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CASE REPORT

Dental and Endodontic Management in a Patient with Familial X-Linked Hypophosphatemic Rickets

Manejo Dental y Endodóntico en un Paciente con Raquitismo Hipofosfatémico Familiar Ligado al Cromosoma X

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ABSTRACT: The term rickets refers to insufficient or retarded mineralization of the osteoide matrix. X-linked hypophosphatemic (XLH) rickets is a rare genetic disorder characterized by biochemical changes in bone mineralization due to inactivation of the phosphate regulating gene and primary defect of the osteoblasts. The aim of this article was to report a clinical case of XLH, its oral manifestations, periapical changes and dental management. A 31-year old woman female patient was referred to the school of dentistry with pain and sensitivity in the teeth. She had a childhood history of rickets, hypophosphatemia and alteration in Vitamin D. In the oral exam, enamel hypoplasia, microdontia, fistula, caries and periapical lesions and periodontal disease were diagnosed. The radiographic and tomographic exams exhibited the presence of periapical lesions involving various teeth with radiolucent images, suggestive of granuloma or periapical cysts. The treatment prioritized the urgency of eliminating pain and removing the foci of infection. Endodontic treatment began in the teeth that had fistula or periapical lesions and in parallel, oral hygiene guidance was provided and periodontal treatment was performed. There was an improvement in the clinical condition with reduction in inflammation and mobility of the teeth. Dentists and health professionals must evaluate the patient as a whole, considering the relations between systemic and oral health. Knowledge of systemic diseases associated with rickets and their characteristics is essential for making a correct oral diagnosis and planning the dental treatment.

KEY WORDS: familial hypophosphatemic rickets. dental care. prevention and control. endodontic. tooth calcification.

INTRODUCTION

Rickets is characterized by changes in the levels of serum calcium and phosphate, bone growth and deficient mineralization, in addition to deformities, predominantly of the long bones. Hypophosphatemic rickets results in an increase in the excretion of phosphate through the proximal renal tubule. The genetic hereditary pattern of familial hypophosphatemic rickets may be linked to the autosomal dominant or autosomal recessive X chromosome. The best-known pattern is the XLH which, despite being rare, accounts for 80 % of the existent cases in a proportion of 1:20.000 individuals (Baroncelli *et al*., 2012; Pavone *et al*., 2015).

The main clinical manifestations of XLH are low stature, deformities in the lower limbs (bowed legs), widening of the metaphyseal region, rachitic rosary (prominence of the costochondral junction) and in the skull, flattening of the frontal and parietal bones is observed, as well as neonatal convulsions, decreased muscle tone and increase in infections (Baroncelli *et al*.).

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XLH is diagnosed by the medical and family history, physical, biochemical and radiographic exams (Chanchlani *et al*., 2020; Gentile & Chiarelli, 2021), by identifying reduced or normal levels of 1,25-Di-hidroxyvitamin D (vitamin D), low levels of phosphate, high levels of FDF23 and high or normal levels of alkaline phosphatase in patients with XLH (Baroncelli *et al*.; Carpenter, 2012). Radiographic analysis exhibits loss of definition, increase in the zone of calcification of the cartilaginous plate, and "short bone" aspect with increase of bone trabeculae (Pavone *et al*.).

The main clinical dental manifestation of XLH is the formation of recurrent spontaneous abscesses and facial cellulite in non-carious teeth in the same individual in both primary and permanent dentitions. Deficient dentin mineralization, characteristic enamel defects and delay in tooth eruption are also common in patients with XLH. In panoramic and periapical radiographs it is possible to verify teeth with wide pulp chambers (taurodontia) and prominent horns that extend up to the amelo-dentinal junction, in addition to lower radiopacity of enamel and dentin, short roots and open apexes. These defects may be caused by the exposure of odontoblasts to hypophosphatemia and disturbances in intrinsic cells associated with the PHEX gene. The pattern of mineralization is characterized by porosity and lower mineral density close to the pulp linked to low availability of calcium and phosphate in the periods of enamel formation. Pulp necrosis occurs at the time when root formation is incomplete, thus justifying the permanence of open apexes. Histological sections have demonstrated microfissures in abnormal enamel and dentin with deficient mineralization in the intertubular space. Deficient mineralization and the structural defects in dentin are observed by means of scanning electron microscopy (Vital *et al*., 2012; Gjorup *et al*., 2018; Bradley *et al*., 2021; Gentile & Chiarelli) and by microCT (Ribeiro *et al*., 2015).

