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RESEARCH ARTICLE

DENTAL FINDINGS AND MANAGEMENT IN COCKAYNE SYNDROME: A CASE AND A REVIEW

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ABSTRACT

Cockayne syndrome is a rare autosomal recessive disease clinically characterized by growth failure, neurological and sensory dysfunction, photosensitivity and visual abnormalities. Dental and cranio-facial abnormalities are common but rarely studied. ***Methods:*** We performed a review of literature about oro-dental findings and dental management in Cockayne syndrome infants. We reported a 7-year-old girl with genetically confirmed Cockayne syndrome. We focused on oro-dental phenotype and management. ***Results:*** Sixteen articles were reviewed. Oro-dental findings reviewed were bad oral hygiene (N=5) (33.33%) , dental caries (N=16) (100%) , enamel hypoplasia (N=6) (37.5%) , white opacities(N=3) (18.75%) , narrow dental arches (N=4) (25%) , teeth malposition(N=4) (25%) ,agenesis (N=5) (31.25%), anomalies of form(N=4) (25%) , hyposialia (N=5) (31.25%), temporo-mandibular joint defect (N=1) (6.25 %) and other non-detailed features(N=4) (25%) . Dental management in CS patients was detailed in (N=7) (43.75%) of retained articles. ***Conclusion:*** Early dental check-up and management of CS is very important as preventive option. More oro-dental signs need to be explored as skeletal diagnosis, temporal-mandibular joints, and salivary and pulp tests.

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INTRODUCTION

Cockayne syndrome (CS) is a rare autosomal recessive disease belonging to the family of premature aging syndromes (1,2). Its worldwide in cidenceis 1 in 250 000 live births (1). It can be caused by mutations of two genes, the ERCC8/CSA (Excision-Repair Cross- Complementing Group 8), and the ERCC6 /CSB (Excision-Repair Cross Complementing, Group 6) ,located on chromosomes 5 and 10q11 respectively (1,2). The aim of the present study is to describe oro-dental findings as long as dental management in CS patients throughout a review of literature and a case report.

We performed a review of literature about oro-dental findings and dental management in CS infants. PubMed, Cochrane library and Google scholar were databases used. The keywords that were used were Cockaynesyndrome, dental management, growth delay and dental caries. Among the sixty three included articles, only sixteen(16) have been retained in our review [Figure 1]. We reported a clinical case of a young girl with a genetically confirmed CSB. We noticed neurological signs,oro-dental ones and detailed dental management.

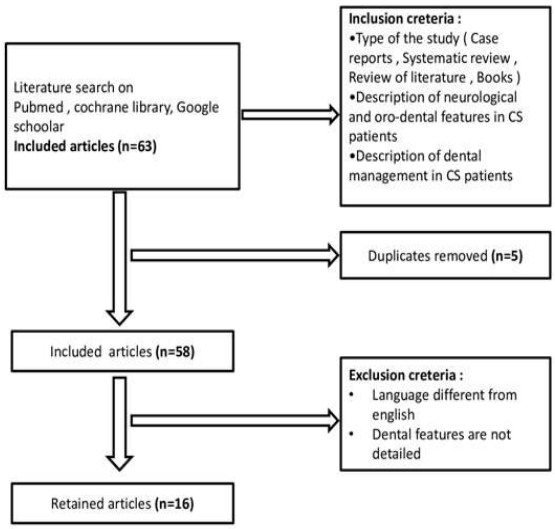

Figure 1. Flowchart of review of literature

Figure 2. Clinical view of the patient: stooped posture, cachectic dwarfism, microcephaly, wizened facies, sunken eyes, beaked nose , sparse hair and oral respiration

Case Report: A seven-year-old girl was sent to the department of pediatric dentistry for dental checkup. She came from healthy consanguineous parents. Pregnancy and delivery were uneventful. In fact, her birth weight was 2300gr,her birth height was 45cm andher birth head circumference was 32 cm (-2SD).

She had normal developmental milestones during the first year of life; however, unaided walking was never achieved. She witnessed then a growth failure and a loss of ability to walk and speak. The patient continued to experience a decrease in her growth rate, in her height, weight and head circumference. At the age of 18 months, parents remarked a photosensitivity and a hear loss. Her mother also reported feeding problems associated with a delayed eruption of primary teeth. Unfortunately, they were lateraffected by multiple dental caries. Dermatologist suspected CS and brain stem evoked response confirmed bilateral and profound deafness. Physical examination at the age of 7 years showed a height of 75 cm (-6SD), a weight of 8 kg (-4SD) and a head circumference of 44 cm (-8SD). The patient had a profound deafness, cachectic dwarfism, facial dysmorphism with wizened facies, sunken eyes, beaked nose,sparse hair and scaly skin [Figure2]. Neurological examination showed good contact, severe language delay, spastic tetarparesis, areflexia in lower limbs and cerebellar signs. Brain CT scan showed putaminal calcifications. Brain MRI showed cerebellar atrophy and hypomyelinatingleukodystrophy [Figure 3].

