

SYSTEMATIC REVIEW

Dentomaxillofacial variability of cleidocranial dysplasia: clinicoradiological presentation and systematic review

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Objectives: The aim of this study was to determine the clinical and radiological presentation of cleidocranial dysplasia (CCD) in our patient group and to compare them with other reported cases by a systematic review (SR) of the literature.

Methods: The study comprises two elements, a complete series of all diagnosed patients at the Center for Craniofacial Genetics at the University of Regensburg, Germany, and a SR. Relevant literature was identified by electronic databases, review of citation lists and hand searching of key journals. The principal selection criterion was that the study should contain as many pertinent cases as possible. The presented signs and symptoms were assigned to the following categories: “supernumerary teeth”, “failure of eruption”, “hypoplastic maxilla” and “clavicular sign”. Additionally, the family history was taken into account.

Results: From the 410 English, German or French articles, 40 single case presentations and 17 multiple case studies remained that met the selection criteria. This report reviews the data of 283 patients with CCD including our own patient cohort of 24 individuals. Dental signs such as supernumerary teeth and eruption failure were expressed in over 93.5%. Skeletal symptoms such as hypoplastic maxilla and the clavicular sign were exhibited in over 84.3%. The prevalence of spontaneous mutations differs slightly when comparing the single case studies (72.0%) with our patient data (58.3%). The fraction of spontaneous mutations in multiple case studies was 5.0%.

Conclusion: The diagnosis of CCD can be difficult when typical features are not clearly expressed. Since the multiple case studies concentrated on specific clinical aspects, an overall ranking including all associated findings was not possible. Owing to their prevalence, we recommend referencing to the described list of clinical signs as major symptoms for the pathognomy in CCD, since they are infrequent in other conditions and in the general population. To categorize the expression of CCD, more interdisciplinary studies are necessary. Nevertheless, a subjective classification is possible according to the related restrictions in the patients' quality of life.

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Introduction

Cleidocranial dysplasia (CCD) is a rare congenital disorder, primarily affecting bones that undergo intramembranous ossification, *i.e.* generally the calvarian but also clavicular bones (Figure 1). The skull base is dysplastic and reduced in growth. Radiographs of the newborn demonstrate poor or absent ossification of the parietal bones.^{1,2} Owing to reduced growth of bones developing

from the chondrocranium, increased skull width and resulting hypertelorism usually appear with associated biparietal and frontal bone bossing. Together with underdevelopment of the facial bones, which often results in a midface deficiency and narrow paranasal sinuses, the dysostotic growth attributes to many patients an almost familiar resemblance. Chief intraoral expressions include retained deciduous dentition, delayed eruption or retention of the permanent dentition, multiple supernumerary teeth and a high palate.³ The thoracic cage is small and bell shaped with short ribs. The pelvis shows a delayed closure of wide symphysis pubis. The dysplastic pelvis often

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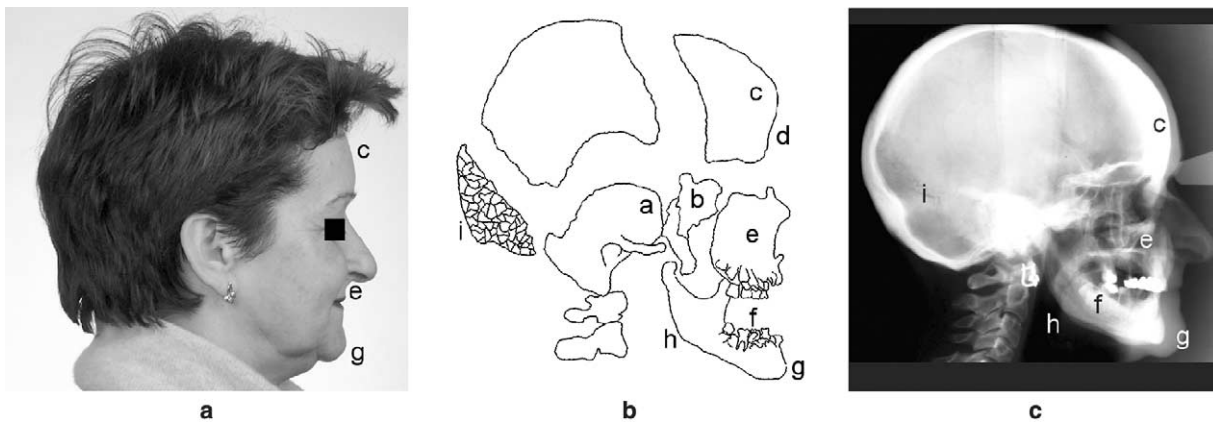


Figure 1 Dentomaxillofacial characteristics of cleidocranial dysplasia, with the first description in the literature: a, deformation of the temporal squama⁷⁶; b, kyphotic spheno-occipital synchondrosis⁷⁶; c, frontal bossing⁷⁵; d, metropic fontanel⁷⁶; e, midface hypoplasia⁷⁵; f, supernumerary teeth⁷⁷; g, prognatic mandible⁷⁵; h, missing gonion angle⁷⁴; i, multiple Wormian bones (Worms, 1643; cited after⁷⁸). (a) Facial morphology in a 50-year-old female; (b) exploded view of the skull; (c) cephalometric radiograph

necessitates Caesarean section of the pregnant female. Hands and feet have pseudoepiphyses at the base of the metacarpal bones and abnormal phalangeal tufts, and often cone-shaped epiphyses of the distal phalanges.

