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REVIEW

Review of the dental implications of X-linked hypophosphataemic rickets (XLHR)

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Abstract
Objectives The aim of this article was to review the dental implications of X-linked hypophosphataemic rickets (XLHR) and to provide suggestions regarding the dental treatment of these patients.
Materials and methods The following search items "x-linked hypophosphataemia, hypophosphataemic rickets, vitamin D-resistant rickets" were used for literature search. Only full-text articles were analysed and summarized to get an overview of the different treatments and outcomes of hypophosphataemic patients.
Results Radiographically, very large pulp chambers with an abnormally high pulp volume/tooth volume ratio, suggesting taurodontism, are often evident. The affected teeth are characterised by a thin enamel layer and dentinal defects. The gender distribution of hypophosphataemic patients is almost equal, but postpubertary males seem to show a trend to develop more severe dental symptoms of the disease. Abscesses without any signs of dental caries or trauma are frequent findings. The most often affected teeth are incisors followed by molars and premolars.
Conclusions Treatment options include frequent dental examination, application of topical fluoride varnish and sealing of pits and fissures to prevent microbial invasion that may result in pulpitis and further endodontic complications.
Clinical relevance X-linked hypophosphataemic rickets is associated with marked structural alterations of dental hard tissues and the development of multiple abscesses and sinus tracts of dental origin. Therefore, profound knowledge of the various dental implications of XLHR is required to provide these patients with the best possible treatment options.

Keywords Dental treatment · Endodontic · Hypophosphataemic rickets · Taurodontism · Vitamin D-resistant rickets

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Classic rickets

Rickets is a metabolic disorder mainly found in children. The disease includes different symptoms such as disturbance of normal bone ossification resulting in failure to mineralize bone and thus a defective bone growth, alteration of calcium and phosphate blood levels, and different neurological alterations such as tetany [1]. Rickets can be cured by administration of vitamin D and/or sufficient sunlight [2].The predominant causes of Rickets disease are the following:

- Lack of sun exposure as the production of vitamin D3 from 7-dehydrocholesterol (7-DHC) in the skin is stimulated by ultraviolet-B radiation (wavelengths 290–315 nm) [1]. The hormonally active form of vitamin D is 1,25-dihydroxyvitamin D [1,25$(OH)_2$D] (calcitriol) [3]. Concentrations of 1,25-dihydroxyvitamin D of less than <50 nmol/L or 20 ng/mL are an indication of vitamin D deficiency, while concentrations of above 30 ng/mL are considered to be appropriate [4].
- Insufficient intake of calcium by nutrition [3]. This insufficient intake may be due to severe diarrhoea or vomiting. Vitamin D is oil soluble, and therefore, it is naturally found mainly in oily fish such as herring, mackerel, salmon and oils from fish, caviar, oysters, and to a lesser extent, tofu and soymilk, salami and sausages, eggs, and mushrooms [2].

Rickets-like hereditary hypophosphataemic diseases

Besides the known classic rickets, there are also hereditary rickets, which show similar symptoms but different reasons [5]. Different rickets-like hereditary hypophosphataemic diseases have been described [5, 6]. The therapy of patients with rickets-like disorders is in contrast to the classic rickets more difficult because of the genetic origin of the diseases. Hereditary rickets can be divided into autosomal dominant (ADHR), autosomal recessive (ARDR) and X-linked dominant (XLHR) [5]. In addition, the Debré-de-Toni-Fanconi-Syndrome is also known as a rickets-like syndrome [7]. These hereditary hypophosphataemic rickets display a group of different diseases whereby the X-linked dominant hypophosphataemic rickets (XLHR) is the most common form of inherited metabolic rickets [8]. This hereditary disease was first described by Albright in 1937 as vitamin D-resistant rickets [9]. In the literature, various synonyms such as familial hypophosphataemia and phosphate diabetes [10] are used as well. It is a genetic disorder that is inherited as an X-linked dominant trait [11, 12]. The corresponding gene is located on the short arm of the X-chromosome (locus Xp22.2-22.1). Known symptoms of rickets and rickets-like diseases are deformities of the limbs especially the lower limbs and other skeletal deformities [5]. XLHR is characterized by bone deformities, bone pain, reduced growth, hypophosphataemia, inappropriately normal serum $1,25(OH)_2D$ level and, additionally, a defective renal reabsorption of phosphate that leads to a phosphate wasting [13, 14]. Due to the dependency between phosphate and calcium homeostasis, X-linked hypophosphataemic rickets is also a disorder of the calcium homeostasis. XLHR is the most common form of inherited hypophosphataemia in industrialized countries; the prevalence is reported to be around 1:20,000 [15, 16].

