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CASE REPORT:

Tetralogy of Fallot Associated with Amelogenesis Imperfecta: a Case Report

Tetralogía de Fallot asociada a amelogénesis imperfecta: reporte de un caso

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ABSTRACT: Tetralogy of Fallot (TOF) is the prevalent cyanotic congenital cardiac anomaly, accounting for 80% of all cases. Despite the incidence rate, the etiopathogenesis of TOF remains unknown. Amelogenesis imperfecta (AI) is a hereditary condition that impacts enamel development, resulting in morphological and functional tooth modifications. This report aims to present the case of a young patient with TOF and AI who received direct restorative treatment, emphasizing the medical and dental factors involved in enhancing oral health and dental esthetics. The patient has a history of cardiac procedures, including the implantation of a metallic pulmonary valve, along with moderate intellectual disability and a prior seizure episode. The intraoral examination indicated extensive gingivitis, inadequate oral hygiene, hypomineralized enamel with structural deterioration, and numerous plaque retention niches, resulting in pain during mastication and oral hygiene practices. Due to the high risk of infective endocarditis, infected foci were eliminated, and antibiotic prophylaxis was administered according to the American Heart Association guidelines. Restorative therapy was conducted utilizing direct composite resin veneers to restore dental aesthetics and functionality. Post-treatment, the patient had enhanced self-esteem, maintained dental hygiene, and achieved remission of gingivitis. This case demonstrates the significance of comprehensive dental care for patients with complex congenital heart conditions and enamel developmental disorders, stressing the necessity for preventive measures, effective periodontal management, and advanced restorative techniques to reduce the risks of systemic infections.

KEYWORDS: Tetralogy of Fallot; Amelogenesis imperfecta; Infective endocarditis; Dental prophylaxis; Composite resin.

RESUMEN: La tetralogía de Fallot (TF) es la anomalía cardíaca congénita cianótica más frecuente, representando el 80% de los casos. A pesar de su incidencia, se desconoce su etiopatogenia. La amelogénesis imperfecta (AI) es una afección hereditaria que afecta el desarrollo del esmalte, provocando modificaciones morfológicas y funcionales de los dientes. Este informe presenta el caso de un paciente joven con TF e AI que recibió tratamiento restaurador directo, destacando los factores médicos y odontológicos que contribuyen a mejorar la salud bucal y la estética dental. El paciente presenta antecedentes de procedimientos cardíacos, incluyendo la implantación de una válvula pulmonar metálica, además de discapacidad intelectual moderada y un episodio convulsivo previo. El examen intraoral reveló gingivitis extensa, higiene bucal inadecuada, esmalte hipomineralizado con deterioro estructural y numerosos nichos de retención de placa, lo que provoca dolor durante la masticación y la higiene bucal. Debido al alto riesgo de endocarditis infecciosa, se eliminaron los focos infectados y se administró profilaxis antibiótica según las directrices de la Asociación Americana del Corazón. Se realizó una terapia restauradora con carillas directas de resina compuesta para restaurar la estética y la funcionalidad dental. Tras el tratamiento, el paciente mejoró su autoestima, mantuvo una higiene dental adecuada y logró la remisión de la gingivitis. Este caso demuestra la importancia de la atención odontológica integral para pacientes con cardiopatías congénitas complejas y trastornos del desarrollo del esmalte, destacando la necesidad de medidas preventivas, un tratamiento periodontal eficaz y técnicas restauradoras avanzadas para reducir el riesgo de infecciones sistémicas.

PALABRAS CLAVE: Tetralogía de Fallot; Amelogénesis imperfecta; Endocarditis infecciosa; Profilaxis dental; Resina compuesta.

INTRODUCTION

Congenital cardiac disorders are currently the leading cause of death from non-communicable diseases in individuals under 30 and the principal cause of mortality resulting from congenital defects. Tetralogy of Fallot (TOF) is the most common cyanotic congenital heart defect, affecting approximately 3 out of every 10.000 live births and accounting for 5-10% of all congenital heart defects (1,2).

While approximately 20% of cases of TOF are syndromic with an identified pathogenic gene, such as DiGeorge Syndrome (22q11.2 deletion), trisomy 21, Alagille Syndrome (JAG1), Ritscher-Schinzel-like Syndrome (WASHC5), and CHARGE Syndrome (CHD7), 80% of TOF cases are unrelated to any known disease or chromosomal abnormality, consequently the etiology remains unknown (1-3).

A recent study performed exome sequencing of 362 probands with non-syndromic Tetralogy of Fallot (TOF) and their parents identified rare, de novo variants. Gene ontology analyses revealed enrichment in processes such as cell cycle progression, chromatin remodeling, myocyte contraction, calcium transport, and ventricular septum development, as well as target genes of SOX9. These findings, absent in controls, suggest that intrinsic molecular defects in cardiac progenitor cells impacting their viability and contractile function are key to non-syndromic TOF pathogenesis, with potential implications for patient stratification and personalized care (3).