Since its first description in 1898 by Pierre Marie and Paul Sainton,⁴ over 1000 cases have been published in the medical literature. Most of the articles are presentations of single cases, probably owing to the rareness of the disorder (incidence 1:1 000 000). More than 100 other symptoms have been affiliated with CCD, although the association with the syndrome was not always obligatory.⁵ Therefore, papers with a large patient group are rare and tend to focus on certain clinical aspects.⁶

Since early diagnosis of CCD is essential for initiating the appropriate treatment approach, physicians should be aware of the prevalence of the characteristic symptoms. The aim of this study was to compare the symptoms of our large, 24 patient group with reports in the literature by a systematic review (SR). A detailed review regarding the entire clinical picture does not exist, despite the large number of reports. This might explain the absence of a detailed classification of the clinical severity. In this study we concentrated on the prevalence of the most frequently associated symptoms to determine the cardinal symptoms ascribed to CCD.

Patients, material and methods

The study was divided into two elements, a complete series of CCD patients presented at our clinic and a SR.

Systematic review

The overall aim of the SR was to include as many pertinent studies as possible. The principal inclusion criterion was that selected studies should present a complete collection of cases of CCD occurring in the caseload, and not merely a selection of those cases. Case reports and studies that were primarily concerned with specific pathological findings or radiological modalities were not included, as they did not represent the complete collection of CCD

cases. Literature meeting the inclusion criterion was then subjected to more specific exclusion criteria determined prior to the literature search. Criterion A excluded own reports whose data had already been reported and included in the review; Criterion B excluded all reports that contained only genotype descriptions; finally Criterion C excluded those reports written in languages other than English, German or French.

The PubMed interface of Medline (<http://www.ncbi.nlm.nih.gov>) was searched using the following key words: “Cleidocranial dysplasia”, “Dysostose cléido-crânienne”, “Cleidocranial dysostosis” and “Osteodental dysplasia”. This was supplemented by a manual search of journals on medical and dental radiology, maxillofacial surgery, oral pathology and craniofacial development. The strategy was further completed by referring to the bibliographies (or citation lists) of all reports identified by Medline and by hand searching.

The cases presented include literature reference, gender distribution and patients' age at time of presentation. Signs and symptoms were divided into the categories “supernumerary teeth”, “failure of tooth eruption”, “hypoplastic maxilla”, “clavicular sign” and “other skeletal disorders”. Since the literature description was not always complete, we abstained from naming the quantity of supernumerary teeth. The “clavicular sign” was defined by the patient's ability to appose the shoulders in front as a result of hypoplastic or aplastic clavicles (Figure 2). This criterion was included owing to its easy diagnosis and the reliability of the symptom even if not expressed in all patients.⁷ In addition, the family history was also taken into account. The criterion of Wormian bones, small epactal bones in the lambdoid suture, although recurrently expressed in CCD, was not included since this information was often not given.

Local patient cohort

At the Center for Craniofacial Genetics at the University of Regensburg, Germany, we were able to offer a specific molecular genetic analysis of the underlying gene in addition to an interdisciplinary approach. This approach



Figure 2 Abnormal shoulder mobility due to hypoplastic or aplastic clavicles

included maxillofacial, orthodontic as well as medical examination as well as treatment after informed consent. To facilitate a direct comparison of the two study elements described, the diagnostic criteria of our patient cohort was limited to those of the SR. Each patient's family history was recorded before examination. The study was approved by the local ethics committee at the University of Regensburg.

Results

The results of single case and multiple presentations pertaining to the SR process is presented first, followed by the specific details of the local patient cohort.

Systematic review

Through the described search protocol using the PubMed interface to Medline, 410 English, German or French articles were found. Following the three exclusion criteria, 40 single case presentations (Table 1)^{3,8-46} and 17 multiple case studies (Table 2)⁴⁷⁻⁶³ remained.

Single case studies Between the years 1962 and 2002, a total of 25 males and 15 females were examined (Table 1). The mean age was 22.7 years. Supernumerary teeth were

reported in all presented cases. There was an eruption failure of permanent teeth in 97.2% of the patients. The maxilla was hypoplastic in 84.3% and the clavicular sign was expressed in 93.9%. 73.0% of the patients had no knowledge of affected parents. Numerous further findings such as clinodactily or onychodystrophy were described in the patients.

