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Original Article

Dental Manifestations and Management of a Young Patient with Cardio-Facio-Cutaneous Syndrome – A Case Report

Atheer I. Almulayfi[1]*, Sama S. Alsaad[1], Abdulrahman S. Alshalaan[1], Abdullah M. Alassaf[1], Sarah S. Alotaibi[1], Rahaf M. Almansour[1], Raghad A. Albarrak[2]

[1]Department of Pediatric Dentistry, King Saud Medical City, Riyadh First Cluster, Riyadh, Saudi Arabia, [2]Department of Pediatric Dentistry, Specialized Dental Center, Riyadh Second Cluster, Riyadh, Saudi Arabia

***Corresponding Author:**
Atheer I. Almulayfi
E-mail: a.almulifi@rfhc.med.sa

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ABSTRACT

Background: Cardio-facio-cutaneous syndrome (CFCS) is a rare autosomal dominant disorder that is considered one of the neuro-CFCS that occur due to a genetic mutation. The clinical presentation of this syndrome includes mental retardation, facial features, and others.

Objectives: The purpose of this article is to describe the clinical manifestations, dental considerations, oral findings, and management strategies in CFC-affected pediatric patients.

Case Description: A 9-year-old Saudi male presented with his mother to the pediatric dentistry clinic at King Saud Medical City, Riyadh, Saudi Arabia. The patient was a known case of CFCS and complained of dental pain that affected his quality of life. Full mouth rehabilitation was done under general anesthesia, and the case was followed up 14 days after the procedure.

Conclusion: Strict oral hygiene and preventive measures would help to prevent early tooth loss and eliminate the risk of exposing patients to general anesthesia. Prenatal and postnatal education are needed to prevent extensive treatment in such cases.

Keywords: Cardio-facio-cutaneous syndrome, Dental management, Oral health, Oral manifestations

Introduction

Cardio-facio-cutaneous syndrome (CFCS) is a rare autosomal dominant disorder with multiple congenital anomalies and intellectual disability, mainly due to mutations in the *BRAF*, *MEK1*, and *MEK2* genes.[1-3] The key features of CFCS include heart defects, distinct facial features, and skin abnormalities. Other characteristics consist of threatening feeding difficulties, intellectual disability ranging from moderate to severe, and short stature, along with macrocephaly.[4] CFCS is mainly caused by mutations in the *BRAF* gene, which is the most common type, making up 75% of cases.[2] Cardio-facio-cutaneous (CFC) is a clinical syndrome that affects more than one system of the body; it significantly impacts the nervous system, causing intellectual disabilities, behavioral abnormalities, and an increased incidence of epilepsy, reaching up to 64%.[2,5] Moreover, individuals with CFCS may also have a risk of developing certain neoplastic disorders such as acute lymphoblastic leukemia and lymphomas.[2] The cardiac defects in CFCS encompass pulmonary stenosis, atrial and ventricular septal defects, hypertrophic cardiomyopathy (HOCM), heart valve anomalies (mitral valve dysplasia, tricuspid valve dysplasia, and bicuspid aortic valve), and rhythm disturbances.[5] Craniofacial features often include a high forehead, macrocephaly, bitemporal narrowing, hypoplasia of the supraorbital ridges, ocular hypertelorism, downslanting palpebral fissures, epicanthal folds, droopy eyelids, short broad nose, upward-pointing nostrils, and low-set ears.[3,5] Airway presents a high-arched palate, relative micrognathia, laryngomalacia, tracheomalacia, and hypersalivation.[3,5] Dental manifestations include crowding, posterior crossbite, parafunctional habits, and malocclusion.[1,3] Therefore, this case report was conducted to address

the dental findings, clinical manifestations, medical considerations, and management approach for a pediatric patient with CFC.

