanelles. This triad is considered to be pathognomonic for diagnosis of CCD (1). If the triad is not complete, it is necessary to

Correspondence to Dr. Jefferson L. O. Tanaka, Faculdade de Odontologia de São José dos Campos - UNESP - Disciplina de Radiologia Odontológica, Av. Engenheiro Francisco José Longo, 777 - Jd. São Dimas, São José dos Campos - SP 12245-000 Brazil
Tel: +55-12-3947-9054
Fax: +55-12-3947-9010
E-mail: jefftanaka@uol.com.br

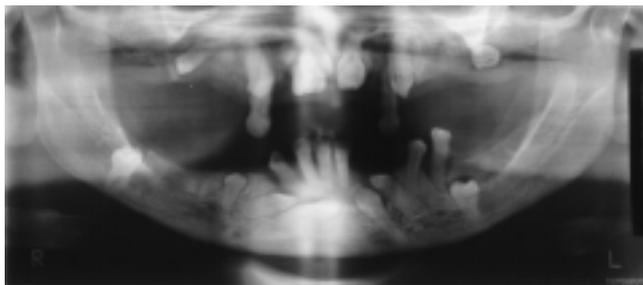


Fig. 1 Panoramic image of the mother, showing the condition of the maxillomandibular complex.

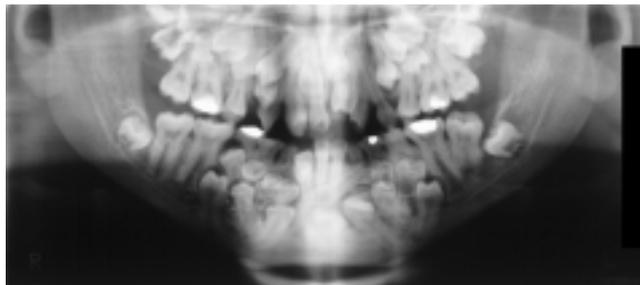


Fig. 2 Panoramic image of the daughter, showing the condition of the maxillomandibular complex.

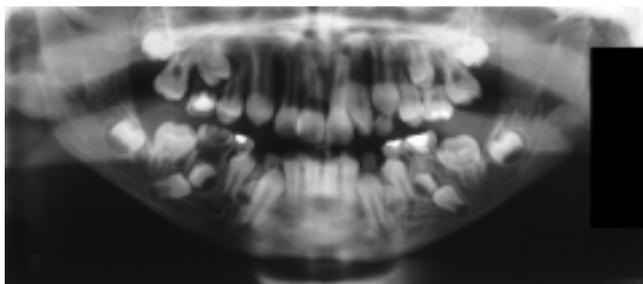


Fig. 3 Panoramic image of the younger son, showing the condition of his maxillomandibular complex.

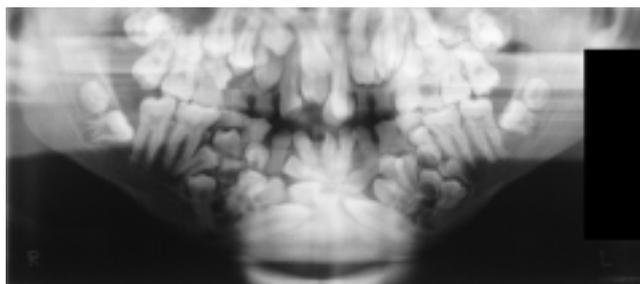


Fig. 4 Panoramic image of the older son, showing the condition of his maxillomandibular complex.

consider the possibility of other entities in a differential diagnosis. Congenital pseudoarthrosis is characterized by the absence of one of the clavicles (usually the right clavicle). Features that suggest pyknodysostosis include malformed bones, osteosclerosis, delayed suture closures, dysplasia of distal phalanges, anodontias, and delayed eruption of permanent teeth. Together, the presence of osteosclerosis and the absence of supernumerary teeth are sufficient to distinguish CCD from pyknodysostosis.

Since CCD patients generally have multiple impacted permanent teeth, prolonged retention of primary teeth, and multiple supernumerary teeth, they can develop masticatory problems with ageing. Many approaches have been suggested for treatment of such problems, including the following: removal of the impacted permanent, supernumerary and deciduous teeth, combined with installation of over-dentures (9,10); surgical removal of the deciduous and supernumerary teeth, combined with orthodontic traction of the impacted permanent teeth (9,11); removal of the supernumerary teeth immediately after completion of mineralization of their crowns, combined with removal of the overlying bone of the permanent teeth to facilitate their eruption. Jensen and Kreiborg (9) evaluated different types of treatment. They concluded that the combination of prosthetic and surgical treatment may not be completely successful, because late eruption of some permanent teeth may occur. They found that the prognosis of the surgical/orthodontic approach

depends on the quantity of supernumerary teeth. Thus, 2 critical factors in the success of these treatments are the correct timing of the treatment and the number of supernumerary teeth.