Multiple case reports Additionally, 17 multiple case studies were reported on 219 CCD patients between the years 1960 and 2002 (Table 2). In total, 106 males and 113 females with a mean age of 17.3 years were listed. The fraction of reported patients with supernumerary teeth was 93.5%. An eruption failure of permanent teeth was described in 97.8% of the cohort. A hypoplastic maxilla was found in 94.3%. 98.4% of the described patients expressed the clavicular sign. The fraction of spontaneous mutations was 6.1%.

Local patient cohort

Our patient cohort consisted of 24 individuals (15 males and 9 females). The mean age was 18.9 years (Table 3).^{5,64-69} The symptom of supernumerary teeth was expressed in 95.8%, and all patients exhibited a failure of eruption. A hypoplastic maxilla was present in 90.1%. The clavicular sign was expressed in 90.1%, and 59.0% were spontaneous mutations. One case was misdiagnosed due to his broad thumbs as Rubinstein-Taybi syndrome, which is associated with mental retardation and limited life-span.⁶⁹

Synthesis

Overall, 283 patients were reviewed (146 males and 137 females), with an average age of 18.1 years. 94.9% had supernumerary teeth and 98.7% had an eruption failure. 92.1% had a hypoplastic maxilla and 97.2% demonstrated the clavicular sign.

Discussion

Although there are many case reports available in the literature, scientific interdisciplinary studies of large groups are rare. This report reviews the data of 283 patients with CCD. Comparing the corresponding variables of the SR and our patient cohort, the prevalence of dental signs such as supernumerary teeth and eruption failure was $\geq 93.5\%$. Skeletal symptoms such as hypoplastic maxilla and the clavicular sign were $\geq 84.3\%$. Since only the permanent dentition is affected in CCD, and the midface deficiency can be masked before the pubertal growth spurt, these symptoms should not be used for diagnosis in infancy. The prevalence of spontaneous mutations is slightly different with respect to the comparison between the single case studies (73.0%) and our patients' data (59.0%). The fraction of spontaneous mutations in multiple case studies was 6.1%. Since the multiple case studies contained all affected family members in the corresponding studies, the case amount was raised without elevating the incidence of spontaneous mutations.

Table 1 Analysis of single case presentations accepted for the systematic review^{3,8–46}

Authors (date)	Cases (n)	Sex		Age years	Presenting signs and symptoms					Miscellaneous comments
		M	F		Supernumerary teeth	Eruption failure	Hypoplastic maxilla	Clavicular sign	Spontaneous mutation	
Abbas (1982)	1		1	19	yes	yes	yes	yes	ING	
Ballard (1981)	1		1	52	yes	yes	ING	yes	yes	crippled leg
Behlfelt (1986)	1	1		13	yes	yes	yes	yes	no	
Bishop (1984)	1		1	19	yes	yes	yes	yes	ING	
Butterworth (1999)	1	1		9	yes	yes	yes	yes	yes	
Counts (2001)	1	1		22	yes	yes	yes	no	no	
Dann (1980)	1		1	15	ING	yes	yes	yes	ING	clinodactyly
Davies (1987)	1		1	13	yes	yes	yes	ING	ING	
Forest (1976)	1	1		21	yes	yes	yes	yes	yes	conical fingerform
Foret (1976)	1		1	19	yes	yes	yes	yes	yes	
Frohberg (1995)	1		1	11	yes	yes	yes	yes	yes	
Frayse (1985)	1	1		16	yes	yes	yes	yes	no	intrafamilial variability
Fukuta (2001)	1		1	47	yes	yes	yes	yes	ING	osteoarthritis
Halazonetis (1995)	1	1		24	yes	yes	yes	yes	yes	autotransplantation
Hebda (1983)	1	1		23	yes	yes	yes	yes	yes	
Ilic (1980)	1	1		25	yes	yes	yes	yes	ING	
Jung (1962)	1	1		12	yes	yes	no	yes	ING	open mandibular symphysis
Kargul (1997)	1		1	12	yes	yes	yes	yes	yes	
Kirson (1982)	1	1		27	yes	yes	ING	yes	yes	
Koch (1978)	1	1		67	yes	yes	yes	yes	no	
Kreiborg (1999)	1	1		7	yes	yes	no	ING	no	
Lacroux (1965)	1	1		19	yes	yes	yes	yes	yes	
Maw (1978)	1	1		21	yes	yes	yes	yes	ING	rib deformities
Miest (1976)	1	1		42	yes	yes	yes	ING	ING	
Migliorisi (1980)	1	1		16	yes	yes	yes	yes	ING	onychodystrophy
Miller (1978)	1		1	9	yes	yes	yes	ING	yes	
Nebgen (1991)	1		1	57	ING	yes	yes	yes	ING	
Pospieszynska (1998)	1		1	17	yes	yes	yes	ING	yes	severe temporomandibular joint deformities
Rinderer (1966)	1	1		16	yes	yes	no	no	no	
Romette (1974)	1	1		14	yes	yes	no	yes	ING	
Ross (1998)	1	1		2	yes	ING	no	yes	yes	bilateral clinodactyly
Sakai (2002)	1	1		75	ING	ING	yes	yes	yes	further neurological symptoms
Sato (1998)	1	1		14	yes	yes	yes	ING	ING	
Shen (2000)	1	1		4	ING	ING	yes	yes	ING	
Steinhauser (1990)	1	1		22	yes	yes	yes	yes	ING	
Tan (2000)	1	1		11	yes	yes	yes	yes	no	polydactyly
Tasar (1995)	1		1	29	yes	yes	yes	yes	yes	29 impacted teeth
Tyndall (1983)	1		1	27	yes	no	no	yes	yes	nearly subclinical expression
Weintraub (1978)	1		1	14	yes	yes	yes	yes	yes	
Winkler (1976)	1	1		21	yes	no	yes	ING	yes	
Synthesis	40	25	15	22.7	100%	97.2%	84.3%	93.9%	73.0%	