Mutations in the phosphate-regulating gene with homologies to endopeptidases on the X-chromosome (PHEX gene) are the main aetiological factor of X-linked forms [17–19]. Although the PHEX gene seems to be responsible for the phosphate wasting, the gene is not expressed in the kidney but rather than in the bone cell linage such as osteoblasts, osteocytes, odontoblasts [13, 14], ovary and lung [14]. PHEX can also be found in parathyroid, brain and muscles. Because PHEX is located on the X-chromosome [14], random X-chromosome inactivation in females is predicted to result in a less severe phenotype compared with males who are completely PHEX deficient [13]. However, males and females seem to be affected equally with similar biochemical indices and skeletal manifestations [20].

The failure renal reabsorption of phosphate does not depend directly on the loss-of-function of the PHEX gene due to the absence of the expression in the kidney cells. The decreased expression of single-pass cell membrane protein PHEX leads to an increase of fibroblast growth factor 23 (FGF-23) [21]. The increased serum concentration correlates with hypophosphataemia, which is a clinical feature of X-linked hypophosphataemia also known as vitamin D-resistant rickets [5, 22]. However, it is currently unknown how the loss-of-function of PHEX leads to a disruption of osteocyte FGF-23 secretion [21]. In consequence, the dysfunction in renal transepithelial transport of phosphate results in a deficient mineralization of the bone. The decreased tubular reabsorption of phosphate results in a persistent hypophosphataemia [13, 15, 23]. The normal tubular reabsorption of phosphate (%TRP) in children ranges from 80 to 95 %, while the mean %TRP in patients with XLHR is considerably reduced to a range of 40 to 70 % [24]. The clinical signs can vary from one patient to another owing to several factors: family history, the degree of hypophosphataemia and the age of the patient at the beginning of the systemic treatment.

The clinical manifestation is identified in the first year of life if a familial history of the disease is known [21]. In the absence of a known familial history, children suffer from a progressive bowing of the lower extremity between the second and third year of life [21]. This correlates with the age when children usually begin to walk. Bone deformities, particularly bowing of the lower extremities, scoliosis and frontal bossing, are typical for XLHR patients. Other manifestations of rickets are short stature, enlargement of wrists and ankles, and pseudofractures. Bony protuberances of the sites of major muscle attachments are further common findings in these patients [25]. Although the general signs and symptoms of XLHR are well documented since the 1930s, it was until 1960 that Harris and Sullivan for the first time reported on characteristic dental findings associated with this disease [26]. On review of the literature, a linkage between hereditary hypophosphataemic rickets and dental alterations seems to be obvious [27, 28], as the pathways of bone and dental hard tissues mineralization are similar [29]. The availability of inorganic phosphate and calcium is essential [29] for the mineralization process, and thus, the direct link between hypophosphataemia and dental alterations is obvious.

Search of the literature

The aim of this article was to review the dental implications of X-linked hypophosphataemic rickets (XLHR) and to provide suggestions regarding the dental treatment of these patients.

The PubMed and Web of Science databases were searched for full papers and reviews using the following MeSH terms: “x-linked hypophosphataemia, hypophosphataemic rickets, vitamin D-resistant rickets”. In addition, the following keywords were also used: “dental, treatment, alterations”. After an initial screening of the abstracts, relevant full-length peer-

Table 1 Summary of included articles focusing on dental implications of X-linked hypophosphataemic rickets (XLHR)

