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Case Report OMICS International

Endodontic Management of Patients With X Linked Hypophosphatemic Rickets: Case Series Report

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Abstract

Introduction: Familial hypophosphatemic rickets, the most common cause of inherited rickets, is in most cases transmitted as an X-linked dominant trait resulting from a mutation of the phosphate-regulating gene with homologies to endopeptidases on the X chromosome gene. This condition impairs bone, cement and dentin mineralization, resulting in skeletal and oral manifestations. Patients present spontaneous tooth abscesses that occur without any history of trauma or dental decay.

Methods: Two XLH patients were referred to the endodontic department of Charles Foix Hospital. They reported history of multiple dental abscesses. The clinical and radiographic examination showed periapical lesions of central left mandibular incisor and first and second maxillary left molars. Furthermore, the radiographic examination showed enlarged pulp chambers, thin enamel and dentin. Conservative endodontic treatment was performed in the necrotic teeth.

Results: The clinical and radiographic follow-up showed a bone healing in process in these two cases.

Keywords: Dental pulp necrosis; Endodontics; Familial hypophosphatemic rickets; Periapical diseases; Rare diseases

Introduction

Familial hypophosphatemic rickets, the most common cause of inherited rickets, is in most cases transmitted as an X-linked dominant trait resulting from a mutation of the PHEX gene (phosphate-regulating gene with homologies to endopeptidases on the X chromosome) [1,2]. PHEX encodes an endopeptidase, predominantly expressed by osteoblasts, osteocytes and odontoblasts [3]. PHEX has been suggested to be involved in the inactivation of fibroblast growth factor-23 (FGF-23), a phosphaturic hormone, thereby controlling its hyperphosphaturic effect. PHEX mutation causes renal loss of phosphate, increased alkaline phosphatase activity, normal serum calcium levels, with normal or low serum levels of vitamin D [4]. It has been previously shown that the proteins of the extracellular matrix (ECM) were abnormally distributed in dentin, including the acidic proteins matrix extracellular phosphoglycoprotein (MEPE), Dentin Matrix Protein 1 (DMP1), and osteopontin (OPN). Furthermore, some peptides derived from the abnormal cleavage of these proteins have been identified in the ECM and particularly peptides enclosing the acidic serine- and aspartate-rich motif (ASARM) which is a strong inhibitor of the mineralization process [5,6]. Thus, the alteration of the post-translational processing of these proteins or their partial degradation seems to be a key factor in the formation of the pathological hypophosphatemic dentin.

Clinically, X-linked hypophosphatemic rickets is associated with severe bone deformities, especially bowing of the legs, impaired growth, short stature, and severe dental troubles. In fact, patients present spontaneous tooth abscesses that occur without any history of trauma or dental decay. Treatment of rickets with vitamin D and phosphate supplements has been shown to improve the dental manifestations in some [7], but not all patients [8,9]. Beginning in the 1970s, 1-hydroxylated forms of vitamin D have progressively replaced vitamin D itself for the treatment of hypophosphatemic rickets. A combination of Phosphates and Calcitriol is the current standard therapy for familial hypophosphatemic vitamin D–resistant rickets in France [10]. Patients who received no treatment before puberty display a severe dental condition, whereas those who received phosphate supplements along with 1α-hydroxyvitamin D3 from infancy present a correct to normal dental status as compared to reference ranges in the healthy age-matched population.

Decision-making in these patients could be difficult since the teeth seem normal. Radiographically, the enamel layer appears thinner while the dentin layer is more radiolucent. Some clinical studies reported the absence of enamel alterations in subjects affected by XLH [11]. However, Cremonesi et al., have shown by scanning electron microscopy, an irregular structured, slightly hypoplastic enamel in XLH teeth when compared to the images of control group [12].

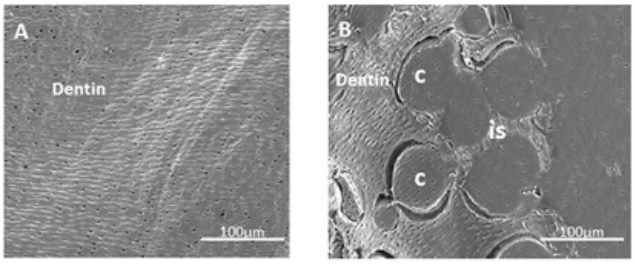

Figure 1: Dental features of hypophosphatemic rickets. Tooth sections observed by Scanning Electron Microscopy (SEM) reveal A: homogenous dentin mineralization with regular tubules for control and B: impaired hypophosphatemic dentin presenting calcospherites (C) between nonmineralized interglobular spaces (IS).