Oral examination was difficult due to lack of cooperation and limited mouth opening. Oral hygiene was extremely bad. In fact, dental plaque and carious lesions were observed in most teeth surfaces [Figure 4A, 4B]. The examination of dental arches revealed an extremely deep palate and quite narrow dental arches [figure 4A, 4B]. The lingual archwidth was respectively 14 mm and20 mm on inter-canine and inter-molar regions. [Figure 4C, 4D] Furthermore, white opacities were observed in most surfaces of erupted permanent teeth [figure 4C, 4D]. The Functional examination was in favor of mouth breathing, infantile deglutition and hypotonic tongue. We should also mention that saliva check with sugar cube confirmed a hyposialia. Radiological explorations have proved that there have been no abnormalities in number but in form in first molars and also proved overcrowded premolars germs [Figure 5]. First, many dental care sessions have been performed under local anesthesia. Then, Nance and lingual arches were realized as space maintainers [Figure 5, 6].The lingual arch was active in order to straighten the axis of mandibular molars. That's why the patient was followed-up monthly.

RESULTS

Sixteen articles were reviewed. Mean age at syndrome diagnosis and at dental management were respectively (7.89 YO) and (9.68 YO). Genetic diagnosis was established in 87.5% of included articles: CSA (N=5) 31.25%, CSB (N=8) 50% and XPD (N=1) 6.25% mutations were reported respectively. Oro-dental findings reviewed were bad oral hygiene (N=5) (33.33%) , dental caries (N=16) (100%) , enamel hypoplasia (N=6) (37.5%) , white opacities(N=3) (18.75%) , narrow dental arches (N=4) (25%) , teeth malposition(N=4) (25%) ,agenesis (N=5) (31.25%), anomalies of form(N=4) (25%) , hyposialia (N=5) (31.25%), temporo-mandibular joint defect (N=1) (6.25 %) and other non-detailed features(N=4) (25%) . Dental management in CS patients was detailed in (N=7) (43.75%) of retained articles. It varied from preventive treatment to surgical one under local or general anesthesia depending on the clinical context. (Table 1)

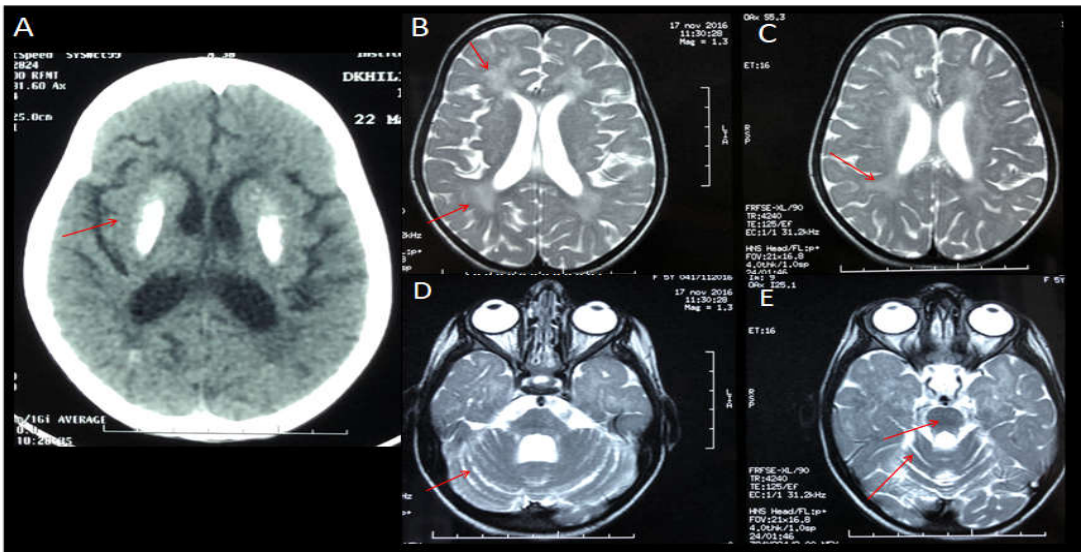

Figure 3. 3D Neuro-imaging A : Brain CT scan showing lenticular calcifications B,C :T2-weighted axial slice MRI images showing a periventricular white matter hypersignal and a ponto cerebellar atrophy (D,E)