ING, information not given

Table 2 Analysis of multiple case studies accepted for the systematic review⁴⁷⁻⁶³

Authors (date)	Cases (n)	Sex		Mean age (years)	Presenting signs and symptoms							Miscellaneous comments
		M	F		Eruption failure							
					Supernumerary teeth	Eruption failure	Hypoplastic maxilla	Clavicular sign	Spontaneous mutation			
Agbessi (1967)	5	2	3	14	yes	yes	yes	yes	yes	no		
Alderson (1960)	3	3	48	yes	yes	ING	ING	ING	ING	no		
Buurman (1978)	2	1	15	yes	yes	yes/no	yes	yes	yes	ING/yes		spina bifida
Fardy (1984)	2	2	12	yes	yes	yes	yes	yes	yes	no		
Farrar (1983)	2	1	9	yes	yes	yes	yes	yes	yes	yes		
Fleischer-Peters (1988)	17	8	9	12	yes	yes	yes	yes	ING	ING		physical growth almost unaffected
Harris (1977)	2	2	17	yes/no	yes/no	yes	yes	yes	yes	no		
Hirschfelder (1991)	17	8	9	15	ING	ING	yes	yes	ING	ING		dysplastic zygomatic arches
Ishii (1998)	14	8	6	12	ING	ING	yes	yes	ING	ING		
Jarvinen (1981)	3	1	2	12	yes	yes	yes	yes	ING	no		
Jarvis (1974)	40	18	22	ING	34 yes/1 no	23 yes/10 no	yes	yes	yes	no		
Jensen (1993)	52	25	27	22	ING	ING	yes	yes	ING	ING		
Jensen (1994)	35	15	20	27	ING	ING	yes	yes	ING	ING		
Job (1965)	3	1	2	2	ING	ING	2 yes/1 no	2 yes/1 no	yes	no		cutis laxa
Monasky (1983)	2	1	1	22	no	no	yes	yes	ING	ING		loss of alveolar bone
Richardson (1994)	17	11	6	ING	15 yes/2 no	yes	yes	yes	ING	ING		
Steiniger (1996)	3	2	1	20	yes	yes	yes	yes	yes	ING		
Synthesis	219	106	113	17.3	97.8%	94.3%	98.4%	98.4%	6.1%			

ING, information not given

Ishii *et al*⁵⁵ assessed craniofacial morphology in young and adult individuals with CCD obtained from lateral head films. They demonstrated that young CCD subjects showed relatively normal jaw proportions and morphology of the mandible, while older CCD individuals tended to express the typical signs of CCD. These differences can be attributed to pronounced horizontal mandibular growth resulting from lack of vertical maxillary growth as well as impaired eruption of permanent teeth. These findings are supported by Richardson *et al*⁶¹, who analysed the cephalometric radiographs of 17 patients with CCD and found a mandibular prognathism due to increased mandibular length and a short cranial base. Jensen⁵⁹ described a detailed quantitative analysis of craniofacial morphology in 35 adult patients with CCD, analysing 216 reference points of lateral, frontal and basal projections. They concluded that all craniofacial regions are affected with CCD to a lesser or greater extent, and suggested that the abnormal craniofacial morphology in CCD may be explained by skeletal dysplasia, combined with early cranial deformation and dysplastic and compensatory skeletal growth.

Clinical expression

According to the literature, in addition to the discussed craniofacial findings the following skeletal features are typically associated with CCD: deformities of the thorax and pelvis, scoliosis, kyphosis, missing ribs, clinodactyly and onychodystrophy.⁷⁰ In the extremities coxa vara, coxa valga and notching capital femoral epiphysis are frequently found. Other changes include hypoplasia and anterior rotation of the iliac wings and wide sacroiliac joints. Various findings such as cone-shaped epiphysis or Wormian bones were not considered owing to their subclinical nature.

Frequently, craniofacial as well as skeletal symptoms were reported to be associated with CCD, which later proved to be unrelated or overinterpreted. Yamachika *et al*⁷¹ reported an association of CCD with cleft palate, while according to the patient's history an independent inheritance had to be assumed.⁷² Despite the frequently described reduced body growth in CCD,⁷⁰ a long-term study on patients by Fleischer-Peters and Müßig⁵² showed no correlation between CCD and reduced skeletal growth.