Case Description

A 9-year-old Saudi male presented with his mother to the pediatric dentistry clinic at King Saud Medical City (KSMC), Riyadh, Saudi Arabia. The patient was referred by a general pediatrics physician for comprehensive dental management, and this was his first dental visit, as he had no prior history of dental care. As reported by the mother and after reading the patient's medical record, the patient had been diagnosed with CFCS by the genetics department at KSMC. He had mild segmental left ventricular hypertrophy, mild pulmonary stenosis, cardiomegaly, global developmental delay, and intellectual disability. The patient was born at full term and was shifted to the intensive care unit after delivery for 5 days due to meconium aspiration syndrome. His family history was unremarkable for CFC or other neurological diseases. The patient has four healthy siblings. The patient resides with both parents, with the mother serving as the primary caregiver. Furthermore, for the past 2 years, the patient had been attending a special needs institution focused on early intervention and rehabilitation. According to dietary history, the child was limited to a soft diet because of swallowing difficulties. No history of night bottle feeding or gastrointestinal tube was found. The mother mentioned that she could not brush her child's teeth because he is uncooperative.

Investigation

Upon extra-oral examination, the patient had a long face, sparse and friable hair, posteriorly angulated ears with prominent helices, a high forehead, hypertelorism, a short nose, full lips, and hyperkeratosis skin lesions. Intra-oral examination showed that the patient was in the mixed dentition stage, with badly decayed teeth, drooling of saliva, malocclusion, and open bite. Clinical pre-operative photographs are shown in Figure 1.

While the patient was anesthetized and positioned on the operating table, radiographs were limited to erupted teeth due to the patient's cooperation level and to minimize unnecessary radiation exposure, as shown in Figure 2. Full mouth periapical radiographs showed deep caries of upper and lower canines, primary molars, and all permanent first molars (PFM), which were deemed non-restorable. Periapical radiograph of lower permanent incisor teeth showed proximal caries of the lower central incisors.

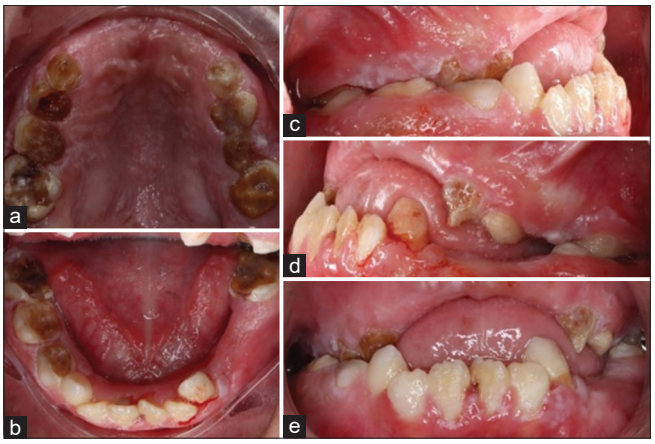

Figure 1: Pre-operative clinical photographs intraorally that are taken when the patient is under general anesthesia. (a) Upper occlusal view, (b) lower occlusal view, (c) right lateral view, (d) left lateral view, and (e) frontal view of the teeth

Management

All procedures were explained to the child's caregiver, and full written informed consent was obtained for dental treatment under general anesthesia. Furthermore, consultation from a pediatric cardiologist was obtained and recommended subacute bacterial endocarditis (SBE) prophylaxis 1 h before a dental procedure. 1 g of ampicillin was administered intravenously (IV) 1 h before the operation. Anesthesia was induced with IV administration of sevoflurane and oxygen, followed by propofol, after which endotracheal intubation was performed using the standard laryngoscopy technique by the anesthesia team. Dexamethasone was given to minimize post-operative oral edema, and anesthesia was maintained with an oxygen–sevoflurane mixture. Throughout the procedure, the patient's vital signs remained stable. The total surgical duration was 60 min, excluding induction and extubation. The procedure started with prophylaxis of all teeth, then caries excavation was done for the lower central incisors. 37% phosphoric acid etch was used, and adhesive was applied and cured according to the manufacturer's instructions. Then the cavities were restored with shade A2 light-cured composite resin restoration. Whereas, all primary molars, canines, and PFMs were extracted. All PFMs extraction was done with the help of an oral and maxillofacial surgeon. 2% lidocaine (1:100,000) without epinephrine was used as suggested by the cardiologist. Oxidized regenerated cellulose gauze was applied to all extraction sites to accelerate the clotting mechanism, then the socket areas were sutured with 3-0