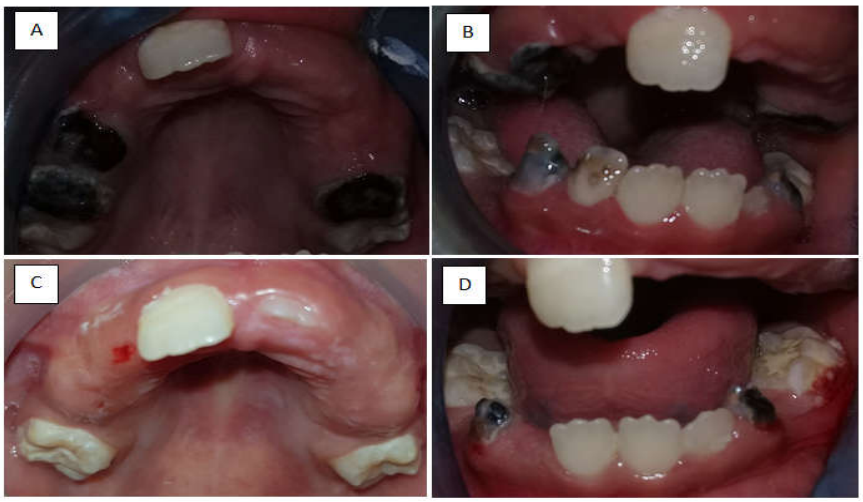

Figure 4: Intra-oral view at the first dental check-up (A, B) and during dental care sessions (C, D) A : Maxillary intra-oral view showing poor oral hygiene , carious lesions on all primary molars rated(ICDAS 6) , the eruption of the permanent right central incisor and permanent first molars . The palate was extremely deep. B: Mandibular intra-oral view showing carious lesions on primary right lateral incisor and primary canines, a narrow dental arch and a limited mouth opening. C: Maxillary intra-oral view showing an improved oral hygiene after the mechanic tooth brushing. Sealant on the permanent first molars and the extraction of all primary ones were realized. White opacities were obvious on the remaining teeth. D: Mandibular intra-oral view showing conservative treatment on the permanent left first molar with glass ionomer. Sealant on the right one and the extraction of the primary right lateral incisor were realized.

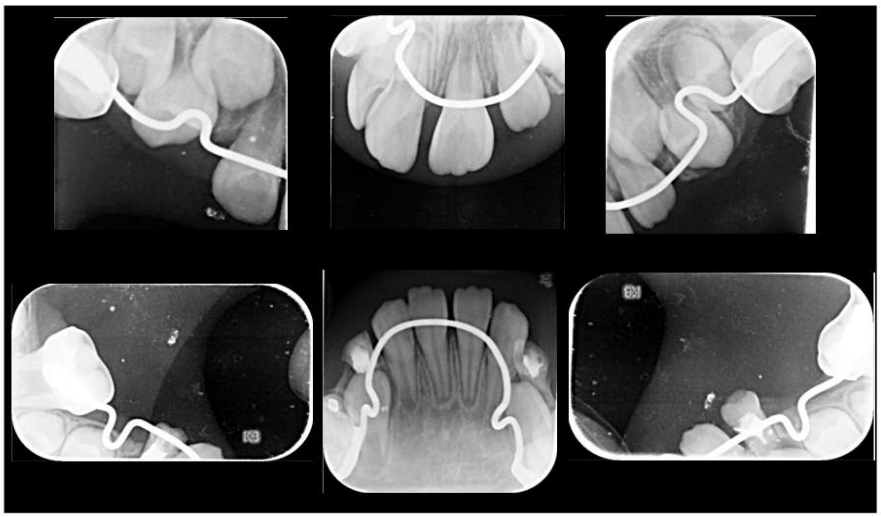

Figure 5. A full mouth series of radiographs after dental management showing no agenesis in the permanent dentition, taurodontic permanent maxillary and mandibular first molars , overcrowded maxillary and mandibular premolars' germs(A,C,D,F) and versed axis of the permanent mandibular first molars (D,F)

Table 1. Review of literature about oro-dental findings and management in CS patients