Diagnosis and differential diagnosis

In 1997, the aetiological factor of CCD, the *RUNX2* gene, was mapped on the short arm of chromosome 6.⁷ *RUNX2* is considered a master gene in the formation of bone and dental tissue. To find a general quantitative relationship between the developmental mechanisms and the gene dosage of CBFA1, the genotype has to be correlated with the phenotype. Yoshida *et al*,⁷³ for example, reported on a strong correlation between body height and supernumerary teeth as a function of the involvement of the "runt homology domain", a structural feature of the *RUNX2* protein involved in DNA binding site recognition.

Jensen and Kreiborg⁵⁸ recommended early diagnosis of CCD to initiate the appropriate treatment approach in order

Table 3 Maxillofacial features of cleidocranial dysplasia in the 24 presented cases^{5,64–69}

Case	Sex		Age (years)	Presenting signs and symptoms					Reported
	M	F		Supernumerary teeth	Eruption failure	Hypoplastic maxilla	Clavicular sign	Spontaneous mutation	
1	1		7	yes	yes	yes	yes	yes	
2		1	9	yes	yes	no	yes	yes	
3	1		10	yes	yes	no	yes	no	Golan (2003)
4	1		10	yes	yes	yes	yes	yes	
5	1		11	yes	yes	yes	yes	no	
6	1		12	yes	yes	yes	no	no	Golan (2000)
7	1		14	yes	yes	no	yes	yes	Golan (2002)
8	1		14	yes	yes	yes	yes	no	Hrala (2003)
9	1		14	yes	yes	yes	yes	yes	
10		1	14	yes	yes	yes	yes	yes	
11		1	16	yes	yes	yes	yes	yes	
12		1	17	yes	yes	yes	yes	no	Golan (2003)
13		1	19	yes	yes	yes	yes	no	Müßig (1991)
14		1	23	yes	yes	yes	yes	yes	
15	1		23	yes	yes	yes	yes	yes	Fleischer-Peters (1983)
16	1		23	no	yes	no	no	no	
17	1		37	yes	yes	yes	no	yes	Golan (2001)
18	1		44	yes	yes	yes	yes	yes	
19		1	50	yes	yes	yes	yes	yes	
20		1	19	yes	yes	yes	yes	no	
21	1		7	yes	yes	yes	yes	no	
22	1		16	yes	yes	yes	yes	yes	
23		1	38	yes	yes	yes	yes	yes	
24	1		6	yes	yes	yes	yes	no	Golan (2003)
Synthesis	15	9	18.9	100.0%	100.0%	90.1%	90.1%	59.0%	

to minimize the extent of later surgical and orthodontic intervention. Since the striking dental signs such as supernumerary teeth or eruption failure are correlated with the second dentition, and a hypoplastic midface usually only becomes apparent after the pubertal growth spurt of the mandible, CCD patients are often not recognized in younger years. With identification of the responsible gene, molecular genetic diagnosis has become possible and should therefore be utilized for diagnosis confirmation.⁷⁴

In conclusion, the diagnosis of CCD can be difficult when typical features are not clearly expressed. Owing to the rareness of the disorder, medical consultation is often associated with the “one-patient-one-doctor” phenomenon, where the clinician has consulted one case with CCD.⁷⁴ This might explain the relatively low number (17) of multiple case studies, with only 7 reporting on more than three affected individuals. Since these studies concentrated on specific clinical aspects, an overall ranking including all associated findings was not possible. Owing to their

prevalence, we recommend referencing to the described list of clinical signs as major symptoms for the pathognomy in CCD, since they are infrequent in other conditions and in the general population. Various attempts have been made to categorize the expression of CCD. As many findings manifest subclinically, their contributions for diagnostic specificity remains indicative. To circumvent this problem, more interdisciplinary case studies are necessary. This will elucidate the contributions of the various clinical and subclinical findings to the whole view of CCD. Nevertheless, a subjective classification is possible according to the related restrictions in the patients’ quality of life.

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References

- Golan I, Baumert U, Müßig D. Cleidocranial dysplasia. In: National Organization for Rare Disorders, (ed). *NORD guide to rare disorders*. Philadelphia, PA: Lippincott Williams and Wilkins, 2003, pp 182–183.
- Kaplan SB, Kemp SS, Oh KS. Radiographic manifestations of congenital anomalies of the skull. *Radiol Clin North Am* 1991; **29**: 195–218.
- Tyndall DA. Cleidocranial dysostosis: a nearly unrecognized case. *Gen Dent* 1983; **31**: 390–393.
- Marie P, Sinton P. Sur la dysostose cleido-crânienne héréditaire. *Rev Neurol* 1898; **6**: 835–838.
- Golan I, Baumert U, Held P, Feuerbach S, Mussig D. Radiological findings and molecular genetic confirmation of cleidocranial dysplasia. *Clin Radiol* 2002; **57**: 525–529.
- Aktas S, Wheeler D, Sussman MD. The ‘chef’s hat’ appearance of the femoral head in cleidocranial dysplasia. *J Bone Joint Surg Br* 2000; **82**: 404–408.