Author	Year	Number of patients	Dental findings	Dental treatment
Witkop [30]	1971		Multiple abscesses, delayed eruption of the teeth, prominent pulp horns with extension to dentino-enamel junction, large pulp chambers	Pulp capping, onlay
Sauk and Witkop [31]	1973	1	Numerous dental abscesses, large pulp chambers, pulp horn extending to dentino-enamel junction, periapical radiolucencies	
Shellis [32]	1983	3 teeth	Extensive interglobular spaces, hypo- and unmineralized interglobular regions, some small calcospherites	
Bender and Naidorf [27]	1985	12	Enamel hypoplasia, hypocalcification, enlarged pulp chambers, wide root canals, pulp horns extending to dentino-enamel junction	Prophylactic veneers and steel crowns
Abe et al. [33]	1988	3	Reparative dentin formed in response to attrition, interglobular dentin, predentin wider with small calcospherites	
Schwartz et al. [34]	1988		Malocclusion, enamel hypocalcification defects, hypoplasia, enlarged pulp chambers, spontaneous abscesses	
Daley et al. [35]	1990	10 teeth	Poorly calcified globular dentin, different Ca/P Ratio	
Shields et al. [36]	1990	17	Larger pulp chambers in younger patients (15–25 years); larger pulp chambers in males compared to females (ratio pulp chamber to tooth volume)	
Hillmann and Geurtsen [37]	1996	2	Large pulp chambers, varying amounts of root resorption, pulp horn extending to dentino-enamel junction, wide zones of interglobular dentin	
Goodman et al. [38]	1998	17	Abscesses in primary dentition, enamel defects, mild hypomaturation and hypoplasia, clinical signs of attritions, enlargement of pulp chambers, large pulp horns to dentino-enamel junction, hypomineralized early-forming coronal dentin, absence of lamina dura around roots	
Murayama et al. [39]	2000	1	Abscess, short roots, large pulp chambers, periapical radiolucencies in primary dentition	Incision drainage, root canal treatment, composite and cast metal restoration
Zambrano et al. [40]	2003	1	Hypoplastic yellowish to brownish enamel, malocclusion, large quadrangular pulp chambers, short roots, periodontitis, gingivitis, variable degree of dentin calcification, variation in sizes of dentinal tubules, abnormal globular dentin, wide predentin layer	
Chaussain-Miller et al. [41]	2003	48	Abscesses, poorly mineralized enamel, thin dentin layer, large pulp chambers, prominent pulp horns, reduced secondary dentin apposition in the furcal area, taurodontism	
Seow [42]	2003		Spontaneous dental abscesses	Prophylactic coverage with steel crowns, coverage with resin
Batra et al. [43]	2006	1	Anterior open bite, spontaneous abscesses, root resorption, taurodontism, enlarged pulp chambers, wide predentin, marked globular dentin, tubular dentinal defects from pulp to enamel	Preventive steel crowns, permanent fissures sealing
Chaussain-Miller et al. [44]	2007	7	Recurrent abscesses, necrotic teeth, severe alteration of circumpulpal dentin, large interglobular spaces between unmerged calcospherites, fissures from pulp horn to dentino-enamel junction	Extraction for orthodontic reason
Douyere et al. [45]	2009	1	Fistula, tooth mobility, abscesses, taurodontism	Extraction, root canal treatment, fluid resin composite on all occlusal surfaces, prophylactic sealing
Souza et al. [5]	2010	14	Malocclusion enamel hypoplasia, dental abscess, enlarged pulp chambers, hypoplasia, dentin abnormalities	
OpsahlVitala et al. [29]	2012	0		Regular dental investigation 2x/y, radiographs, early sealing of occlusal surfaces, root canal treatment of permanent teeth, extraction of deciduous teeth, orthodontic treatment

Table 1 (continued)

Author	Year	Number of patients	Dental findings	Dental treatment
				if patient medicated with 1α-hydroxyvitamin D, prevention of attrition
Rabbani et al. [46]	2012	19	Dental caries, delayed eruption, enamel hypoplasia, taurodontism, dental abscesses, gingivitis	
Andersen et al. [47]	2012	52	Periapical radiolucencies, long pulp chambers, extended pulp horns	Root canal treatment
Rathore et al. [48]	2013	1	Primary teeth: root resorption, hypoplasia, dentin abnormalities, enlarged pulp chambers, permanent teeth: large pulp chambers, short roots, poorly defined lamina dura, hypoplastic alveolar ridge	Pulpotomies, preventive resin restorations, regular follow-up
Souza et al. [16]	2013	1	Fistula, enlarged pulp chambers, pulp horns up to dentino-enamel junction, poorly defined lamina dura, hypoplastic alveolar ridge, geographic tongue, large wear of incisors, crown alterations, rarefication around apices, dental abscesses	Extraction, root canal treatment
Rafaelsen et al. [22]	2013	4 (family)	Decay	
StudartSoares et al. [49]	2013	3 (family)	Tooth loss, spontaneous gingival abscesses, root resorption deciduous, taurodontism, close proximity between pulp horns and dentino-enamel junction, poor demarcation of the lamina dura, irregular wide globular dentin, dental caries, periradicular abscesses	Extraction, root canal treatment, composite and/or sealants

reviewed articles were selected. The reference lists of the articles were also screened for additional relevant articles.

In the attempt to include the most recent publications, a hand search of articles published online, "in-press" and "early view", was performed for the Journal of Endodontics, International Endodontic Journal, Oral Surgery Oral Medicine Oral Pathology Oral Radiology & Endodontology and Australian Endodontic Journal. The date of the last search was November 25, 2014. The reference lists of those articles included were checked for additional articles of relevance.