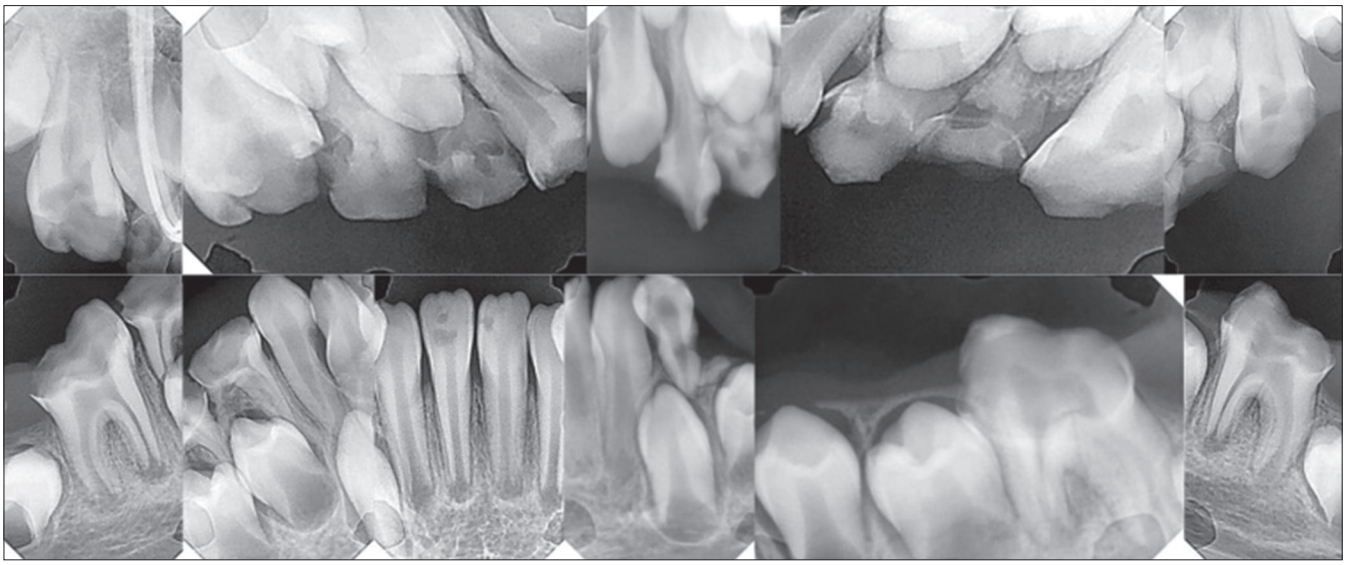

Figure 2: Full mouth periapical radiographs that are taken when the patient is under general anesthesia

synthetic absorbable polyglactin. Following completion of the dental procedure, spontaneous breathing was re-established, the patient was extubated, and supplemental oxygen was administered. The patient was discharged on the same day without any post-operative complications and was given a prescription of 315 mg of amoxicillin with clavulanic acid antibiotic (Augmentin) 2 times a day for 5 days and 200 mg of paracetamol 4 times a day for 3 days. Two weeks after the procedure, the patient was scheduled for a follow-up appointment at the dental clinic and showed good recovery. Finally, the patient booked for a recall visit after 3 months and showed healed extraction sites, and another appointment was given as a 6-month recall for monitoring the growth and eruption of permanent dentition, as well as assisting the occlusion and function. Post-operative photographs are shown in Figure 3. Table 1 shows a summary of dental materials used during the procedure with manufacturer instructions.