A variety of systemic oral signs and symptoms are characteristic of XLH, therefore, treatment must be individualized according to the dental urgencies. It is important to remember that the formation of spontaneous, recurrent abscesses is common in these individuals. Therefore, endodontic treatment and complete elimination of microorganisms are the main focus of dental treatment.

The aim was to report a clinical case of a patient with X-linked hypophosphatemic rickets, and their oral and dental manifestations, and the dental treatment performed.

CASE REPORT

A 31-year old woman female patient was admitted to the hospital of the clinics at the Universidade Federal do Paraná - UFPR (Curitiba- Brazil). The medical diagnosis of hypophosphatemic rickets had been made in early childhood by physical, laboratory and radiographic exams. She was referred for dental treatment in the school of dentistry of the UFPR. The patient's chief complaint was "pain and sensitivity in the teeth". The patient brought the computed tomography and panoramic radiography exams with her.

The medical diagnosis of hypophosphatemic rickets had been made in early childhood by physical, laboratory and radiographic exams. Physical examination revealed, bulging of the frontal bones of the face was observed, in addition to flattening of the parietal bones and bone deformity of the upper and lower limbs, with slightly bowing and genu varum. During dental anamnesis, the patient reported that she received medical follow-up and did not use any systemic medication.

In the panoramic radiograph, radiolucent periapical lesions involving several teeth were observed, suggestive of granuloma and periapical cyst, bilateral absence of third molars, and periodontitis (Fig. 1). The clinical aspects observed were enamel hypoplasia, supragingival calculus, microdontia of tooth 12, caries on the vestibular surface of tooth 31, unilateral crossbite on the right side (Fig. 2) and fístula in the alveolar mucosa of tooth 22 (Fig. 5A. In the cone beam computed tomograph, extensive bone lesions were observed in tooth 22, and in the mandibular central and lateral incisors and canines (Figs. 3A-C).

Fig. 1. Panoramic radiograph taken at beginning of treatment. Note the periapical lesions in maxillary and mandibular central and lateral incisors, microdontia of tooth 12, alveolar bone loss of tooth 27 and provisional restorations in mandibular incisors.

Periapical radiographs were taken using exposure time of 0.2 s (70 kVp and 7 mA) of the maxillary central and lateral incisors and mandibular central and lateral incisors and canines (Figs. 4A-C). The patient reported that the mandibular central and lateral incisors had been treated with endodontic dressings since the time of adolescence. Another radiographic finding suggested that teeth 41 and 11 had incomplete rhizogenesis. Exams for endodontic purposes involving percussion, palpation and pulp sensitivity tests indicated that the pulp of these teeth was compromised.

Fig. 2. Clinical aspect of enamel hypoplasia, gingivitis in mandibular anterior teeth and unilateral crossbite on right side.

Periodontal exam detected periodontal pockets in specific sites of teeth 26 and 27, with tooth mobility grade 3. Teeth 31, 41 and 22 showed grade 2 dental mobility and absence of periodontal pockets. Gingivitis was observed in the mandibular anterior teeth 31 to 41. Supra and subgingival calculus was observed in teeth 33 to 43. After obtaining the data and making critical analysis of the patient's oral condition, a treatment plan was established based on the scale of priorities.

