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Case Report

Oral Features in Children with X-Linked Hypophosphatemic Rickets: An 8-Year Follow-Up Case Report

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Abstract

X-linked hypophosphatemic rickets (XLHR) is a hereditary metabolic disease caused by the loss of phosphate through the renal tubules into the urine and an associated decrease in serum calcium and potassium phosphate, resulting in bone and dental abnormalities. We report this case, aiming to describe, through an 8-year follow-up case report, the clinical approach adopted in managing dental features in both primary and permanent dentition in a child diagnosed with XLHR. The oral manifestations were mainly premature exfoliation of primary teeth with no history of dental caries or trauma, spontaneous abscesses, enamel hypoplasia, and facial cellulite. The panoramic X-ray revealed pathognomonic features of XLHR, such as high pulp horns extending up to the dentin-enamel junction, unclear limits of the lamina dura, hypoplastic alveolar ridge, and taurodontism. To manage these dental alterations, space maintainer, coverage of the hypoplastic teeth and endodontic treatment were carried out.

Through this 8-year follow-up, we documented the dental management of a child with XLHR, emphasizing the unique oral manifestations and their successful treatment. This case reinforces the importance of early and regular dental interventions to improve the quality of life and functional outcomes for patients with XLHR.

Keywords
Hypophosphatemic rickets; metabolism; hereditary; dental management; child; follow up

1. Introduction

Hypophosphatemic rickets is a group of hereditary metabolic diseases that are characterized by diminished phosphate reabsorption in renal tubules, leading to chronic hyperphosphaturia and hypophosphatemia, associated with normal or low levels of $1,25(OH)_2$ Vitamin D_3 [1].

This condition often presents with normal or low levels of $1,25(OH)_2$ Vitamin D_3. Hereditary hypophosphatemic rickets exist in various forms, distinguished by transmission mode and genetic causes [2]. Among these, the X-linked dominant form, hypophosphatemic rickets, is the most prevalent inherited variant, affecting approximately 1 in 20,000 to 60,000 individuals [3]. Its annual incidence is typically fewer than 6 cases per newborn [4]. This type, abbreviated as XLHR, arises from dysregulated fibroblast growth factor 23 (FGF23) due to mutations in the PHEX gene. This mutation leads to decreased phosphate tubular reabsorption, reduced renal 1α-hydroxylase activity, and heightened renal 24-hydroxylase activity [5]. Additionally, XLHR involves disturbances in calcium and phosphate metabolism, leading to mineralization disorders primarily affecting bone and teeth tissues [6].

The main clinical symptoms are severe bone deformities. Indeed, the primary sign of the disease is the bowing of the legs, most evident from the first walking steps. In addition, patients present frontal bulging due to sagittal suture synostosis, costochondral joint enlargement, genu valgum, genu varum, and short stature [7]. The main dental manifestations reported were spontaneous abscess in noncarious teeth, hypoplastic enamel, abnormal lamina dura, and rickety bone trabeculation [8].

Numerous cases of XLHR with dental features have been documented in the literature. To the best of our knowledge, this is the first reported case that documented the dental features of this rare disease and its management in both primary and permanent dentition. This case highlights the importance of early diagnosis and an interdisciplinary approach to managing XLHR, demonstrating how targeted dental interventions can significantly improve oral health and overall quality of life in affected individuals.

2. Case Report

2.1 Ethics Statement

This study was conducted in accordance with ethical guidelines and was approved by the Comité d'Éthique pour la Recherche Biomédicale (CERB). The approval identification code is CERB 30/2024, and the approval was granted on August 26, 2024. In Tunisia, ethical committees for biomedical

research operate under Law No. 2004-93 of November 3, 2004, which regulates research involving human participants. This law establishes the ethical and legal framework for biomedical research, ensuring the protection of participants' rights, dignity, and well-being. Signed informed consent was obtained from the legal guardian.

2.2 Patient Information and Initial Presentation (March 2014)

A 4-year-old boy presented to the Department of Preventive and Pediatric Dentistry with a chief complaint of spontaneous premature exfoliation of the upper and lower primary incisors (Figure 1). He was born to consanguineous parents and diagnosed with XLHR at age three. The family pedigree chart revealed an X-linked dominant transmission (Figure 2).