Since the radiographic appearance of CCD is almost sufficient for diagnosis (2,5), the purpose of the present study was to present the radiographic characteristics of 4 cases of CCD in the same family.

Report of the Cases and Discussion

The report of the cases was approved by the ethics committee of the Dentistry School of São José dos Campos - Sao Paulo State University.

Four patients diagnosed with CCD in the same family (the mother, 2 sons and 1 daughter) were referred to the Oral and Maxillofacial Radiology Department of our school for routine radiographs. The ages of these patients were 47 years 7 months, 16 years 3 months, 14 years 1 month and 12 years 5 months, respectively. Because of the familial occurrence, it is reasonable to conclude that there was a genetic cause for CCD in these cases, at least in the siblings.

Supernumerary teeth and impacted permanent teeth are among the most common features of CCD (2,12,13). Extra teeth were observed in all 3 present siblings. Although we could not confirm the exact number of supernumerary teeth of the mother (Fig. 1), because she had already had most of those teeth extracted, we confirmed that she did

have supernumerary teeth, because at least 7 supernumerary teeth were visible on her panoramic image. The daughter (Fig. 2) had 19 supernumerary teeth, the younger son (Fig. 3) had 5, and the older son (Fig. 4) had more than 30 (we could not confirm the exact number because they were so numerous). We noted the great differences in the number of supernumerary teeth among the siblings. It is possible that these differences were caused by differences in the level of expression of the CCD gene.

It is probable that in CCD patients, at the time at which mineralization of the crowns of the permanent teeth is completed, remnants of the dental lamina are activated to form the extra teeth. The presence of multiple supernumerary teeth may be one of the causes of impaction of permanent teeth in CCD (9). In the 3 present siblings, teeth with delayed mineralization blocked the eruption path of more-developed teeth (Figs. 2, 3 and 4). Previous findings suggest that these teeth with delayed mineralization are the supernumerary teeth, and that the blocked teeth are the

permanent teeth. This pattern is found only in patients with CCD.

We could not confirm the number of supernumerary teeth on the mother's panoramic radiograph, because most of them had already been surgically extracted. However, we included the mother in this report to demonstrate the inheritance pattern (2,5,14) and penetration (15) of the CCD gene; i.e. all 3 of her offspring are also affected by CCD.

Another common dental feature of CCD patients is for the extra teeth to be located mainly in the anterior and premolar region (5,16). This pattern was observed in the 3 present siblings (Figs. 2, 3 and 4), although the girl (Fig. 2) and the older boy (Fig. 4) also had extra teeth in the molar region (fourth molars). Reports describing extra molars in CCD patients indicate that the incidence of extra molars is lower than the incidence of extra anterior or premolar teeth (17). It is important to note that most of the extra teeth in the 3 present siblings resembled permanent teeth.

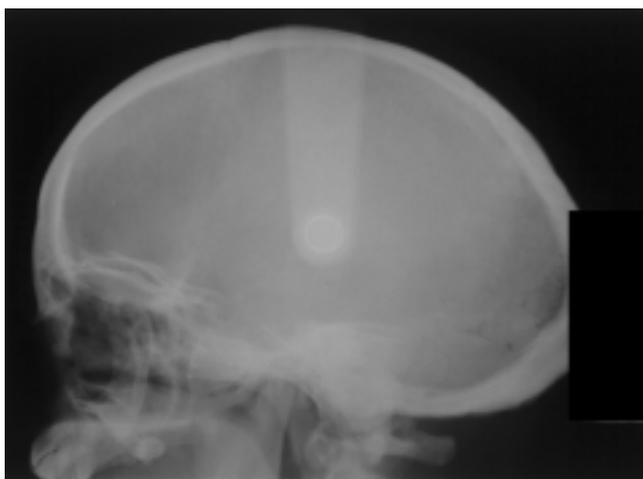


Fig. 5 Calvaria radiograph of the mother.



Fig. 6 Calvaria radiograph of the daughter.