Age at diagnosis	Genetic mutation	Oro-Dental findings											Age of dental management	Dental management	Authors' names
		Bad Oral hygiene	Dental caries	Enamal hypoplasia	White opacities	Norrow dental arches	Teeth Malposition	Agenesis	Abnormalities of form/shape	Others /non detailed dental abnormalities	Hyposialia	TMJ defect*			
4 YO	-	+	+	-	-	-	-	-	-	-	-	-	-	+	Boraz R A [3]
P 1 : 21YO P 2 : 1 Y and 11 months P3 : 6 YO P 4 :5YO P5 : ND	P1, P2: DNA Exision repair defect P 3,4, 5 : -	-	+	-	-	+	+	+	+	-	+	-	-	+	Nance MA, Berry SA [8]
9 YO and 4 months	CSB	+	-	+	-	+	-	+	+	-	-	+	9 YO and 4 months	-	Arenas-Sordo M de la L, Hernández-Zamora E, Montoya-Pérez LA [12]
4YO	-	+	+	-	-	+	-	-	-	-	-	+	14YO	+	Gaddam D, Thakur MS, Krothapalli N, Kaniti S [9]

TMJ : Temporo-mandibular joint ; P1, P2P3, P4, P5 : Respectively patient 1, 2, 3, 4,5

Age at diagnosis	Genetic mutation	Oro-Dental findings											Age of dental management		Dental management	Authors name
		Bad Oral hygiene	Dental caries	Enamal hypoplasia	White opacities	Norrow dental arches	Teeth malposition	Agenesis	Abnormalities of form	Others/ non detailed dental abnromalities	Hyposialia	TMJ Defect*				
ND	CSA CSB	+	+	+	-	-	+	-	+	-	-	-	8.75YO	+	Bloch-Zupan A, Rousseaux M, Laugel V [11]	
CSA : 7.84 Y CSB : 6.21 Y	ERCC8/CSA ERCC6/CSB	-	-	-	-	-	-	-	-	+	-	-	ND	ND	Calmels N, Botta E , Jia N and al[10]	
11.5 Years	CSB CSA XPD	-	+	+	-	-	-	-	-	-	-	-	-	+	Wilson BT, Stark Z, Sutton RE and al [5]	
ND	ND	-	+	+	-	-	+	+	-	-	-	-	-	+	WissemHafsi; Talel Badri [7]	

TMJ :Temporo-mandibular joint

Age at diagnosis	Genetic mutation	Oro-Dental findings											Age of dental management	Dental management	Authors name
		Bad Oral hygiene	Dental caries	Enamal hypoplasia	White opacities	Norrow dental arches	Tooth malposition	Agenesis	Abnormalities of form	Others / Non detailed dental anomalies	Hyposialia	TMJ defect*			
-	-	-	+	-	-	+	+	-	-	+	+	+	-	+	Kubota M [14]
P 1*: 22 YO P2*: 20 YO	-	- -	- -	- -	- -	- -	+ -	- -	- -	- -	- -	- -	- -	- -	Sowmini PR, Kumar MS, Velayutham SS and al [4]
P1*: 18 months P 2*:7 months	-	-	+	-	-	-	-	-	-	-	-	-	-	-	Scaioli V, D'Arrigo S, Pantaleoni C [17]
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
-	CSA CSB	-	+	+	-	-	-	-	-	-	+	-	-	-	Karikkineth AC, ScheibyeKnudsen M, Fivenson E, [1]
-	CSA CSB	-	+	+	-	-	+	+	+	+	+	-	-	-	Laugel V [6]

*P1,P2 :Patient 1 ,Patient 2 ; *TMJ :Temporo-mandibular joint

Age at diagnosis	Genetic mutation	Oro-Dental findings											Age of dental management	Dental management	Authors name
		Bad Oral hygiene	Dental caries	Enamal hypoplasia	White opacities	Norrow dental arches	Tooth malposition	Agenesis	Abnormalities of form	Others / Non detailed dental anomalies	Hyposialia	TMJ defect*			
P 1*: 3 YO P 2*: 1.6 YO	ERCC6 (c.2382+2T>G) and (c.3259C>T)	-	+	-	-	-	-	-	-	-	-	-	-	-	Sanchez-Roman I, Lautrup S, Aamann MD [15]
7.17 YO (Mean age)	-	-	+	-	-	-	-	-	-	-	-	-	-	-	Alan R Lehmann, Annette F Thompson, et al[8]
4YO	RRSdeficiency	-	+	-	-	-	-	-	-	-	-	-	-	-	Pasquier L, [13]
7YO	CSB	+	+	-	+	+	+	-	+	+	+	+	7 and 1/2 YO	+	Our case report (Bourguiba E , Jazi I , Kraoua I and al)