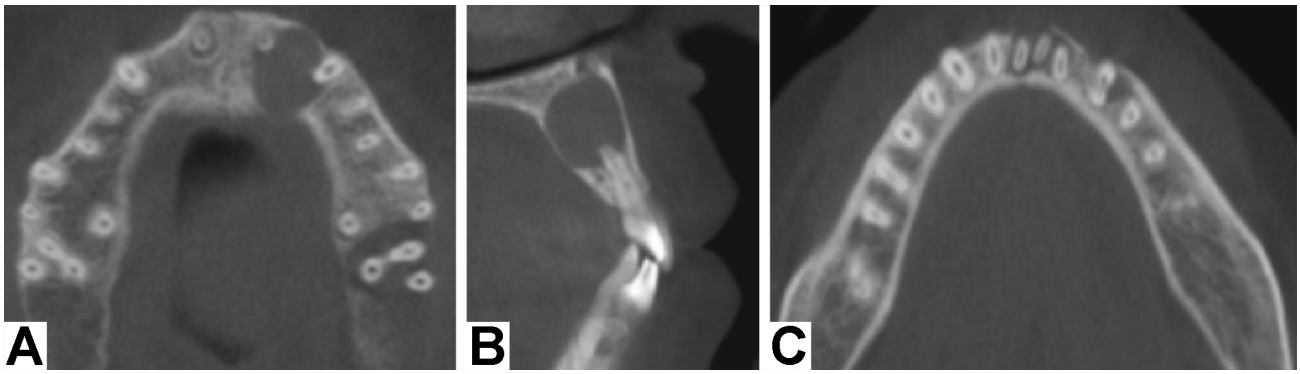

Fig. 3. Cone beam computed tomography images in axial and sagittal sections in maxilla and axial section in mandible. Hypodense bone lesion involving roots of teeth 21 and 22 (A); narrowing of vestibular and palatal bone corticals (B); bone loss around roots of tooth 27 and in mesial region of 26 (A). Hypodense bone lesion on roots of mandibular central and lateral incisors and canines in mandible.

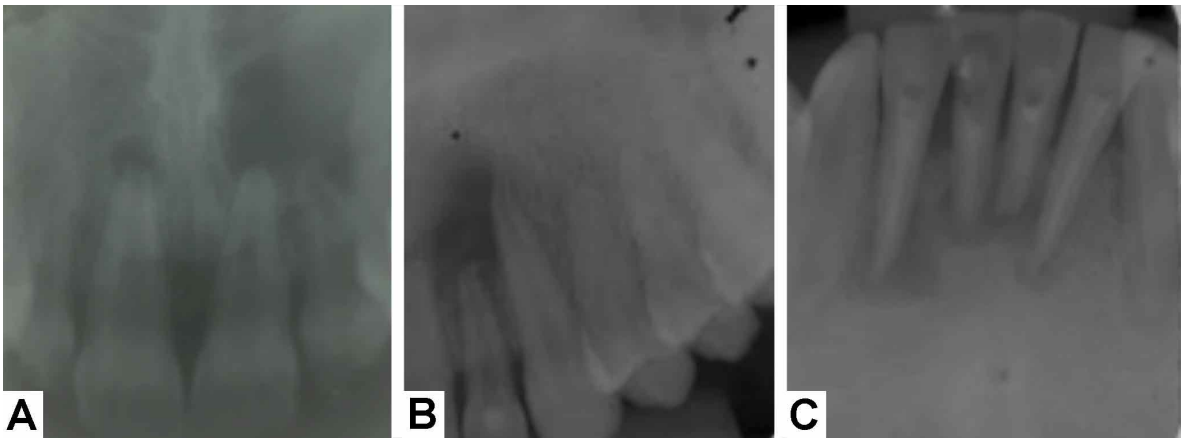

Fig. 4. Radiolucent periapical lesions in maxillary and mandibular incisors and canines at the beginning of endodontic treatment (A and B). Wide root canal in maxillary central incisors and (A) short roots, with open apexes in teeth 31 and 41 (C).

Endodontic access to teeth 11, 21 and 22 was initiated, and the purulent secretion was drained from teeth 21 and 22 (Fig. 5B). The crown-down mechanical preparation technique was performed by means of using the ProT (MK LIFE, Brazil) rotary system, under constant irrigation with 1 % sodium hypochlorite, and final irrigation with 17 % EDTA. Teeth 21 and 22 were cleaned until the flow of exudate was controlled. As intracanal medication, the Ultracal XS (Ultradent Products, Inc. USA) used was injected until the entire extension of the root canal was filled.

In a second time interval, the mandibular central and lateral incisors and canines, and tooth 12 were submitted to the same steps and techniques of chemical-mechanical preparation. Parallel to endodontic treatment, oral hygiene was performed, the patient was provided with oral hygiene instructions (toothbrushing technique and use of dental floss). Formulas and fissures in the maxillary and mandibular premolars were sealed, and root scraping and planing were performed.

The intracanal dressings were maintained and changed until cicatrization of the tissues occurred, and purulent exudation from teeth 21 and 22 was eliminated so that the canals could be filled. The partial results of endodontic treatment demonstrated reduction in the periapical lesions (Fig. 6A) this meant that contamination and the number of bacteria present had diminished. The patient reported regression of the pain on vestibular palpation of teeth 21 and 22, and absence of symptoms and exudation. The root canals were filled by means of the lateral condensation technique followed by vertical condensation. 6 B).