In both deciduous and permanent teeth, pulp chambers could be enlarged, resembling taurodontism and prominent pulp horns extend up to the dentino–enamel junction [13]. Histologically, hypophosphatemic patients have been reported to display large interglobular spaces in the dentin consequent of a lack of fusion of calcospherites in the circumpulpal dentin (Figure 1) [5,14]. The mantle dentin is usually unaffected [15] Extensive enamel cracking and fissuring can be observed on histologic sections, as well as dentin mineralization defects. The endodontic infections are believed to result from rapid dental pulp necrosis, a consequence of the abnormal dentin mineralization and enamel cracks that allow invasion of the pulp by oral bacteria. Bacterial invasion of the pulp results in pulpal necrosis and infection, constituting a host defense reaction in the periradicular tissues that prevents dissemination of pathogens beyond the root canal. Endodontic treatment is performed to control the infection, to allow healing of the periradicular tissues. Mechanical instrumentation coupled with irrigation of the root canal with sodium hypochlorite dramatically reduces the bacterial load in the root canal. Then, the root canal is filled with gutta-percha and an endodontic sealer. The present study reports endodontic management of two unrelated patients with XLH.

Case Report

Case #1

A 15-year- old boy was referred to the endodontic department of Charles Foix hospital (Ivry sur seine France). He was first seen in the reference center of rare diseases at Kremlin Bicêtre hospital (Le Kremlin Bicetre, France). There, the patient and his parents reported a history of multiple abscesses in the mandibular incisor area, repetitively treated by amoxicillin and metronidazole. The medical history of the patient revealed a familial history of X-linked hypophosphatemic rickets, which has been transmitted by his affected mother and diagnosed at walking acquisition. Since the diagnosis, he had been treated with phosphate supplements and calcitriol, with irregular compliance. The dental history revealed dental abscesses in deciduous teeth and a two-arch multibrackets fixed orthodontic treatment from 12-14 years.

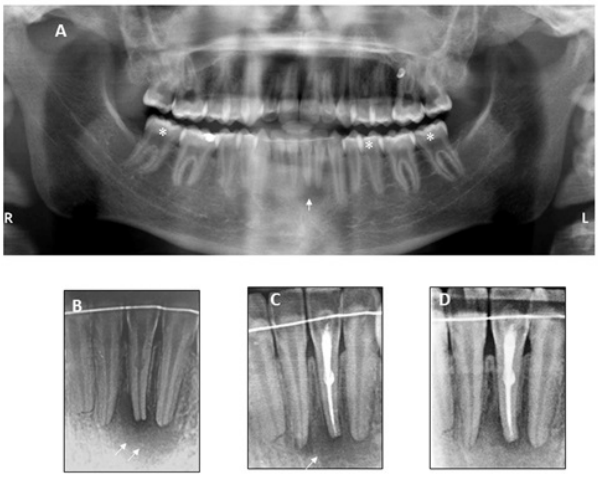

Figure 2: (A) Orthopantomograph of Patient 1 showing characteristic dental manifestations of XLH including: a normal (but slightly thinner) enamel layer, a radiolucent dentin layer with enlarged pulp chambers (asterisks *) and prominent pulp horns, and apical periodontitis associated with the mandibular incisors (arrows). (B) Periapical radiograph of mandibular incisors from a patient with XLH. Note for the left central incisors the large periapical lesion associated with internal root resorption and apical root resorption. (C) Postoperative radiograph showing endodontic filling of the canal and the resorptive lacunae. (D) At the 6-month post-operative visit, the patient reported no inflammatory experience. No clinical symptom was detected and the periapical radiograph revealed that the apical lesion size was reduced.

On physical examination, the patient displayed short stature and bowed legs. The oral examination showed normal periodontal tissues and an orthodontic contention was fixed on the lingual surface of mandibular incisors and canines. The left lower central incisor did not response to thermal and electric pulp tests [16], whereas other teeth responded positively to these tests. Panoramic examination showed premolars and molars with large pulp chamber, characteristic of dental manifestations of XLH (Figure 2A). Furthermore, large radiolucent area were observed on the mesial aspect of both second upper molars. Periapical radiograph of the left lower central incisor revealed the presence of a resorption lacunae in the middle part of the root canal (Figure 2B). Two different X-ray incidences confirmed an internal resorption. Thus, an endodontic lesion was diagnosed on the left lower central incisor and an endodontic treatment was planned. The endodontic therapy of the necrotic tooth was performed under operative microscope. The left central incisor was isolated with rubber dam. The difficulty here was to deal with the lingual orthodontic contention. Then, the access cavity was performed under operative microscopy using rotary access cavity burs. Ultrasonic tips were used for access refinement. The visual access and superior control that ultrasonic tips provide during access procedures make them a most convenient tool. Granulation tissue located inside the resorption lacunae was removed and surprisingly the bleeding stopped rapidly. Root canal shaping was performed conventionally under an abundant cleaning using 3% sodium hypochlorite. The root instrumentation was completed using nickel-titanium rotary files (ProTaper System; Dentsply Maillefer, Ballaigues, Switzerland) up to an F3 finishing file.