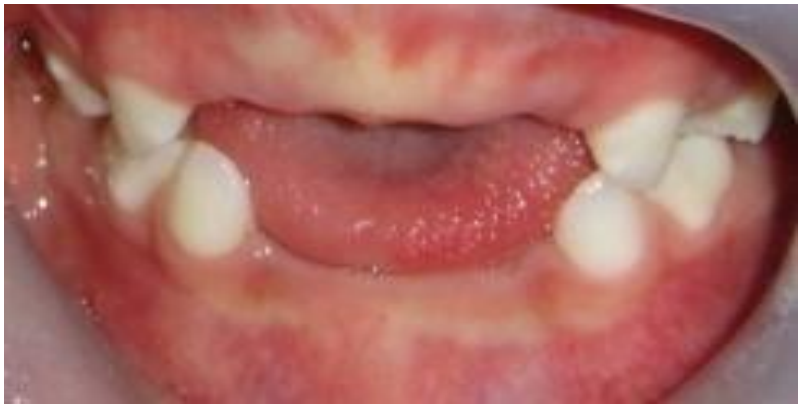

Figure 1 Spontaneous exfoliation of all primary incisors.

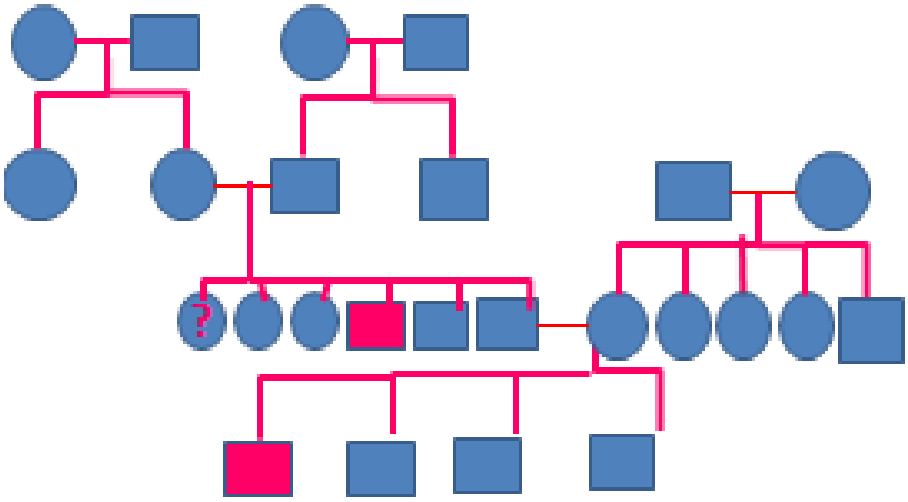

Figure 2 Pedigree chart.

2.3 Clinical and Diagnostic Findings

Physical examination revealed skeletal deformities characteristic of XLHR:

- Bulging frontal bone
- Occipital protuberance
- Increased anteroposterior diameter of the skull (Figure 3a)
- Enlarged wrists (Figure 3b)

- Bowing of the legs (Figure 3c)