It was not possible to fill the mandibular teeth that remained with inflammatory exudate and without regression of the periapical lesions after changes of the intracanal dressing for the period of one and a half years (Fig. 6 C; Teeth 31 and 41 continued with grade 2 mobility). In an attempt to control mobility and preserve the bone tissue, fixed splinting was performed with composite resin. The patient has been maintained with splinting and oral hygiene care. After performing the endodontic procedures end with periodontal maintenance, a favorable prognosis of the case is expected. The patient will continue to be under treatment until conclusion of the proposed treatment has been reached.

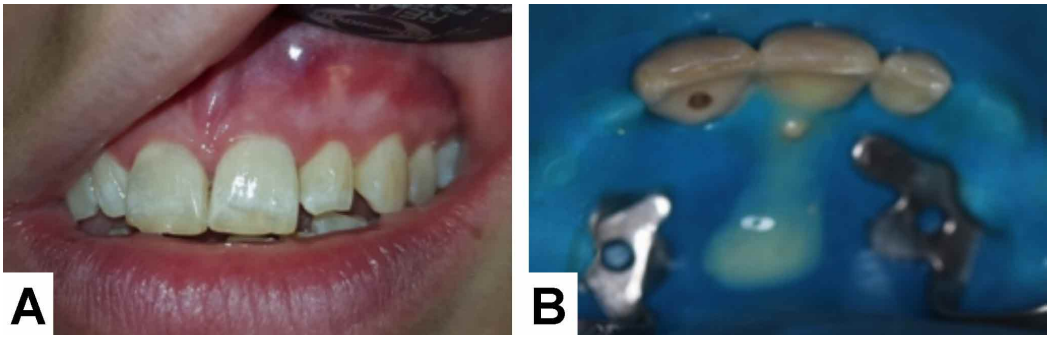

Fig. 5. Translucence in crowns of teeth 12, 11, 21 and 22 and presence of fístula in alveolar mucosa of 22 (A). Drainage of purulent secretion from tooth 21 during first session of endodontic treatment (B).

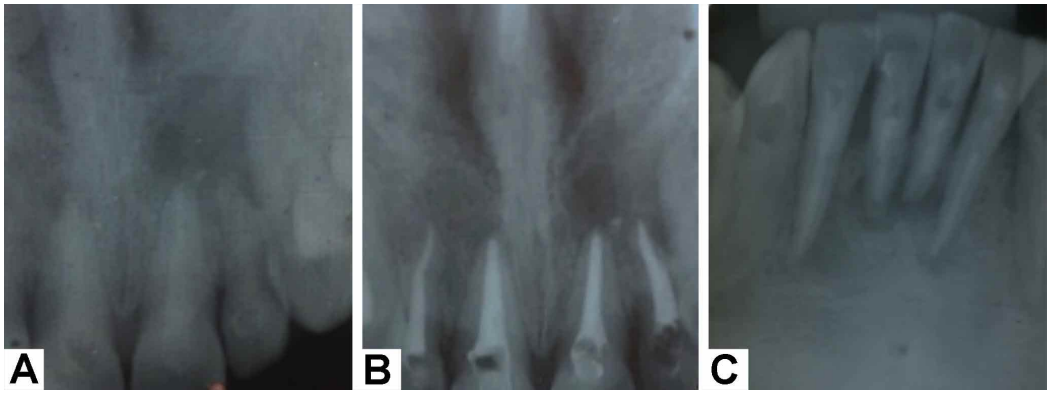

Fig. 6. Reduction in periapical lesions of incisors after 1 and 1/2 year of follow-up (A). Filling of root canals of maxillary central and lateral incisors (B). Mandibular central and lateral incisors and canines with intracanal medication. There was no regression of the periapical lesions after treatment (C).

DISCUSSION

XLH is common and affects 1:20.000 individuals according to a world estimate (Baroncelli *et al*.). The classical clinical signs of XLH in bone growth observed in the patient of the present case were similar to the findings that have been reported by otherauthors (Omdurman *et al*., 2013; Gjorup *et al*.; Bradley *et al*.). The patient reported having constant muscle fatigue and pain in bone and joints in the lower limbs. Adults with XLH are predisposed to having muscle fatigue, osteomalacia, pseudofractures and fractures, pain, bone and joint rigidity, reduction in joint mobility and physical function (Lecoq *et al*., 2020).