The apical diameter was determined at 35 with a manual K-file. Then a step back was used to prepare this apical part of the root canal. The working length was electronically (Propex II Dentsply Maillefer, Ballaigues, Switzerland) and radiographically determined. The irrigation solution used was 3% stabilized sodium hypochlorite (Parcan, Septodont Saint Maur des fosses, France) and was activated using ultrasonic passive activation tips (Irisafe, Acteon Satelec, Merignac, France). At the end of shaping and cleaning, the root canal could be dried and the decision to fill was made. The root canal was filled for the apical third with warm Gutta percha compaction (Calamus Dual, Dentsply Maillefer, Ballaigues, Switzerland). Then, the middle and coronal parts of the canal were backfilled with warm gutta percha gun Calamus Dual, Dentsply Maillefer, Ballaigues, Switzerland). Glassionomer cement was used to fill the cavity access and a dental composite was placed within 30 days (Figure 2C). At the 6-month post-operative visit, the patient reported no inflammatory experience. No clinical symptom was detected and the periapical radiograph revealed that the apical lesion size was reduced (Figure 2D).

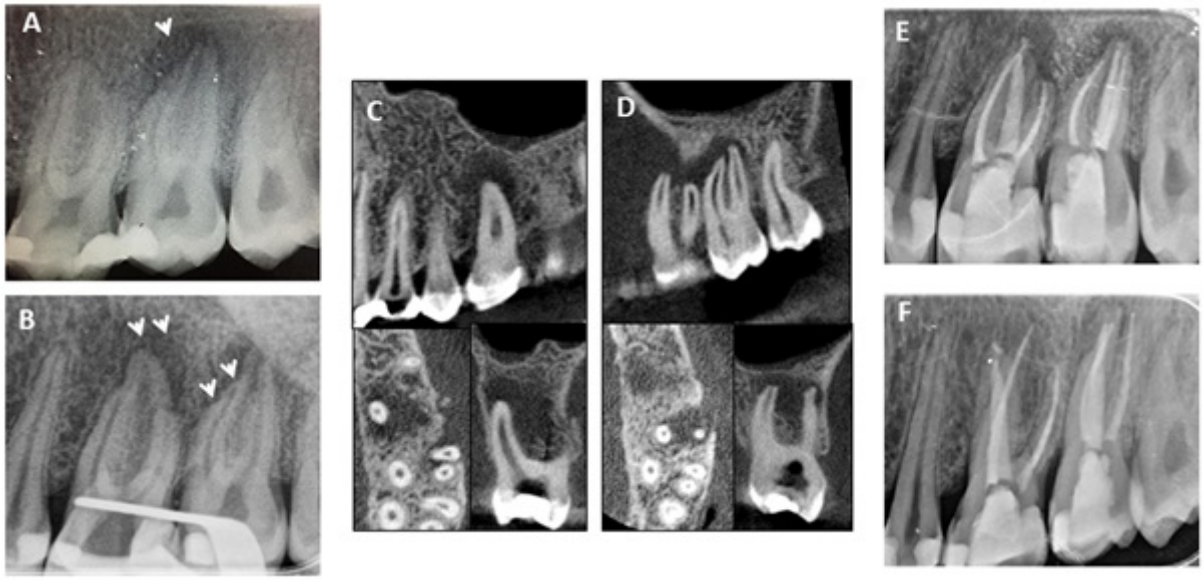

Figure 3: (A) Preoperative periapical radiograph showing a periapical lesion on the second upper left molar. (B) The patient missed the endodontic treatment appointment and a new periapical radiograph 2 months after showed a periapical lesion on the first upper left molar (arrows). (C) Sagittal, axial and coronal CBCT slides of the first upper left molar confirm the presence of large apical lesion on the palatal root (CBCT PAI: 5). (D) Sagittal, axial and coronal CBCT slides of the second upper left molar show extensive apical lesion of buccal and palatal roots (CBCT PAI: 5 +D). (E, F) The follow up at 6 months and 1-year showed progressive periapical healing evidenced by i) the disappearance of the clinical symptoms, and ii) the reduction of the size of the lesions.

Case #2

A 35 year old male patient was referred to the endodontic department of Charles Foix hospital (Ivry sur seine France) for the endodontic management of the first and second left maxillary molars (26 and 27). The intra oral examination revealed a gingiva globally sound. The patient reported recurrent abscesses with fistulae in this left posterior area with a small swelling associated with mild discomfort. He had rarely needed antibiotics since the sinus tracts were often drained. At the time of the oral examination, the fistulae had been resorbed. Thermal and electric pulpal tests revealed that both 26 and 27 were necrotic. The periapical radiograph showed large periapical lesions for 27 and indicated external root resorption on the mesiobuccal root of 27 (Figure 3A and Figure 3B). The patient missed his endodontic appointment and came back 2 months later. The new periapical radiograph showed a periapical lesion on the first upper left molar. In this case, a tridimensional examination by Cone Beam Computerized tomography was performed in order to evaluate:

- The size of the lesions and
- The presence of external root resorption.