Dental implications

Table 1 provides a summary of published articles related to dental implications of XLHR. One of the main findings in patients with known XLHR is recurrent abscesses or sinus tracts associated with carious free teeth of the primary and the permanent dentition [5, 16, 30, 31, 34, 38, 39, 41–46, 49] (Figs. 1 and 2). Other dental-related findings are delayed tooth eruption [30, 46], both in the primary and in the permanent dentition. Radiographically, very large pulp chambers [5, 16, 27, 30, 31, 34, 37–41, 43, 46, 48] with an abnormally high pulp volume/tooth volume ratio, suggesting taurodontism, are often evident [41, 43, 45, 46, 49] (Fig. 3). The affected teeth are characterised by a thin enamel layer [5, 27, 38, 40, 41, 46] and dentinal defects [5, 33, 40, 41, 43, 48] (Fig. 3). Additionally, short roots [39, 40, 48] and root resorptions in primary dentition [37, 48, 49], poorly defined lamina dura [16, 38, 48, 49] and hypoplastic alveolar ridge [16, 48] are common findings.

Histopathologically, the dentin is characterized by large tubular clefts or lacunae [16, 40, 45], and the pulp horns are prominent [16, 27, 30, 31, 37, 38, 41, 44, 47, 49], often extending up to or beyond the dentin-enamel junction [16, 27, 30, 31, 37, 38, 41, 43–45, 49], particularly in the primary teeth [28, 30, 37–39, 41, 50, 51] (Fig. 2b). The structure of the enamel is normal but thinner and with long cracks [29, 34,

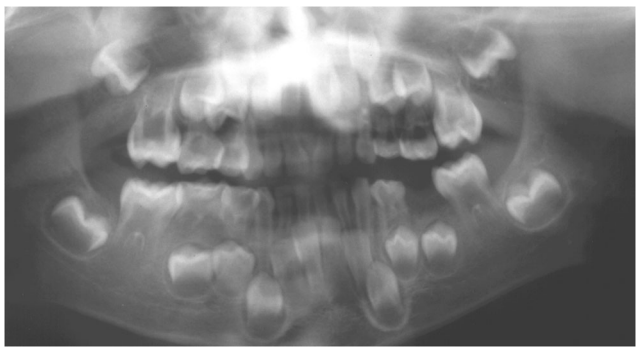

Fig. 1 Panoramic radiograph of a 5-year-old boy suffering from XLHR. Although no dental decay was obvious, teeth 54, 84 and 63 were associated with sinus tracts with discharge of pus

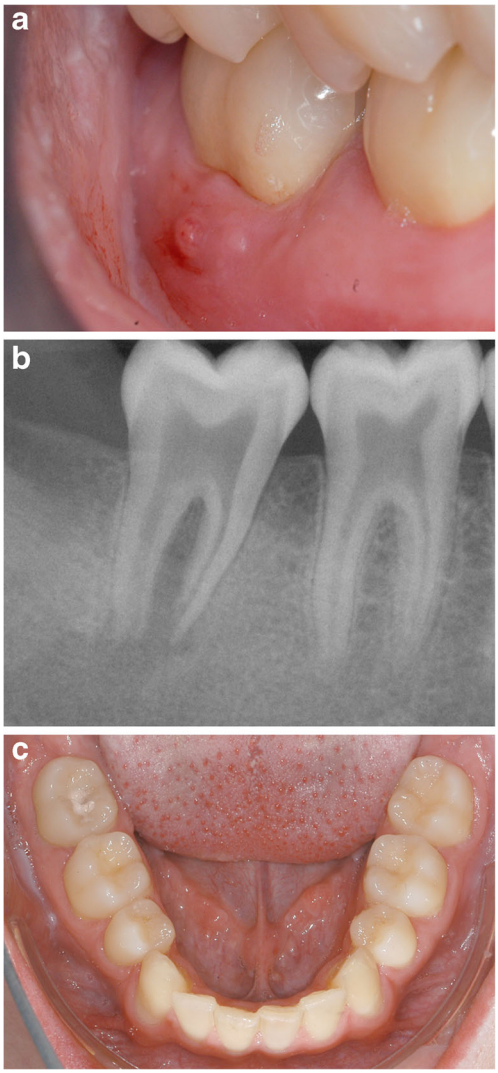

Fig. 2 **a** Sinus tract associated with the caries-free tooth 47 of a 15-year-old boy suffering from XLHR since the age of 8 months. The familial history revealed that his mother developed XLHR as well. **b** Radiograph of tooth 47 showing periradicular radiolucency and incomplete root formation and a prominent mesial pulp horn at tooth 46. **c** Clinical situation showing caries-free mandibular teeth