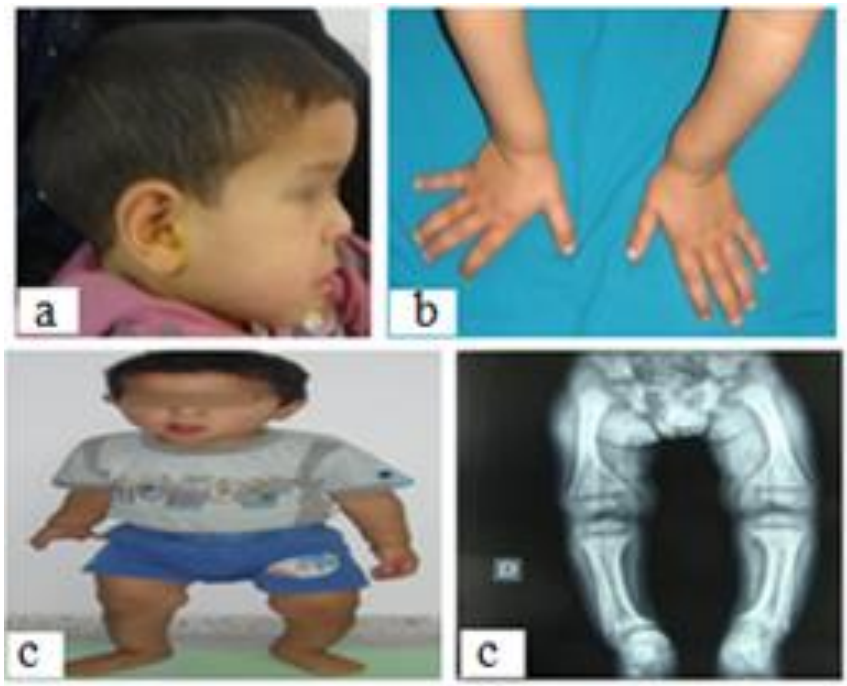

Figure 3 Bone deformities at the age of 4. a: Bulging frontal bone, occipital protuberance, increased anteroposterior diameter of the skull; b: Enlargement of the wrists; c: Bowing of the legs.

Laboratory tests indicated:

- Reduced serum phosphorus: 20.4 mg/L (normal range: 50-70 mg/L)
- Elevated alkaline phosphatase: 1011 U/L (normal range: 1-720 U/L)
- Elevated 24-hour urinary calcium: 22.95 mg/24 h (normal range: 2-4 mg/kg/24 h)
- Normal parathormone: 43 pg/mL (normal range: 15-72 pg/mL)

Panoramic X-ray findings included high pulp horns extending to the dentin-enamel junction, poorly defined lamina dura, hypoplastic alveolar ridges, and taurodontism (Figure 4).

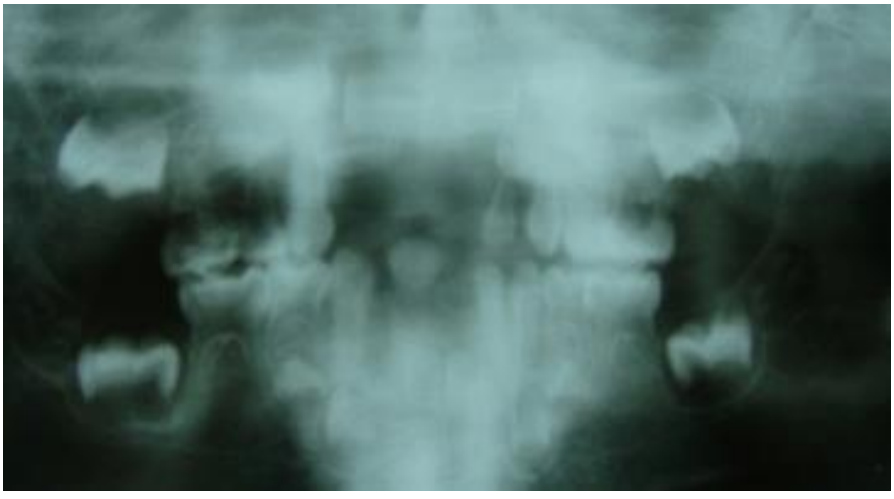

Figure 4 Panoramic X-ray.

At this age (4 years), the priority of dental treatment was to maintain the space of the lost primary incisors in order to prevent malocclusions and to restore function and aesthetic appearance as well.

A fixed space maintainer was fabricated and sealed with glass ionomer cement to preserve space following the loss of primary incisors (Figure 5).