This three-dimensionnal exam showed the presence of large lesions interesting all roots of 27 (Figure 3C and Figure 3D). Concerning 26, axial slides showed a bone perforation on the buccal size and a periapical lesion. According to the treatment plan, endodontic treatment was performed under operative microscope for 26 and 27. All steps of the treatment were similar to those explained above. However, at the end of shaping and cleaning, the root canal could not be dried. A Ca $(OH)_2$ intracanal medication was placed during 2 weeks to allow the canal to dry. Then, the root canal was filled for the apical third with warm Gutta percha compaction (Calamus Dual, Dentsply Maillefer, Ballaigues, Switzerland). Then, the middle and coronal parts the canal were backfilled with warm gutta percha gun Calamus Dual, Dentsply Maillefer, Ballaigues, Switzerland). Glassionomer cement was used to fill the cavity access. The follow-up at 6 months and 1-year showed progressive peripapical healing evidenced by:

- The disappearance of the clinical symptoms, and
- The reduction of the size of the lesions (Figure 3E and Figure 3F).

Discussion

The existence of periapical lesions in XLH patients had been shown to be a consequence of the structural dental defects observed at the microscopic level [17]. These defects create a way for microorganisms or toxic substances to the pulp, causing spontaneous necrosis and dental abscesses [11,18]. The present study showed that the anterior teeth of a 15-year old XLH patient was affected, which is consistent with the previous study of McWhorter and Seale [19]. In this study, 57% of the abscesses involved an anterior tooth and 83% of the patients first developed an anterior tooth abscess. Chaussain - Miller et al. have shown that well-treated patients with 1α-$(OH)D_3$ and phosphorus during growth displayed less dental manifestations including less dental abscesses [20]. Although the therapeutic improvement of phosphate and vitamin D metabolism normalizes the dental status of XLH patients, some alterations remain detectable even in early treated, compliant patients, especially an abnormally high pulp area/tooth ratio of primary and permanent teeth, prominent pulp horns on deciduous molars, and, less frequently, prominent pulp horns and enlarged pulp chambers on permanent teeth. In the present clinical cases, the medical examination revealed that the patients were not-well treated meaning the chemical therapy was not well followed. This observation can explain the presence of abscesses in these patients. Local prophylactic measures have been proposed as a complementary but mandatory treatment to improve dental defects. Prophylactic covering with metal crowns and extraction have been accepted as a preventing treatment in the primary dentition but are considered rather invasive for permanent teeth [21]. More recently, Douyere et al. proposed the appliance of fluid resin composite associated with a self-etching system to all primary molars as a preventive therapeutic treatment and may be extended to the permanent teeth [22]. Because of the low viscosity of the resins, this procedure allows to seal pits and fissures and avoids bacterial penetration through enamel to dentin and pulp.

Managing resorptive lesions can be challenging with unknown outcomes [23]. Success depends on type of resorptive lesion (internal vs external resorption), location of lesion and size of the lesion. Treatment of root resorption is dependent on the etiology. In case where the resorption is due to pulpal necrosis nonsurgical pulp therapy is performed. Complete chemomechanical preparation is considered as an essential step in root canal disinfection. Use of concentrated sodium hypochlorite has been shown to be the most effective of antibacterial agent. The disinfection is improved with ultrasonic passive activation [24]. However, total elimination of bacteria is difficult to accomplish. A $Ca(OH)_2$ intracanal medicament may help to enhance bacterial elimination between appointments. Interestingly, more recent studies have advocated the root canal filling as soon as the 3 following parameters are respected: canal shaped and disinfected, dried canal, no pain. Indeed, no significant difference has been shown between one and multiple visits. Thus, in the case of internal root resorption, calcium hydroxide removal out of the lacunae could be incomplete and so detrimental for the sealing.

In these two cases, the follow-up becomes mandatory to intercept any new periapical lesion. Indeed, as the dentin is still porous the risk of bacterial invasion remains high and the coronal seal must be optimal. Thereby, occlusal coverage should protect teeth from new endodontic infection. Healing of the periapical lesions requires optimal blood concentrations of phosphate and calcium. If recurrent lesions appear after endodontic treatment, extraction and prosthetic management should represent the therapeutic option.

Authorship Declaration

All authors have contributed significantly, and they are in agreement with the manuscript.

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Conflict of Interest Statement

The authors declare no conflict of interest.

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