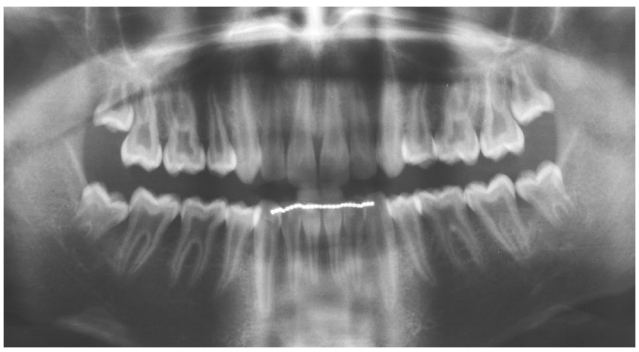

Fig. 3 Panoramic radiograph of the patient from Fig. 2 at the age of 14 years showing numerous taurodontic molars

45]. In some cases, alterations such as hypoplasia [5, 27, 34, 38, 40, 46] of the enamel were reported. Typically, the dentin layer is thin [41, 52], and the dentin consists of numerous microscopic abnormalities, such as interglobular dentin, unmineralized dentin [5, 27, 32, 35, 38, 40, 43, 49, 52], wide predentin zones and tubular defects [31, 33, 38, 40, 43]. The lack of fusion of calcospherites and consequently the presence of large interglobular spaces [33, 37, 44] constitute the characteristic traits of the human X-linked hypophosphataemic dentin [29, 32, 35, 45, 53, 54]. In addition, an absence of secondary dentin formation in teeth of patients with XLHR was reported [55]. These conditions facilitated microbial penetration into the endodontium and dentin [37] resulting in pulp infection, pulp necrosis and finally periradicular periodontitis both in the deciduous and the permanent dentition. In consequence, multiple gingival and periapical abscesses without concurrent evidence of trauma or caries are often evident [5, 16, 30, 31, 34, 38, 39, 41–46, 49].

The older the patients are, the more often dental abscesses are detected [47]. The most frequently affected teeth are incisors (Fig. 4) and canines followed by molars and premolars [47]. The order of the affected teeth is determined not only by the time of eruption but also by the rate of natural attrition as a result of mastication. There is an obvious correlation between

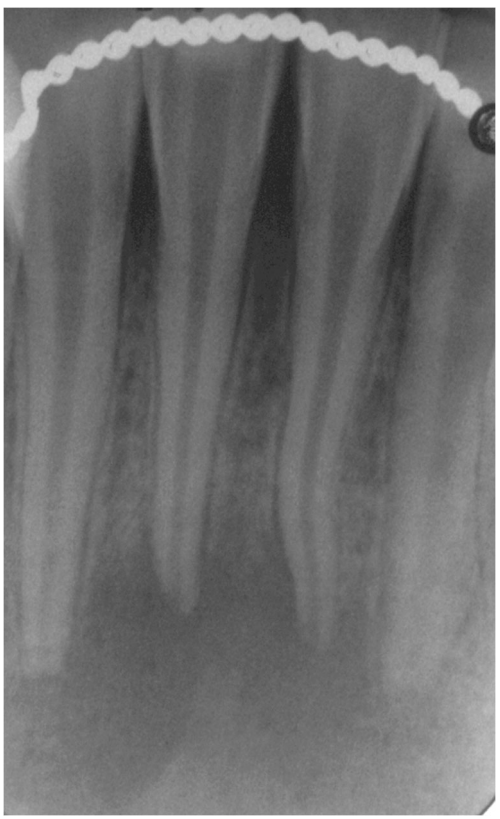

Fig. 4 Radiograph of teeth 32, 31 and 41 of an XLHR patient showing apical translucency. These teeth were not tender to percussion and caries-free. Clinical and radiographic examination indicated pulp necrosis with apical periodontitis

the apposition of reparative dentin as a response to attrition [33] and an increased attrition of especially anterior teeth [16, 33, 38].

Treatment

Systemic treatment

The primary treatment goals of XLHR and other rickets-like diseases are to prevent the renal loss of phosphate in order to reduce the clinical symptoms related with rickets or osteomalacia and furthermore to allow the patient to achieve normal growth. Standard treatment consists of a combination of oral phosphate supplement and calcitriol. The concomitant use of calcitriol enhances the intestinal calcium absorption and prevents the development of secondary hyperparathyroidism, which may occur with phosphate therapy alone [24]. The treatment with phosphate supplements has been shown to prevent or cure the dental anomalies in some [30, 41, 56], but not all, patients [34, 36, 41, 57].