Clinically, TOF comprises four cardiac anomalies: right ventricular hypertrophy, pulmonary stenosis, ventricular septal defect, and an

overriding aorta. Due to these anatomical anomalies, Tetralogy of Fallot permits the combination of pulmonary and systemic circulations. To improve survival, surgical correction is recommended within the first year of life. Due to ongoing improvements in surgical methods and postoperative management, almost 87% of patients with TOF achieve adulthood following surgical intervention (4,5).

Enamel features may be inherited as autosomal dominant, autosomal recessive, or X-linked Mendelian disorders, resulting from mutations in many genes that influence enamel development. This set of genes encompasses those encoding extracellular matrix (ECM) proteins, including AMELX and ENAM, with genes that regulate ion transport, transcription factors, and other functions (6).

Amelogenesis imperfecta (AI) is a hereditary genetic disorder caused by defective genesis of enamel, leading to abnormal structure and function. This condition can result in a variety of dental issues, including increased susceptibility to caries, sensitivity, and aesthetic concerns, worsening the oral health of individuals with pre-existing cyanotic conditions. AI exclusively affects the ectodermal component of teeth, while the mesodermal component remains intact (7-9).

Witkop's 1988 categorization, with subsequent adjustments, categorizes AI into three types: hypoplastic, hypomature, and hypomineralized. The resulting enamel phenotypes are highly variable, including thin enamel characterized by hypoplasia and hypomineralized enamel, which can manifest as discolouration and reduced structural integrity, resulting in tooth sensitivity. MicroRNAs (miRNAs) are linked to enamel formation and genetic abnormalities, and may interact with environmental factors in conditions such as dental fluorosis. AI is defined by the presence of defective enamel in the absence of other systemic problems (6, 10-12).

Individuals with AI frequently experience a significant, progressive reduction in vertical occlusal dimension, complicating dental rehabilitation and markedly impacting quality of life. The enamel is delicate, soft, and fragile, enabling plaque buildup, dental caries, and periodontal diseases, and which may result in premature tooth loss. Consequently, both direct and indirect treatment modalities are commonly used for restorative rehabilitation. In permanent dentition, treatment goals include reducing dental sensitivity and restoring vertical dimension, functionality, and aesthetics. Definitive treatment is initiated once the clinical crown height is determined and pulp tissue has diminished. A multidisciplinary approach integrating prosthodontic, endodontic, restorative, periodontic, and orthodontic management is recommended for full-mouth rehabilitation. Crown lengthening and gingival recontouring are advised for cases with short gingival crowns and hyperplasia. Anterior open bites, frequently linked to AI, necessitate orthodontic intervention. Root canal therapy is recommended for individuals with significant tooth attrition. Collaboration with specialists is crucial for formulating a comprehensive treatment strategy for those affected by different forms of AI (8,13,14).

Some authors describe a suggests a possible relationship between congenital heart disease and enamel formation disturbances. Studies show enamel abnormalities and microdontia in congenital cardiac individuals. Furthermore, some authors describe that cases of children exhibiting cyanosis and prolonged hypoxia may experience ameloblastic activity impairment during odontogenesis. However, the impact of these heart defects on tooth development is still under investigation (14,15).

The objective of this report is to describe the case of a young patient with TOF and AI who underwent direct restorative treatment, highlighting

the medical and dental considerations aimed at improving oral health and dental esthetics.

CASE REPORT

A 19-year-old white male patient with TOF, pulmonary valve agenesis, and patent ductus arteriosus returned for dental consultation. Before consultation, a written informed consent was obtained from the patient's legal guardian, using the standard institutional consent form of our dental school, which covers both treatment and publication including images. According to his mother, he had previously undergone metallic pulmonary valve prosthesis placement, duct ligation, right ventricle-pulmonary trunk (RV-PT) conduit placement, and ventricular septoplasty. Postoperative complications included pneumonia, requiring a 19-day hospitalization.

In 2020, he underwent additional stent placement surgery. The patient also has mild intellectual disability and a history of a controlled isolated seizure, for which he uses carbamazepine (200 mg). Additional medications included acetylsalicylic acid (100 mg) and metoprolol succinate (25 mg). His mother reported deleterious oral habits, including nighttime lip sucking, and biting of lips, hands, objects, and nails.

Referred from a cardiology hospital, his main complaint was pain and discomfort with his smile. Extraoral examination revealed no significant findings, and the patient was cooperative. Intraoral examination revealed poor oral hygiene, generalized gingivitis, malocclusion, carious lesions, unsatisfactory restorations, and hypomineralized AI (Figure 1.A). A panoramic radiograph confirmed these findings (Figure 1.B).