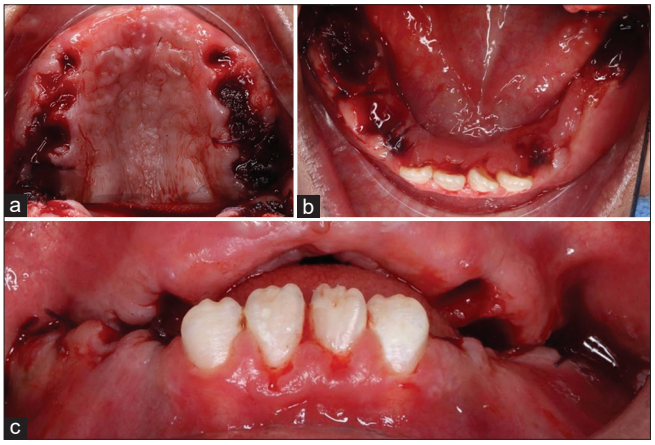

Figure 3: Post-operative clinical photographs intraorally during general anesthesia. (a) Upper occlusal view, (b) lower occlusal view, and (c) frontal view of the teeth

Discussion

CFCS represents a rare genetic disorder with autosomal dominant inheritance, involving multiple congenital anomalies and cognitive delay.[1,3,5] In our case, the patient was diagnosed with mild pulmonary stenosis, as individuals with a BRAF mutation are more commonly associated with this condition, which happens to be the only anomaly that demonstrates a significant genotype-phenotype correlation statistically.[2] 2% lidocaine (1:100,000) without epinephrine was used in our case. Epinephrine was not added to the local anesthetic, and the amount of epinephrine was reduced to prevent the risk of left ventricular outflow tract obstruction.[4] During invasive dental procedures, bacteremia can potentially lead to the development of infective endocarditis in high-risk individuals with cardiac conditions.[11] Mitral valve defect requires the mandatory use of antibiotic prophylaxis to prevent endocarditis.[4] In our case, we administered SBE prophylaxis to the patient 1 h before the procedure. There has been considerable debate about whether CFCS is regarded as a more severe phenotypic variant within the Noonan syndrome spectrum. Although CFCS is phenotypically related to Noonan syndrome, mutation analysis in typical cases has not demonstrated *PTPN11* gene involvement, suggesting it has a distinct etiology.[12] Differential diagnosis with other neuro-CFC (NCFC) syndromes, such as Costello syndrome and severe Noonan syndrome, relies on characteristic ectodermal

Table 1: Materials used in the operative room (name, company, and manufacturer instructions)

Material	Company	Manufacturer instructions
Scotchbond™ Etchant	3M, ESPE, St. Paul, MN	"1- Clean: If the surface isn't freshly cut, polish it with a pumice-water mixture. Avoid prophy pastes containing oil or fluoride, as they can interfere with etching. Rinse thoroughly. 2-Isolate: Maintain a dry working area using a rubber dam is best. 3-Etch: Place the etchant on a pad or dish, then apply it to the target surface with a brush or suitable tool for about 15 s. Stir if a thinner consistency is needed. 4-Rinse: Rinse the etched area for 15 s and suction away the water. Prevent saliva contact; if contamination occurs, re-etch for 5 s and rinse again. 5-Dry: Keep the surface uncontaminated; if contamination happens, repeat the etching and rinsing steps. 6-Bond: Begin the bonding process immediately after drying."[6]
Scotchbond™ universal adhesive	3M, ESPE, St. Paul, MN	"1-After selectively etching the enamel or performing total etching on both enamel and dentin, apply the adhesive to the prepared surface and actively rub it for about 20 s. 2-Lightly air-dry for around 5 s to remove the solvent. 3-Cure the adhesive for 10 s."[7]
Z100™ composite	3M, ESPE, St. Paul, MN	"1-Properly isolate the tooth and follow the adhesive system's guidelines. 2-Apply the composite using a syringe or capsule. 3-Build the restoration in small increments, start with a 1 mm layer in the proximal box, and cure each layer. 4-Slightly overfill and shape before curing, keeping the material away from strong ambient light. 5-Choose shades carefully, use opaque shades for deeper areas and incisal shades on the surface for better esthetics. 6-Finish by polishing to achieve a smooth, glossy, and durable surface."[8]
Oxidized regenerated cellulose gauze (Surgicel™)	Ethicon, New Jersey, USA	"Used as an aid during surgical procedures to help control bleeding from capillaries, veins, and small arteries when traditional methods such as ligation are difficult or ineffective."[9]
Synthetic absorbable polyglactin 910 (VICRYL®)	Ethicon, New Jersey, USA	"Used for general soft-tissue approximation and ligation, including ophthalmic surgery, but not recommended for use in cardiovascular or neurological tissues."[10]