Dental treatment

Diverse treatment options were suggested by different authors (Table 1). The most common recommendation is regular dental control that should include sensibility testing of all teeth and routine radiographic control of the entire dentition [29]. Most of the patients with this disease are affected by early tooth loss [29, 43, 45, 49] or develop abscesses and sinus tracts of dental origin [29, 39].

Unfortunately, there is currently no method available that allows determining how widespread the formation of dentin and enamel is affected by this disease. The primary treatment options in XHLR patients are frequent dental controls, professional dental care, application of topical fluoride varnish and fissure sealing. Early sealing of hypophosphataemic teeth is the primary treatment option to preserve pulp vitality as fissure sealing is the most effective approach to prevent bacterial penetration. Regular professional dental care and frequent dental examination are required to detect gingival recessions and exposition of dentin areas at an early stage. It should be a rule of thumb in these patients that any exposed dentin areas require immediate bacteria-tight sealing to prevent penetration of microorganisms into the dentinal tubules towards to pulp.

The treatment of choice for teeth associated with apical periodontitis, abscess or sinus tract is non-surgical root canal treatment, preferably with the use of an interappointment temporary dressing (Fig. 5). The obturation of the root canal system should aim at avoiding any voids and at achieving the best possible density of the root canal filling, due to the increased risk of reinfection of the root canal system in these patients because of the structural abnormalities of the dentin.

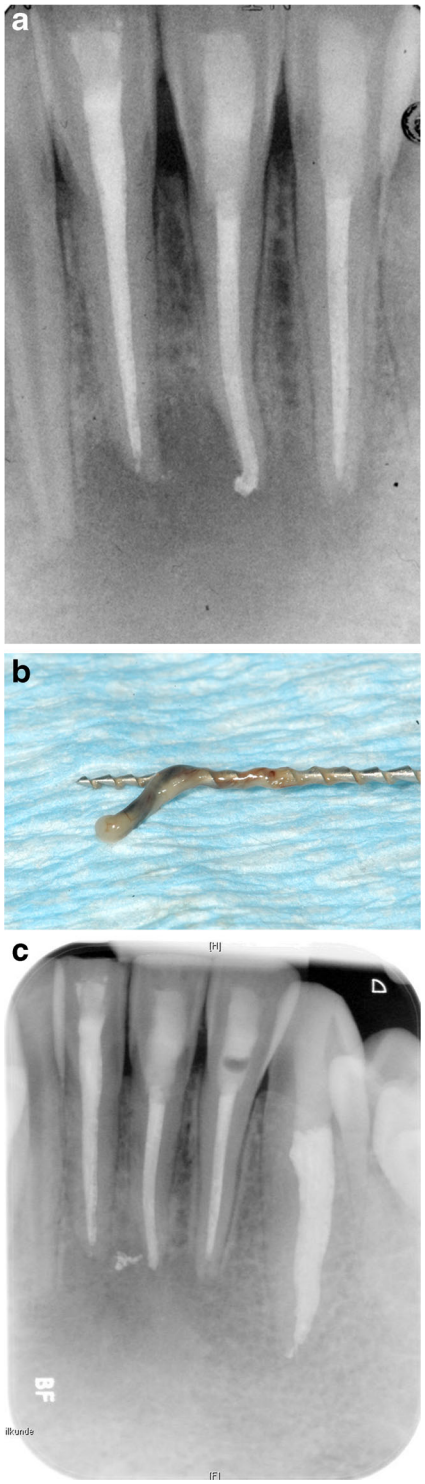

Fig. 5 **a** Radiograph taken immediately after root canal obturation of teeth 32, 31 and 41 (same patient as in Fig. 4). **b** During root canal treatment, ischemic and non-vital pulp tissue was removed. **c** Radiograph taken at the 1-year follow-up showing that healing of the periradicular tissues was in progress. The patient was free of pain, but meanwhile, also tooth 33 required root canal treatment

Therefore, the use of thermoplasticized obturation techniques using a virtually insoluble sealer (e.g. epoxy resin-based

sealers) is advisable. Due to the short roots regularly found in XHLR patients, working length should be determined very accurately and thoroughly, preferably by using electronic apex locators. There is currently no evidence available suggesting that the success rates of root canal treatment in XLHR patients are considerably reduced when compared to non-XHLR patients. Follow-ups should be scheduled on a regular basis until complete healing of the periradicular pathology. As often even in young patients, teeth become non-vital and develop apical pathology root canal treatment of teeth with incomplete root formation that is quite common with XHLR patients. Therefore, besides root canal preparation, proper and copious irrigation, and intracanal dressings, the creation of an apical plug using mineral trioxide aggregate (MTA) is often required before obturation (Fig. 6). Regarding the coronal restoration of root canal-treated teeth, posts should be avoided wherever possible.