- 7 Mundlos S, Otto F, Mundlos C, Mulliken JB, Aylsworth AS, Albright S, et al. Mutations involving the transcription factor CBFA1 cause cleidocranial dysplasia. *Cell* 1997; **89**: 773–779.
- 8 Abbas KED, Prabhu SR. Cleidocranial dysplasia in a Sudanese female. *J Oral Med* 1982; **37**: 45–48.
- 9 Ballard Jr W. Cleidocranial dysostosis: report of an interesting case. *J Colo Dent Assoc* 1981; **60**: 3–4.
- 10 Behlfelt KM, Gundlach KK. Dysplasia cleidocranialis. Symptome im Kieferbereich und deren Behandlung. *Fortschr Kiefer Gesichtschir* 1986; **31**: 175–178.
- 11 Bishop RG. Dental management of cleido-cranial dysostosis. Case report. *Aust Dent J* 1984; **29**: 1–4.
- 12 Butterworth C. Cleidocranial dysplasia: modern concepts of treatment and a report of an orthodontic resistant case requiring a restorative solution. *Dent Update* 1999; **26**: 458–462.
- 13 Counts AL, Rohrer MD, Prasad H, Bolen P. An assessment of root cementum in cleidocranial dysplasia. *Angle Orthod* 2001; **71**: 293–298.
- 14 Dann III JJ, Crump P, Ringenberg QM. Vertical maxillary deficiency with cleidocranial dysplasia. Diagnostic findings and surgical–orthodontic correction. *Am J Orthod* 1980; **78**: 564–574.
- 15 Davies TM, Lewis DH, Gillbe GV. The surgical and orthodontic management of unerupted teeth in cleidocranial dysostosis. *Br J Orthod* 1987; **14**: 43–47.
- 16 Forest D, Fontaine JN. Dysostose cléido-crânio-dentaire: présentation d'un cas. *J Can Dent Assoc* 1967; **33**: 141–145.
- 17 Foret J. Un cas de dysostose cléido-cranienne. I. Etude clinique. *Acta Stomatol Belg* 1976; **73**: 173–184.
- 18 Frohberg U, Tiner BD. Surgical correction of facial deformities in a patient with cleidocranial dysplasia. *J Craniofac Surg* 1995; **6**: 49–53.
- 19 Fraysse E, Fraysse H, Dubertrand Y, Bonifassi J, Flach F, Damery C, et al. Contribution à l'étude du syndrome de Pierre Marie et Sainton. *Rev Stomatol Chir Maxillofac* 1985; **86**: 103–106.
- 20 Fukuta Y, Totsuka M, Fukuta Y, Takeda Y, Yoshida Y, Niitsu J, et al. Histological and analytical studies of a tooth in a patient with cleidocranial dysostosis. *J Oral Sci* 2001; **43**: 85–89.
- 21 Halazonetis J, Halazonetis DJ. Autotransplantation in cleidocranial dysplasia: case report with 5-year follow-up. *J Oral Maxillofac Surg* 1995; **53**: 1472–1475.
- 22 Hebda TW. Cleidocranial dysplasia: case report. *Mil Med* 1983; **148**: 938–941.
- 23 Ilic D. Cleidocranial dysostosis. *Proc Eur Prosthodontic Assoc* 1980; 101–104.
- 24 Jung C. Befunde im Zahn- und Kiefersystem bei Dysostosis cleidocranialis. *Fortschr Kieferorthop* 1962; **23**: 273–279.
- 25 Kargul B, Salih IM, Yilmaz L, Dumlu A. Cleidocranial dysostosis: report of a case. *J Clin Pediatr Dent* 1997; **22**: 83–86.
- 26 Kirson LE, Scheiber RE, Tomaro AJ. Multiple impacted teeth in cleidocranial dysostosis. *Oral Surg Oral Med Oral Pathol* 1982; **54**: 604.
- 27 Koch PE, Hammer WB. Cleidocranial dysostosis: review of the literature and report of case. *J Oral Surg* 1978; **36**: 39–42.
- 28 Kreiborg S, Jensen BL, Larsen P, Schleidt DT, Darvann T. Anomalies of craniofacial skeleton and teeth in cleidocranial dysplasia. *J Craniofac Genet Dev Biol* 1999; **19**: 75–79.
- 29 Lacroux R, Delahaye RP, Raynaud S, Pellerin C. Dystrophies unguéales et macrochéilite dans la dysostose cléido-crânienne. *Bull Soc Fr Dermatol Syphiligr* 1965; **72**: 366–369.
- 30 Maw RB. Cleidocranial dysostosis: report of case. *J Am Dent Assoc* 1978; **96**: 306–309.
- 31 Miest D, Malevez C, Putz M. La dysostose cléido-cranienne (maladie de Pierre Marie et Sainton). *Acta Stomatol Belg* 1976; **73**: 163–171.
- 32 Migliorisi JA, Blenkinsopp PT. Oral surgical management of cleidocranial dysostosis. *Br J Oral Surg* 1980; **18**: 212–220.
- 33 Miller R, Sakamoto E, Zell A, Arthur A, Stratigos GT. Cleidocranial dysostosis: a multidisciplinary approach to treatment. *J Am Dent Assoc* 1978; **96**: 296–300.
- 34 Nebgen D, Wood RS, Shapiro RD. Management of a mandibular fracture in a patient with cleidocranial dysplasia: report of a case and review of the literature. *J Oral Maxillofac Surg* 1991; **49**: 405–409.