The treatment plan included elimination of infectious foci, hygiene instructions, prophylaxis, endodontic treatment, and direct composite restorations. Given his cardiac history, antibiotic prophylaxis (2 g amoxicillin one hour before invasive procedures) was administered according to the American Heart Association (AHA) guidelines (16). The patient's mother was instructed to administer the medication in the dental clinic waiting room prior to treatment.

Following periodontal treatment, all carious lesions were removed, and temporary direct restorations were applied. After the improvement of oral hygiene and the patient's willingness to cooperate, we initiated aesthetic rehabilitation. Direct composite veneers were placed from premolar to premolar across both dental arches. (composite resin Z350/3M, shades C2B and A1E; Maplewood, Minnesota, USA) ((Figure 1.C).

In the 24-month post-treatment follow-up, both the patient and his mother reported high satisfaction with the results. The patient maintained excellent oral hygiene, and gingivitis was completely resolved.

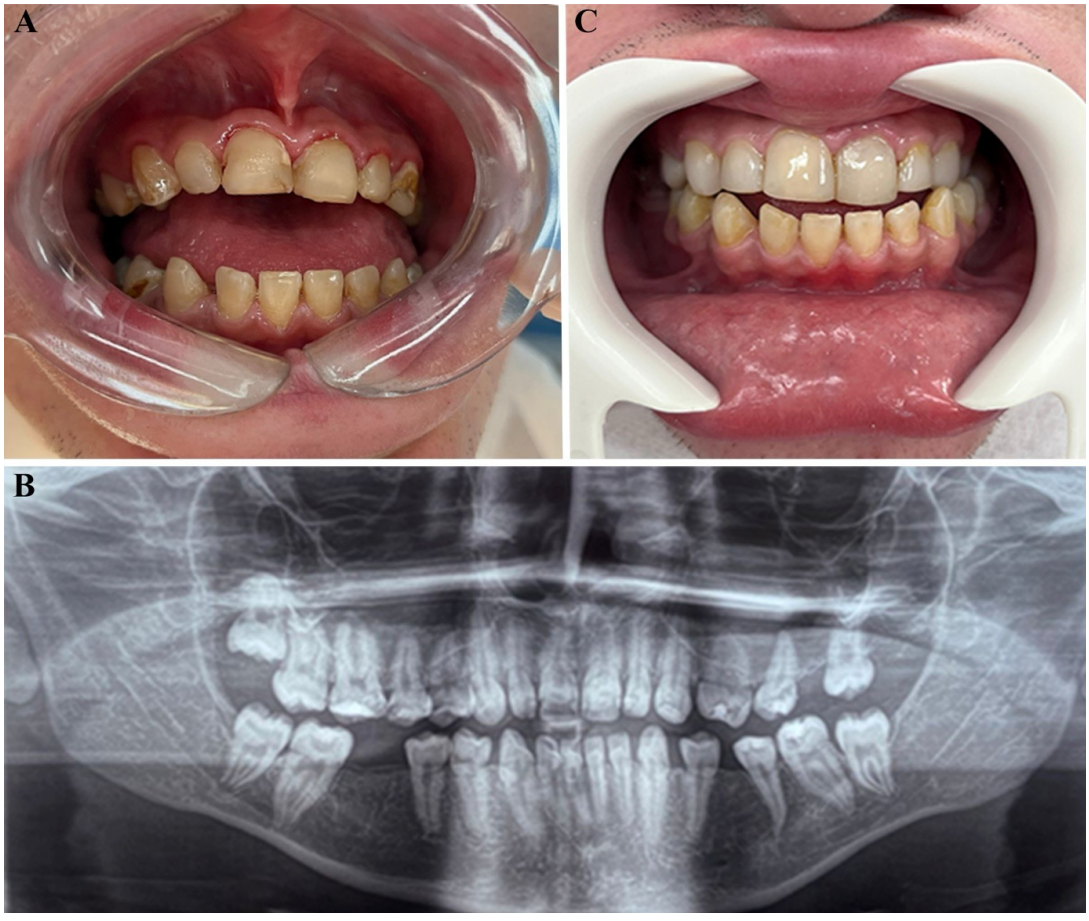

Figure 1. Initial clinical presentation showing generalized gingivitis, carious lesions, unsatisfactory restorations, and hypomineralized amelogenesis imperfecta, with enamel structure loss creating niches for biofilm accumulation (A); Panoramic radiograph of the patient before treatment, revealing significant dental issues, including multiple carious lesions unsatisfactory restorations, and missing teeth (B); final result after rehabilitation with direct composite veneers, showing complete remission of gingivitis, improved oral hygiene, and enhanced smile aesthetics following the proposed treatment for amelogenesis imperfecta (C).