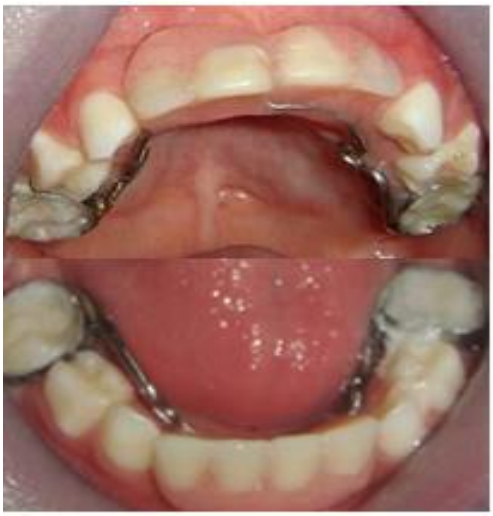

Figure 5 Maxillar and mandibular fixed space maintainer.

2.4 Follow-Up and Therapeutic Interventions

2.4.1 (Age 6)

- At six, despite a normal physical overall growth, the dental examination revealed spontaneous loss of the upper left primary canine and all primary molars.
- Permanent teeth, including the first molars and lower incisors, exhibited hypoplastic yellowish or brownish enamel (Figure 6a).
- Hypoplastic teeth were restored with composite materials (Figure 6b).
- A removable space maintainer was fabricated to maintain the space of the deciduous teeth.

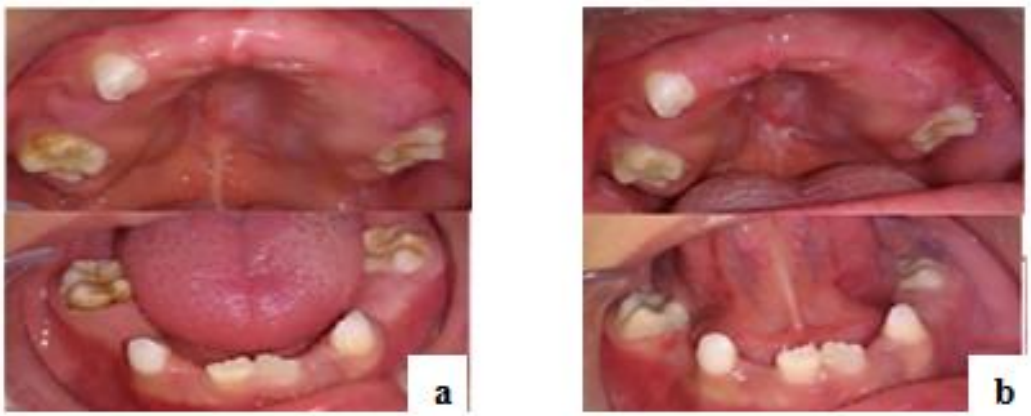

Figure 6 a: Intra-oral clinical view showing loss of the upper left primary canine tooth and the hypoplastic teeth; b: Clinical view after restoration of the hypoplastic teeth with dental resin.

2.4.2 2017 (Age 7)

- The patient developed a dental abscess related to tooth #83 without dental caries.
- Endodontic treatment was performed, and hypoplastic first permanent lower molars were restored with preformed pedodontic metal crowns (Figure 7).
- Between 2018 and 2021, the patient was lost to follow-up post-surgery, likely due to logistical or personal constraints.

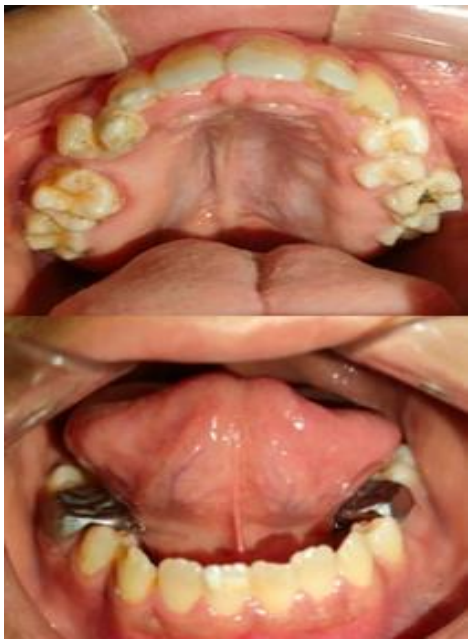

Figure 7 Inta-oral view of maxillar and mandibular arch.