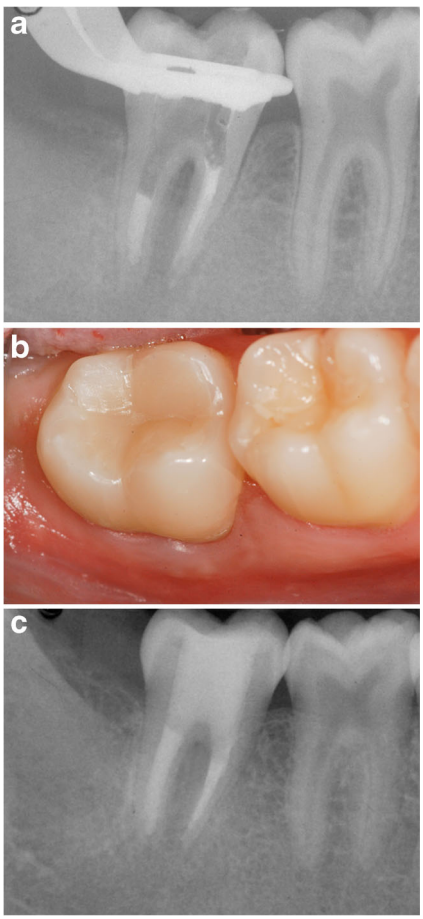

Fig. 6 **a** Radiograph of apical MTA plugs that were implemented in all root canals of tooth 47 under visual control using an operating microscope (same patient as in Fig. 2). **b** Clinical situation following coronal restoration. The coronal part of the root canals and the access cavity were filled with composite to achieve a tight seal and to improve the fracture resistance of the root canal-filled tooth. **c** Radiograph taken at the 6 months following up revealing that healing was in progress

Due to the correlation between attrition and formation of abscesses, early coronal restoration of the teeth with the highest risk (incisors>molars>premolars) is strongly recommended [47]. These restorations include resin fissure sealing [39, 42, 43, 45, 49], stainless steel crowns for deciduous teeth [27, 42, 43] and permanent crowns for permanent teeth [27, 30, 39].

Due to the atypical dentin formation in XHLR patients, with increased areas of interglobular and unmineralized dentin, wide predentin zones and tubular defects, the bonding strength of adhesive composite restorations, such as fissure sealing and composite fillings, is assumed to be reduced. Therefore, the utmost care must be taken to obtain the best possible retention. Moreover, prolonged etching times or the use of total etch systems seem to be related with an increased risk of pulp irritation [58] due to the close proximity between the pulp chamber and the enamel [16, 27, 30, 31, 37, 38, 41, 43, 44, 47, 49] and the wide dentinal tubules [40, 43]. To minimize the risk of pulp irritation, the usage of self-etch bonding and sealant systems is recommended due to the irregular calcified dentin [27, 32, 35, 38, 40] and widened interglobular spaces between the calcospherites of the dentin [33, 37, 44]. These alterations of the dentin may lead to affections of the pulpal tissues, when not adequately taken into consideration.

Steel crowns for primary teeth or definitive partial or full crowns for permanent teeth are generally recommended in these patients [27, 30, 39, 42, 43]. However, in the case of partial or full crowns for permanent teeth, the wide pulp horns that often extend to the dentino-enamel junction [16, 27, 30, 31, 37, 38, 41, 43, 44, 47, 49] and in some cases even beyond [41, 43, 44, 47, 49] and the large pulp chambers [5, 27, 30, 31, 34, 37–41, 43, 46, 48] should be taken into consideration. In young patient with very prominent pulp horns, ceramic restorations should be avoided, as preparation for ceramic partial or full crowns is associated with a greater loss of dental hard substance compared to full metal restorations. It is therefore, wherever indicated, reasonable to restore teeth using all-ceramic occlusal veneers. This treatment option guarantees the currently best possible prevention of occlusal attrition using a minimally invasive approach. Furthermore, adhesive bonding to the unaltered enamel is assumed to be more reliable than to the irregularly formed dentin [59].

Discussion

Up to now, the precise pathogenesis of the dental alterations associated with hypophosphataemic rickets is not completely understood. Males show a trend to more severe dental symptoms of the disease than females [13]. These include taurodontism of molar teeth [5, 27, 30, 31, 34, 37–41, 43, 46, 48] and pulp horns extending to the dentino-enamel

junction [16, 27, 30, 31, 37, 38]. Differential diagnoses which should be taken into consideration are dentin dysplasia, dentinogenesis imperfecta, osteogenesis imperfecta [42] and other systemic diseases that lead to an alteration of the phosphate homeostasis such as genetic defects of phosphate-associated proteins like FGF-23 [60] or PHEX.