- 35 Pospieszynska MD. Morphological changes of the mandible and temporomandibular joints in a patient with cleidocranial dysostosis. *J Orofac Orthop* 1998; **59**: 246–250.
- 36 Rinderer L. Über ein pelvino-dentales Dysostose-Syndrom cleidocranialis. Ein kasuistischer Beitrag zur sogenannten Dysostosis. *Stoma (Heidelb)* 1966; **19**: 74–82.
- 37 Romette D, Pauchard JM. A propos d'un cas de dysostose cléido-crânienne. Observations sur la statique de la tête. *Orthod Fr* 1974; **45**: 285–293.
- 38 Ross DA. Cleidocranial dysostosis—a case report and review of the literature. *J R Army Med Corps* 1998; **144**: 37–39.
- 39 Sakai N, Hasegawa H, Yamazaki Y, Ui K, Tokunaga K, Hirose R, et al. A case of a Japanese patient with cleidocranial dysplasia possessing a mutation of CBFA1 gene. *J Craniofac Surg* 2002; **13**: 31–34.
- 40 Sato K, Sugawara J, Mitani H, Kawamura H. Use of selectively colored stereolithography for diagnosis of impacted supernumerary teeth for a patient with cleidocranial dysplasia. *Int J Adult Orthodon Orthognath Surg* 1998; **13**: 163–167.
- 41 Shen WC. A case of cleidocranial dysplasia confirmed by 3D CT of the cranium. *Am J Neuroradiol* 2000; **21**: 609.
- 42 Steinhäuser EW, Janson IM. Kieferchirurgische und kieferorthopädische Behandlungsmöglichkeiten bei der Dysostosis cleidocranialis. *Dtsch Zahnärztl Z* 1990; **45**: 192–198.
- 43 Tan S, Papndrikos A, Troutman KC. Dental management of cleidocranial dysostosis: a case report. *Columbia Dental Review* 2000; **5**: 8–10.
- 44 Tasar F, Bulut E, Tümer C, Saysel M, Muhtarogullari M. Cleidocranial dysplasia. Case report. *Aust Dent J* 1995; **40**: 352–356.
- 45 Weintraub GS, Yalisove IL. Prosthodontic therapy for cleidocranial dysostosis: report of case. *J Am Dent Assoc* 1978; **96**: 301–305.
- 46 Winkler S, Drinnan AJ, Puengphob R. Cleidocranial dysostosis. A review and case report. *N Y State Dent J* 1976; **42**: 24–26.
- 47 Agbessi V, Couray J, D'Almeida A, Goudote E. La dysostose cleidocranienne en Afrique. Etude de 5 cas familiaux. *Bull Soc Med Afr Noire Lang Fr* 1967; **12**: 277–286.
- 48 Alderson CGP. Hereditary cleido-cranial dysostosis. *Br Dent J* 1960; 157–159.
- 49 Buurman R, Gundlach K, Schmidt-Hoberg W, Vogel H. Die Dysplasia cleidocranialis—Zwei Einzelbeobachtungen. *ROFO Fortschr Geb Röntgenstr Nuklearmed* 1978; **128**: 60–66.
- 50 Fardy MJ. Cleidocranial dysostosis: some problems in the dental management of occlusion. *Dent Update* 1984; **11**: 363–368.
- 51 Farrar EL, Van Sickels JE. Early surgical management of cleidocranial dysplasia: a preliminary report. *J Oral Maxillofac Surg* 1983; **41**: 527–529.
- 52 Fleischer-Peters A, Müßig D. Langzeitbeobachtungen der Zahn- und Gebißentwicklung bei Patienten mit Dysostosis cleidocranialis. *Fortschr Kieferorthop* 1988; **49**: 535–542.
- 53 Harris RJ, Gaston GW, Avery JE, McCuen JM. Mandibular prognathism and apertognathia associated with cleidocranial dysostosis in a father and son. *Oral Surg Oral Med Oral Pathol* 1977; **44**: 830–836.
- 54 Hirschfelder U, Müßig D, Fleischer-Peters A. Untersuchungen zur Schädelmorphologie bei Dysostosis cleidocranialis. *Dtsch Zahnärztl Z* 1991; **46**: 292–296.
- 55 Ishii K, Nielsen IL, Vargervik K. Characteristics of jaw growth in cleidocranial dysplasia. *Cleft Palate Craniofac J* 1998; **35**: 161–166.
- 56 Jarvinen S. Dental findings in three cases of cleidocranial dysostosis. *Proc Finn Dent Soc* 1980; **76**: 56–61.
- 57 Jarvis JL, Keats TE. Cleidocranial dysostosis. A review of 40 new cases. *Am J Roentgenol Radium Ther Nucl Med* 1974; **121**: 5–16.
- 58 Jensen BL, Kreiborg S. Craniofacial abnormalities in 52 school-age and adult patients with cleidocranial dysplasia. *J Craniofac Genet Dev Biol* 1993; **13**: 98–108.
- 59 Jensen BL. Cleidocranial dysplasia: craniofacial morphology in adult patients. *J Craniofac Genet Dev Biol* 1994; **14**: 163–176.
- 60 Job JC, Nahum M, Faure C, Rossier A. La dysostose cléido-crânienne. Son polymorphisme. *Arch Fr Pediatr* 1965; **22**: 669–686.
- 61 Monasky GE, Winkler S, Icenhower Jr JB, Ruane AS, Fielding AF, Defrancis D. Cleidocranial dysostosis—two case reports. *N Y State Dent J* 1983; **49**: 236–238.