DISCUSSION

Amelogenesis imperfecta demonstrates considerable variety in clinical presentation, ranging from mild discoloration to total enamel degradation across all teeth. It is classified into three types: hypoplastic, hypomature, and hypomineralized (8). The patient in this case exhibited hypomineralized amelogenesis imperfecta, classified as the most severe type.

Hypoplastic AI involves a quantitative alteration in enamel with localized or generalized effects. thickness reduction. Hypomature AI results from a defect in the degradation of enamel matrix protein; it is the mildest form and often goes undiagnosed. Hypomineralized AI, the most severe form, is characterized by reduced mineral content in the enamel, causing pain during chewing and brushing. As a result, it is commonly associated with gingivitis and periodontal disease due to heightened sensitivity and difficulty maintaining oral hygiene (8). The present case described a patient with TOF who had this type of AI.

A recent study investigated the impact of congenital heart disease (CHD) on children's oral health, comparing those with CHD to healthy

children. Key findings indicate a correlation between CHD severity and enamel defects; children with lower oxygen saturation levels exhibited a higher prevalence of enamel hypoplasia and hypomineralization. While reduced oxygen saturation was significantly linked to a greater number of teeth with enamel defects, the study found no significant differences in enamel defects based on whether the CHD was acyanotic or cyanotic, or its hemodynamic significance (17).

Other authors discussed the role of hypoxia affecting ameloblast function, reducing essential enamel proteins and impairing mineralization, which can lead to enamel defects characteristic of amelogenesis imperfecta. These studies highlights the importance of adequate oxygen supply in normal enamel development and suggests that hypoxia may play a role either directly or as a modifier in the pathogenesis or severity of AI (15,17).

Our patient presented two congenital disorders and intellectual deficit, a study evaluated the genetic overlap between autism spectrum disorder, intellectual disabilities, and TOF. While the precise reasons for this overlap were not fully understood, researchers discussed the potential shared molecular pathways impacting both myocyte and axon cytoarchitecture, with a notable enrichment of variants involved in neural cell progenitor proliferation and differentiation. Also they suggest that these genetic variants, besides affecting brain development, may also influence cardiac neural crest cells and cardiac development (3).

In case of patients with cyanotic congenital heart disease corrected with prosthetic material and concomitant amelogenesis imperfecta, the dentist must proceed with extreme caution and diligence in formulating a treatment plan due to the high risk of infective endocarditis (IE). The hypomineralized AI type presents challenges for oral hygiene maintenance, as discomfort during brushing and plaque accumulation occur in cavities resulting from the progressive degradation of enamel. This increases the likelihood of spontaneous IE related to inadequate oral health (8,15).

Transient bacteremia following dental procedures is prevalent, ranging from 58% to 100% in adults and 30% to 76% in children. It has been associated with an increased risk of IE in high-risk patients, such as those with prosthetic heart valves. Odontogenic bacteremia accounts for 10% to 15% of IE cases (18, 19).

According to the 2007 AHA guidelines, antibiotic prophylaxis is recommended for high-risk patients undergoing invasive dental procedures involving manipulation of gingival tissue, periapical regions, or mucosal perforation (16, 20, 21).

In this case, the patient and his mother were educated on the importance of oral health, particularly given the patient's surgically repaired congenital heart disease with a metallic prosthesis, which significantly elevates IE risk.

We faced a cycle requiring careful intervention: hypomineralized AI led to poor hygiene due to pain, but restorative treatments couldn't proceed in a setting of uncontrolled gingivitis. Thus, it was essential to first control gingivitis and improve hygiene before proceeding with restorations. Without treating the AI, however, the patient would continue struggling to maintain oral health, perpetuating the risk. In children with systemic conditions, close monitoring of permanent tooth development is crucial to promptly identify and address enamel anomalies, preventing caries and enamel deterioration (15).

The present report has limitations, as a single case report, the findings cannot be generalized; further studies are required to better understand the relationship between congenital cyanotic heart disease and enamel defects.

CONCLUSION

In congenital heart disease, it is essential to plan multidisciplinary treatment that recognizes potential enamel developmental defects. Preventive measures must be implemented to ensure that these patients oral conditions remain free of infectious foci. Direct composite resin veneers offer both functional and aesthetic benefits, highlighting the necessity of rigorous oral hygiene and preventive measures for these patients.

CONFLICT OF INTEREST: The authors declare that there is no conflicts of interest.

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DATA AVAILABILITY STATEMENT: The data analyzed during this study are partially included in this article, with only the most relevant data being included. Further data and questions can be directed to the corresponding author.

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