There is a correlation between the severity of dental manifestation and the first appearance of oral symptoms: The younger the patients when a dental abscess emerges for the first time, the more severe the dental manifestations tend to be [61]. Moreover, the appearance of abscesses typically seems to follow a certain pattern according to the sequence of the eruption of teeth [37, 47, 62]. Younger patients show more often non-carious-related abscesses associated with incisors and/or canines, while in older patients, the likelihood of affected molars is increased [47]. Generally, premolars are only affected in older patients [47]. It seems to be that attrition of enamel over time in combination with the extended pulp horn and the large pulp chamber leads to the exposition of the defective dentin, thereby allowing microorganisms to penetrate dentinal tubules and finally invading the pulp tissue [37].

Although the function of the odontoblasts is not compromised in XLHR patients, hypophosphataemia is responsible for dysplastic and poorly mineralized circum pulpal dentin [44] with wide areas of interglobular dentin [33, 37, 44] thus limiting growth and fusion of calcopherites. Tubular defects can particularly be found in the region of pulp horns. Due to the irregular structured dentin, the enamel fissures may extend into the pulp horns [41, 43, 44, 47, 49], exposing the pulp to a high risk of microbial invasion [37]. This may be an explanation for the seemingly spontaneous pulp necrosis without any signs of caries or dental trauma [38, 39, 44, 51, 54]. The formation of dental hard tissues (enamel and dentin) takes place in the uterus so it is not feasible to prevent structural dentin defects in primary teeth. Although the application of medicaments soon after birth can theoretically affect the formation of dental hard tissues of permanent teeth positively—since they are formed postnatal—irregularities in mineralization may persist nonetheless. In many cases, however, early diagnosis and medical treatment are beneficial [41]. When examining an affected family over different generations, a less severe phenotype of hypophosphataemia of the younger generations is a typical finding. This observation corroborates the speculation that an early onset of medical treatment by administration of the lacking metabolites is correlated with milder manifestation of the disease [13].

Numerous preventive measures have been suggested to avoid infected pulp necrosis, i.e., professional cleaning of dental surfaces, topical application of fluoride varnish, prophylactic fissure sealing of permanent teeth, resin composite covering of the anterior teeth [5, 6, 46, 49] as well as placement of prefabricated metal or polycarbonate crowns [39, 45] to protect the entire clinical crown of primary molars [6, 39, 42, 45, 63, 64] (Table 1). Pit and fissure sealants are useful when the teeth are erupting as they prevent ingress of bacteria into the enamel microfractures as well as initiation of caries in the deep pits and fissures. Placement of steel crowns has been recommended for a long time, but there seems to be an increased risk of pulp infection during preparation [64].

Concerning root canal treatment of hypophosphataemic teeth, it should be taken into consideration that the dentinal irregularities may compromise the mechanical debridement of the root canal system. The formation of globular dentine or calcospherites may entrap intracanal microorganisms inside the dentin gaps [33, 37, 44, 62]. Even properly disinfected and obturated root canals may be reinfected when gingival recessions occur [40, 43] or dentin becomes exposed to the oral cavity by attrition [16]. In combination with irregularly formed dentin [5, 27, 32, 35, 38, 40], an infection of the obturated root canal [37] via the gaps between the calcospherites is possible. Following root canal treatment, follow-ups should be scheduled in short intervals, and radiographs should be taken on a regular basis. Additionally, there are problems regarding post-endodontic coronal restorations: Thin dentin walls tend to fracture easily and do not support intracanal posts [42, 65]. In general, the fracture resistance of dentin is considerably reduced in XHLR patients [42]. When a prosthetic restoration is planned, it has to be considered if the placement of a post is possible with a minimum risk of further root fracture. Whenever possible, loss of dental hard tissue should be minimized when restoring hypophosphataemic teeth, and therefore, all-metal crowns should be preferred over all-ceramics ones. Occlusal all-ceramics veneers can prevent further attrition by a minimum of substance loss in order to restore the original shape of the teeth.

Conclusion

XHLR patients require frequent and regular dental care with the main focus on the prevention of attrition due to the fact that the structure of dental hard tissues is severely altered [5, 27, 34, 38, 40, 46, 66]. In the sense of tooth-conserving dentistry bacteria, tight restorations and a preventive sealing should be performed in order to hamper bacterial invasion that may result in pulpitis and further endodontic complications.

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