- 62 Richardson A, Deussen FF. Facial and dental anomalies in cleidocranial dysplasia: a study of 17 cases. *Int J Paediatr Dent* 1994; **4**: 225–231.
- 63 Steiniger A, Pierer K, Dannhauer KH. Interdisziplinäres Vorgehen von Patienten mit Dysostosis cleidocranialis. *Kieferorthop* 1996; **10**: 257–264.
- 64 Fleischer-Peters A, Müßig D. Befindlichkeit und Lebensschicksal von Patienten mit Dysostosis cleidocranialis. *Kinderarzt* 1983; **14**: 1059–1067.
- 65 Golan I, Preising M, Wagener H, Baumert U, Niederdellmann H, Lorenz B, et al. A novel missense mutation of the *CBFA1* gene in a family with cleidocranial dysplasia (CCD) and variable expressivity. *J Craniofac Genet Dev Biol* 2000; **20**: 113–120.
- 66 Golan I, Baumert U, Wagener H, Preising M, Lorenz B, Niederdellmann H, et al. Zur Variabilität der *CBFA1/RUNX2*-Gen-Expression bei Dysostosis cleidocranialis — eine Familienuntersuchung. *Fortschr Kieferorthop* 2001; **63**: 190–198.
- 67 Golan I, Baumert U, Pragnier R, Aknin JJ, Rodde J, Müßig D. L'expressivité inter- et intrafamiliale de la dysostose cléido-crânienne. *Orthod Fr* 2003; **74**: 7–13.
- 68 Hrala BP, Golan I, Laban C, Baumert U, Müller N, Müßig D, et al. Chirurgisches Patientenmanagement bei Dysostosis Cleidocranialis. *Dtsch Zahnärztl Z* (in press).
- 69 Müßig D, Hirschfelder U, Spitzer W. Behandlungsmaßnahmen bei Patienten mit Dysostosis cleidocranialis. *Dtsch Zahnärztl Z* 1991; **46**: 308–312.
- 70 Mundlos S. Cleidocranial dysplasia: clinical and molecular genetics. *J Med Genet* 1999; **36**: 177–182.
- 71 Yamachika E, Tsujigiwa H, Ishiwari Y, Mizukawa N, Nagai N, Sugahara T. Identification of a stop codon mutation in the *CBFA1* domain from a patient with cleidocranial dysplasia and cleft lip. *J Oral Pathol Med* 2001; **30**: 381–383.
- 72 Baumert U, Golan I, Mussig D. Common mutations and independent assortment of CCD. *J Oral Pathol Med* 2002; **31**: 567–568.
- 73 Yoshida T, Kanegane H, Osato M, Yanagida M, Miyawaki T, Ito Y, et al. Functional analysis of *RUNX2* mutations in Japanese patients with cleidocranial dysplasia demonstrates novel genotype–phenotype correlations. *Am J Hum Genet* 2002; **71**: 724–738.
- 74 Golan I, Baumert U, Wagener H, Dauwerse J, Preising M, Lorenz B, et al. Atypical expression of cleidocranial dysplasia: clinical and molecular–genetic analysis. *Orthod Craniofac Res* 2002; **5**: 243–249.
- 75 Hultkranz JW. Über Dysostosis cleido-cranialis. *Zeitschrift für Morphologie und Anthropologie* 1908; **11**: 385–528.
- 76 Scheuthauer G. Combination rudimentärer Schlüsselbeine mit Anomalien des Schädels beim erwachsenen Menschen. *Allgemeine Wiener medizinische Zeitung* 1871; **16**: 293–295.
- 77 Marie P, Sainton P. Observation d'hydrocéphalie héréditaire (père et fils) par vice de développement du crâne et du cerveau. *Bull Mem Soc Méd Hôp Paris* 1897; **14**: 706–712.
- 78 Jeanty P, Silva SR, Turner C. Prenatal diagnosis of wormian bones. *J Ultrasound Med* 2000; **19**: 863–869.

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