*P1, P2 : patient 1, Patient 2 ; *TMJ : Temporo-mandibular joint

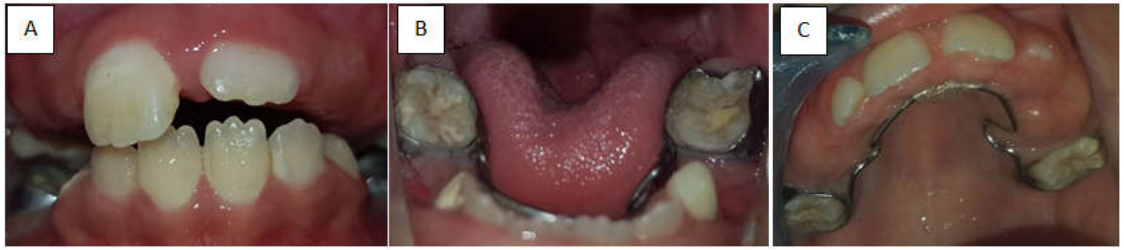

Figure 6: Intra-oral view during the interceptive treatment (A) and the sessions of follow-up (B,C) A: The sealing of Nance and lingual arches is done .White opacities are noted on most dental surfaces. A normal eruption's sequence is noticed. B: At the fifth month of follow-up: The lingual arch is activated and re-sealed . The mandibular arch 'width between primary mandibular right and left canines and permanent mandibular first right and left molars are respectively 20.5 mm and 31 mm. C: At the ninth month of follow-up , Arch's Nance is well adapted to palate , a normal eruption of permanent maxillary lateral incisors is noted

DISCUSSION

CS is belonging to the family of premature aging syndromes that encompasses an expanding spectrum of clinical presentation. Neurologic anomalies and oro-dental affections are constantly characterizing the syndrome (1,3). Its global prognosis depends on the type of CS and the severity of ocular and neurological signs associated (4–8). Our review included studies that focused exclusively on oro-dental abnormalities (1,3,7,9–15). Nance and Berry(9), Zupan and al (12) have the largest cohorts that studied respectively clinical signs and oro-dental phenotype in CS patients. It is obvious that this disease is due to a genetic mutation on ERCC8 and ERCC6 as commonly reported in 70% of included articles(1,5,6,11–13,16). Nevertheless some novel studies have been emerged and discovered novel mutations hidden behind this defect (16,17) Our case report and review of literature reported a wide detailed oro-dental phenotype in CS infants. It includes dental abnormalities of structure, form, number and shape. It also includes dental arches measures; temporal-mandibular joint and saliva check (6,10,12,13,15). Besides, our study permitted to correlate between neurologic signs and oro-dental ones. In fact , autonomic and motor impairment may affect oro-facial functions such as deglutition , respiration , salivation , tongue's and mandibular motricityand dental pulp innervation (1,4,10,15) . Consequently, restriction in motion of temporal-mandibular articulation, hypotonia, decreased salivation and abnormal tooth blood flowand innervation may lead to dental decay in addition to bad oral hygiene in most of cases (6,9,10,15).

Indeed, growth delay has an impact on dental arches 'growth and cranio facial skeleton. Thus, a general tendency to a hypo development of the face and the skull as long as retrognatia were reported in literature (12,13). Moreover, atrophy of alveolar ridge, narrowness of dental arches were also reported leading to severe malocclusions and overcrowded teeth in mixed and permanent dentition (3,11,12,15,18). Besides, there is a delay in syndrome diagnosis because cardinal signs like growth delay, microcephaly and motor impairment, do not appear at first months of life except in the severe neonatal form of the disease(14) .

Therefore, oro-dental findings at early childhood are rarely reported in literature. Moreover, our review confirmed that there is a delay between the syndrome diagnosis (7.87 YO) and the dental management process (9.68 YO). That may be due to long periods of managing multivisceral affections, before addressing the patient to pediatric dentist. In fact, dental management was only detailed in (N=7) (43.75%) of the included articles in spite of considering dental abnormalities cardinal for diagnosing the disease (1,9). That may be due to a lack of studies about oro-dental concerns in CS patients. When reported, the dental management varied from preventive measure to dental extraction because of the lack of cooperation and narrowness of the oral cavity (3,5,9). Knowing that growth delay is a major problem in CS patients (1,9) we expended the treatment to interceptive one, in order to prevent possible severe malocclusion and boost alveolar ridge's growth in addition to the systemic treatments. Interceptive and orthodontic treatments will obviously depend on the severity of the disease and the motivation of parents (12)

CONCLUSION

Early dental check-up and management of CS is very important as preventive option. More or o-dental signs need to be explored as skeletal diagnosis, temporal-mandibular joints, and salivary and pulp tests.

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