The biochemical exams revealed hypophosphatemia, normal levels of calcium and sodium, high levels of alkaline phosphatase, and reduced rate of renal tubule resorption. Lower phosphate absorption by the kidneys implies their greater release from the body, reducing the serum phosphate levels. Whereas alkaline phosphatase is a marker of bone activity in rickets, and when elevated, indicates an increase in bone neoformation and remodeling (Veilleux *et al*., 2012).

Periapical lesions, fístula, caries, gingivitis and periodontitis, and enamel hypoplasia were the main oral findings of XLH in the present case report, therefore treatment was performed to heal these diseases. Enamel hypoplasia, width of the pulp chamber and pulp horns that extended up to the amelodentinal junction predisposed the patient to the development of dental fistulas and abscesses. This occurs secondarily to bacterial invasion into the pulp by means of microfissures present in enamel and dentin. This characteristic resulted from greater access of microorganisms to the dental pulp and could reduce the dentinal resilience (Vital *et al*.; Hernández & Laguna, 2013).

The initial dental treatment consisted of performing urgency treatments and eliminating the foci of infection, in order to subsequently perform the rehabilitation treatment. The endodontic treatments were prioritized according to the protocol recommended by Andersen *et al*. (2012) and Sabandal *et al*. (2015). Infected pulp and root canals are known to be considered a continuous source of infection of the periodontium (Andersen *et al*.; Rabbani *et al*., 2012).

The safest method for decontaminating the root canal is by means of instrumentation, irrigation and aspiration during chemical-mechanical preparation, thus removing a large quantity of bacteria. However, due to the anatomic conditions such as regions of isthmus, ramifications and dentinal tubules, the microorganisms may persist on the dentinal walls of the root canal. Successful endodontic treatment depends on diminishing the number of microorganisms and prevention of re-infection; therefore, disinfection is an important stage in guaranteeing the success of treatment. Calcium hydroxide is the intracanal medication of choice. Its application may significantly eliminate the microorganisms and repair the damaged tissues, due to its high pH. It is biocompatible, has antibacterial properties, promotes destruction of the cell membrane and protein structure of bacteria, and helps with peri-radicular cicatrization (Kim & Kim, 2014). Its efficacy depends on microbial activity, time of permanence in the canal, application of medication throughout the entire extension of the canal prepared, and infection of the microorganisms involved in the canal (Duque *et al*., 2019).

Bacteria capable of growing in a pH of 9-10 may survive in the root canal system even in the presence of calcium hydroxide. There is a reduction in the bacterial load, but this factor explains the limited efficacy of intracanal medication in the complete elimination of bacteria (Jia *et al*., 2019).

In the present case, due to the deficient mineralization and abnormal formation of dentin and enamel, the patient had healthy maxillary central and lateral incisors, and spontaneous periapical lesions and abscesses, so that the pulp of these teeth was contaminated by microorganisms and symptoms characteristic of endodontic disturbances. Frequent changes of the intracanal dressings are necessary as well as clinical and radiographic follow-up to guarantee reduction in intracanal contamination. Another factor that could interfere in the regression of periapical lesions is occlusal trauma due to premature contact during mastication.

Factors such as age, uni- or multi-rooted teeth, occlusion and initial periapical conditions may interfere in periapical cicatrization (Lee *et al*., 2012). In the present case, the intracanal medication was changed every 2 months, and there was regression of the ample periapical lesion that involved teeth 21 and 22. However, the same did not occur with the periapical lesions of the mandibular teeth.

The short roots, incomplete closure of the

foramina of the central incisors and permanence of periapical infection in all of the mandibular incisors for years, may have contributed to failure of the treatment because endodontic access occurred during adolescence. Finally, the dental mobility associated with the unilateral crossbite with occlusal trauma contributed to this outcome. We recognize that long periods of dental treatment demotivate the patients and make it difficult for them to adhere to treatment, however, keeping appointments, consultation and cooperating with treatment are the patients responsibility. Correction of the crossbite and occlusal trauma, patient's cooperation with regard to more frequent changes of dressings performed in the correct manner may be alternatives that would help with reducing the periapical lesions.