features, including dry, hyperkeratotic, scaly skin and sparse, curly, and brittle scalp hair.[13] A hallmark feature is ulerythema ophryogenes, characterized by absent eyebrows with hyperkeratosis.[13] Over time, additional symptoms such as palmoplantar hyperkeratosis and lymphedema can appear. Psychomotor delay in these individuals is typically moderate-to-severe.[13] Cardiac abnormalities are observed in 75% of cases, with pulmonary valve stenosis in 45%, atrial septal defect in 22%, and myocardial disease, often HOCM, in 40%.[14] Unlike other NCFC, CFCS is not generally associated with an increased malignancy risk, though the occurrence of acute lymphoblastic leukemia in one patient raises questions, potentially as a coincidental finding.[13] Intellectual disability hinders oral hygiene practice, which makes those patients more susceptible to dental caries.[15] This exactly reflects our case, which came with multiple hopeless carious teeth due to neglected oral hygiene, resulting in the extraction of all PFM's teeth. Caregivers should remember that patients with these conditions may not be able to brush their teeth on their own and that they need assistance with brushing.[15] Medical conditions can affect the type of treatment given, so dentists might be more aggressive for these patients to minimize risks or the need for further re-admission. For example, when a tooth presents with periapical pathology, extraction is considered a more appropriate treatment option than pulp therapy due to the poor prognosis of the affected tooth.[15] The ideal extraction time of PFM, if deemed non-restorable, falls between 8 and 11.5 years of age for spontaneous eruption of the second permanent molars.[16] Following extraction and satisfactory healing, the patient was managed under space supervision rather than immediate space maintenance. Since all primary molars and first permanent molars were extracted, fixed or removable space maintainers or pediatric prosthetic appliances were not immediately applicable. At the time of reassessment and following the eruption of premolars and upper permanent incisors, arch length was considered adequate, and no functional or esthetic impairment was observed. A 6-month follow-up visit was scheduled to continue monitoring craniofacial growth, eruption pattern, occlusion, and function. The long-term management plan includes regular clinical and radiographic follow-up at 3–6 month intervals, if possible to monitor: Eruption sequence and timing of the permanent successors, arch length preservation and space adequacy, occlusal development and inter-arch relationships, functional outcomes, including mastication and speech. Guidance of eruption and interceptive orthodontic intervention, such as space maintenance or orthodontic appliances, will be considered if signs of space loss, delayed eruption, ectopic eruption, or developing malocclusion are detected during follow-up.[17]

This case report has several limitations. The follow-up duration was limited, and long-term outcomes were not available at the time of reporting. As a result, the long-term stability of the treatment and the occurrence of delayed complications could not be fully evaluated. Moreover, since this report describes a single clinical case, the findings cannot be generalized to all patients with CECS. Future studies involving larger cohorts and extended follow-up periods are warranted to better assess dental management outcomes in this patient population. In addition, post-extraction space management and long-term rehabilitative outcomes could not be assessed due to the short follow-up period and the patient's medical and behavioral limitations.

Conclusion

For patients who cannot be treated in clinical settings, such as patients of CFC, strict oral hygiene and preventive measures would help prevent early tooth loss and eliminate the risk of exposing patients to general anesthesia. An early awareness of caregivers, such as prenatal and postnatal education with multiple close follow-ups, is needed to promote oral health, enhance patients' cooperation, and prevent extensive treatment.

Authors' Contributions

AIA diagnosed and treated the patient, followed up the patient. SSA, ASA, and AMA prepared and edited manuscript. SSA, RMA, and RAA wrote Literature review and initial manuscript, and collected clinical data. All authors read and ap-proved the final manuscript.

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Ethics Declarations

Ethical clearance was obtained from the Institutional Review Board of KSMC (H2RI-22-May25-01). Clinical trial registration: Not applicable.

Consent to Participate

Not applicable.

Consent to Publish

Written informed consent was obtained from the patient's legal guardian for publication of this case report and any accompanying images.

Data Availability Statement

All relevant data supporting the conclusions of this case report are included within the article and its supplementary file. No further datasets were generated.

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Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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