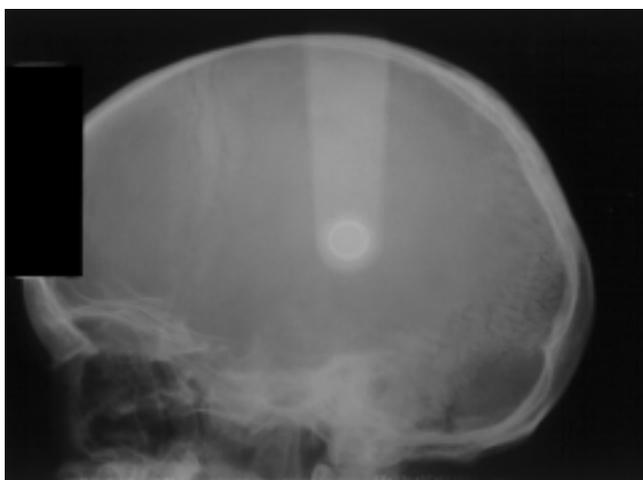


Fig. 7 Calvaria radiograph of the younger son.



Fig. 8 Calvaria radiograph of the older son.

An interesting observation in all 4 present cases was the nearly parallel borders of the ascending ramus of the mandible (Figs. 1, 2, 3 and 4), which has been described in the literature (7,8). Also, the 3 present cases other than the older son exhibited underdevelopment of the maxillary sinuses, the zygomatic bones (consistent with underdevelopment of the zygomatic processes of the maxillary bones) and the nasal bones (Figs. 5, 6, 7 and 8). Those features have been described in the literature (1,7). We could not determine whether the present patients had an upward and posteriorly pointing coronoid process (7,8), because the panoramic film size was 12.5×30 cm. which is not sufficient to register the upper structures of the face.

Lateral cephalometric radiographs of 2 present cases were available (Figs. 9 and 10). A common characteristic of CCD patients is pseudoprognathism, in which the maxilla is underdeveloped in relation to the mandible (2,5,18). Visual inspection of the 2 present lateral cephalometric images indicated that the mandible was indeed anteriorly positioned relative to the maxilla. However, because we did not perform measurements on the present cephalometric radiographs, we could not confirm whether the maxilla was underdeveloped or the mandible was overdeveloped (or both).

The calvaria images of the 3 present siblings showed open sutures of the skull (Figs. 6, 7 and 8). Delayed closure of fontanelles and sutures of the calvaria is another common

feature of CCD (2,5,7,11,16). However, we were unable to check for this feature on the calvaria images. In all 4 present cases, we observed a marked bossing of the occipital bones, and we observed thickening of some segments of the calvaria, which has been reported in the literature (1). The nasal bones were almost absent in all 4 cases.

Partial or total absence of 1 or both clavicles was observed in all 4 present patients (1,2,5). Although use of chest radiographic images is the most reliable method of evaluating clavicular condition, a clinical examination can confirm absence of the clavicle. Most CCD patients are able to bring their shoulders together, which is normally prevented by the presence of the clavicle.

All 4 present patients were able to bring their shoulders near to each other, although they were not able to bring them into contact with each other (Figs. 11, 12, 13 and 14). On clinical palpation, it was possible to feel the absence of the clavicle in all 4 patients. However, only a postero-anterior projection of the thorax would confirm the partial or total absence of the clavicle.

An interesting fact is that most of the features described in the present paper involve the craniomaxillo-mandibular complex. Therefore, it is possible to diagnose CCD based on panoramic radiographs, calvaria radiographs, lateral cephalometric radiographs, hypermobility of the shoulders, and family history (2,5).



Fig. 9 Lateral cephalometric radiograph of the mother.



Fig.10 Lateral cephalometric radiograph of the daughter.



Fig. 11 Photograph of the thorax of the mother.

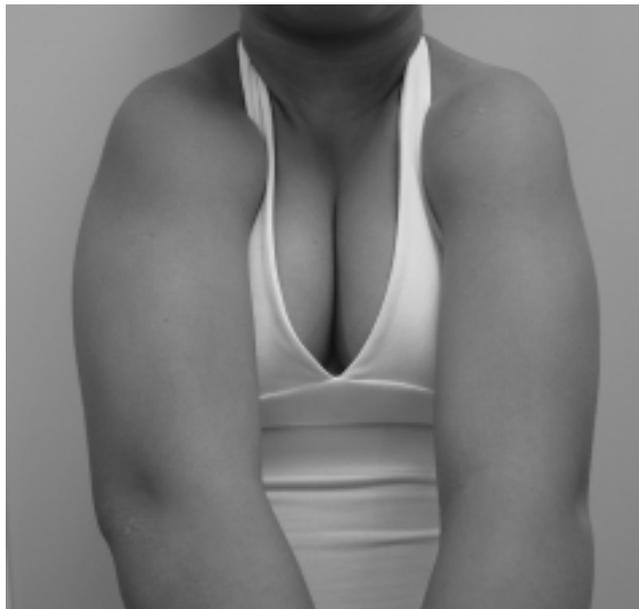


Fig. 12 Photograph of the thorax of the daughter.