Periodontal treatment was performed during the period of exchanging the intracanal dressings, by means of supragingival scraping and root planing of all the teeth, based on the literature of Andersen *et al*. The patient is undergoing support periodontal therapy with the goal of diminishing dental mortality and recurrence of periodontal disease. At the re-consultations, periodontal exam was performed, and when necessary periodontal scraping and planing of the roots of teeth involved were performed. The patient was again motivated with regard to oral hygiene and adequate plaque control.

Topical fluoride application and sealing of the occlusal surface of all posterior teeth was performed, in compliance with the protocol of Vital *et al*. and Sabandal *et al*. with the exception of covering the metal ceramic crown in posterior teeth due to the high cost and financial condition of the patient making this impossible. Tooth 27 was not extracted because the patient refused to have this performed.

A nigh level of prevention with oral hygiene, topical fluoride application and sealing of fossulas and fissures is recommended (Sabandal *et al*.). In cases of dentin exposure or enamel malformation, coronal coverage of anterior teeth (composite resin) and posterior teeth (metal ceramic crown) is indicated (Foster *et al*., 2014). In adults with periodontal disease, clinical follow-up may enable identification of periodontal pockets and root exposures.

The main focus of dental treatment in patients with XLH is to prioritize urgent treatment needs. There is frequent presence of spontaneous abscesses in non-carious teeth, deficient mineralization in dentin, structural enamel defects, short roots and open apexes, with difficult resolution of periapical lesions. Therefore, each case must be individually evaluated so that the priorities can initially be treated, with preference for eliminating foci of infection and thereby improve the systemic and oral conditions of the patient.

CONCLUSION

Based on this case report, it was possible to conclude which the important aspects of the oral condition of patients with XLH were, for dental surgeons to observe.

Recognition of the dental manifestations is fundamental for performing a correct diagnosis and treatment plan.

The main dental manifestations are malformation of enamel and dentin, wide pulp chamber, development of abscesses and periapical lesions, in the absence of caries, short roots and open apexes.

The success of endodontic treatment is effective provided that the infection of periapical tissues can be eliminated so that cicatrization can occur. Therefore, factors such as age, uni- or multi-rooted teeth, occlusion, presence of periodontal disease and initial periapical conditions may interfere in a satisfactory outcome.

SELEME, C. B.; MURAKAMI, G. J. C.; LIMA, M. L. G.; MACIEL, J. V. B.; DE LIMA, A. A. S.; DE ARAÚJO, M. R. & MACHADO, M. A. N. Manejo dental y endodóntico en un paciente con raquitismo hipofosfatémico familiar ligado al cromosoma X. *Int. J. Odontostomat., 16(1)*:81-87, 2022.

RESUMEN: El término raquitismo se refiere a la mineralización insuficiente o retardada de la matriz osteoide. El raquitismo hipofosfatémico ligado al cromosoma X (XLH) es un trastorno genético caracterizado por cambios bioquímicos en la mineralización ósea debido a la inactivación del gen regulador del fosfato y al defecto primario de los osteoblastos. El objetivo de este artículo fue reportar un caso clínico de XLH, sus manifestaciones orales, cambios periapicales y manejo dental. La paciente, una mujer de 31 años, acudió a la Clínica de Semiología de la UFPR con dolor y sensibilidad en varios dientes. Tenía antecedentes infantiles de raquitismo, hipofosfatemia y alteración de la vitamina D. En el examen oral se diagnosticó hipoplasia del esmalte, microdoontia, fístula, caries y lesiones periapicales y enfermedad periodontal. Los exámenes

radiográficos y tomográficos mostraron la presencia de lesiones periapicales en varios dientes con imágenes radiolúcidas, sugestivas de granuloma o quistes periapicales. El tratamiento priorizó la urgencia de eliminar el dolor y remover los focos de infección. Se inició tratamiento de endodoncia en los dientes que presentaban fístula o lesiones periapicales y paralelamente se brindó orientación de higiene oral y se realizó tratamiento periodontal. Hubo una mejoría en la condición clínica con reducción de la inflamación y movilidad de los dientes. Los odontólogos y profesionales de la salud deben evaluar al paciente como un todo, teniendo en cuenta las relaciones entre salud sistémica y oral. El conocimiento de las enfermedades sistémicas asociadas al raquitismo y sus características es fundamental para realizar un correcto diagnóstico oral y planificar el tratamiento odontológico.

PALABRAS CLAVE: raquitismo hipofosfatémico familiar, cuidado dental, prevención y control, endodoncia, calcificación dental.

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