Fig. 13 Photograph of the thorax of the younger son.



Fig. 14 Photograph of the thorax of the older son.

Conclusions

Radiographic images of the face and skull are important tools for the diagnosis of CCD. On traditional dental radiographs, it is possible to observe 2 features of the classical triad of CCD: multiple supernumerary teeth; and open sutures and fontanelles of the skull. Other features that can help with diagnosis (parallelism of the mandibular ramus, underdevelopment of the maxillary sinuses, and impacted permanent teeth) can be observed on dental panoramic radiographs. Therefore, dental radiographs play an important role in the diagnosis of CCD.

References

1. Mundlos S (1999) Cleidocranial dysplasia: clinical and molecular genetics. *J Med Genet* 36, 177-182
2. White SC, Pharaoh MJ (2000) *Oral radiology: principles and interpretation*. 4th ed, Mosby, St. Louis, 588-591
3. Sapp JP, Eversole LR, Wysocki GP (1997) *Contemporary oral and maxillofacial pathology*. Mosby, St. Louis, 30-31
4. Zhou G, Chen Y, Zhou L, Thirunavukkarasu K, Hecht J, Chitayat D, Gelb BD, Pirinen S, Berry

- SA, Greenberg CR, Karsenty G, Lee B (1999) CBFA1 mutation analysis and functional correlation with phenotypic variability in cleidocranial dysplasia. *Hum Mol Genet* 8, 2311-2316
5. Neville BW (1995) *Oral & maxillofacial pathology*. WB Saunders, Philadelphia, 445-446
 6. Ishii K, Nielsen IL, Vargervik K (1998) Characteristics of jaw growth in cleidocranial dysplasia. *Cleft Palate Craniofac J* 35, 161-166
 7. McNamara CM, O'Riordan BC, Blake M, Sandy JR (1999) Cleidocranial dysplasia: radiological appearances on dental panoramic radiography. *Dentomaxillofac Radiol* 28, 89-97
 8. Furuuchi T, Kochi S, Sasano T, Iikubo M, Komai S, Igari K (2005) Morphologic characteristics of masseter muscle in cleidocranial dysplasia: a report of 3 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 99, 185-190
 9. Jensen BL, Kreiborg S (1992) Dental treatment strategies in cleidocranial dysplasia. *Br Dent J* 172, 243-247
 10. Tasar F, Bulut E, Tumer C, Saysel M, Muhtarogullari M (1995) Cleidocranial dysplasia. Case report. *Aust Dent J* 40, 352-356
 11. Davies TM, Lewis DH, Gillbe GV (1987) The surgical and orthodontic management of unerupted teeth in cleidocranial dysostosis 14, 43-47
 12. Becker A, Lustmann J, Shteyer A (1997) Cleidocranial dysplasia: Part I - General principles of the orthodontic and surgical treatment modality. *Am J Orthod Dentofacial Orthop* 111, 28-33
 13. Gorlin RJ, Coldman HM (1970) *Thoma's oral pathology*. Vol 1. 6th ed, Mosby, St. Louis, 534-536
 14. Kalliala E, Taskinen PJ (1962) Cleidocranial dysostosis. Report of six typical cases and one atypical case. *Oral Surg Oral Med Oral Pathol* 15, 808-822
 15. Stiff RH, Lally ET (1969) Cleidocranial dysostosis. Report of a case. *Oral Surg Oral Med Oral Pathol* 27, 202-207
 16. Atasu M, Dumlu A, Ozbayrak S (1996) Multiple supernumerary teeth in association with cleidocranial dysplasia. *J Clin Pediatr Dent* 21, 85-91
 17. Jensen BL, Kreiborg S (1990) Development of the dentition in cleidocranial dysplasia. *J Oral Pathol Med* 19, 89-93
 18. Järvinen S (1981) Cephalometric findings in three cases of cleidocranial dysostosis 79, 184-191