2.4.3 2022 (Age 12)

- General physical manifestations of XLHR persisted, including frontal bone prominence, occipital protuberance, and bowing of the legs.
- Dental examination revealed lower labial cellulitis involving tooth #41, attributed to enamel hypoplasia rather than caries or trauma.
- Endodontic treatment was conducted, and the tooth was restored with composite resin.
- The patient presented with Class III malocclusion characterized by maxillary skeletal retrusion and anterior crossbite (Figure 8).

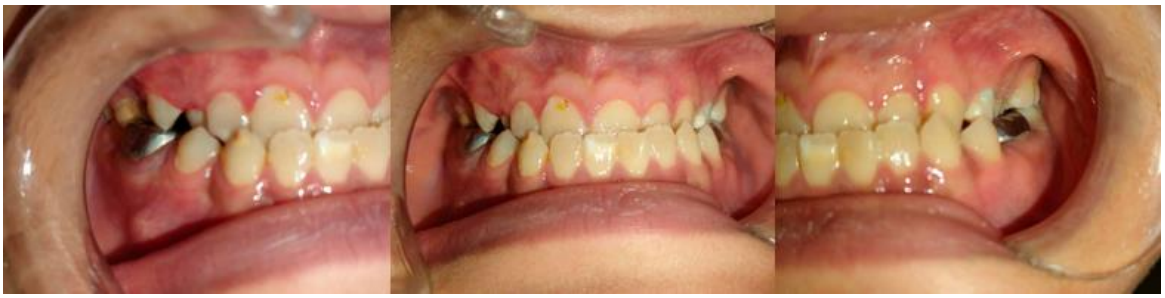

Figure 8 View of the anterior and posterior occlusion.

Le Petit face mask was used without maxillary expansion due to the absence of posterior crossbite (Figure 9). Glass ionomer wedges were placed on teeth #46 and #36 to disarticulate the maxilla. The patient wore the face mask for 14 hours daily, applying a protraction force of 400-600 g per side with an antero-inferior vector of 15°-30° to the occlusal plane. After three weeks, anterior crossbite correction was achieved (Figure 10).

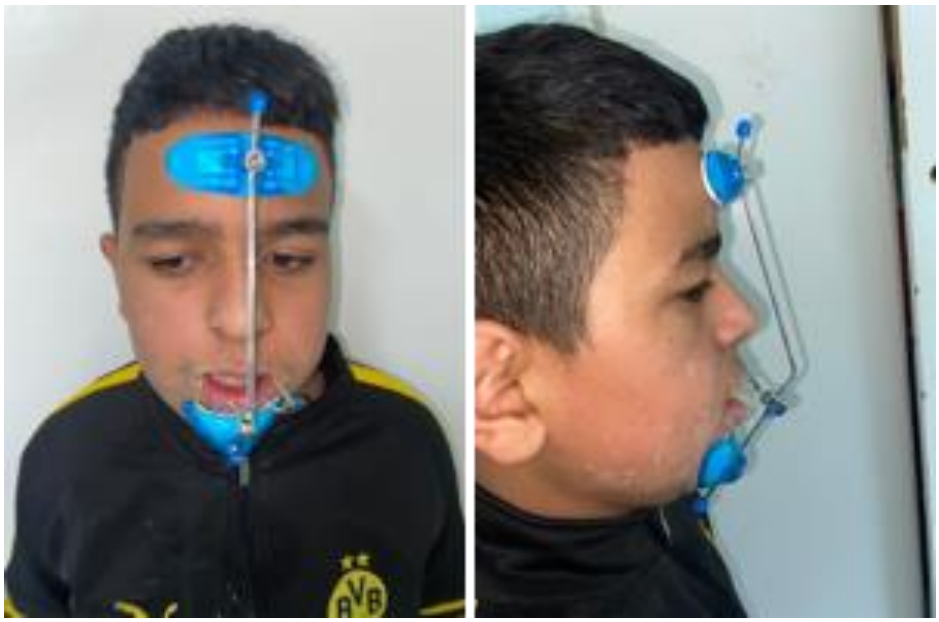

Figure 9 Le petit facial mask.

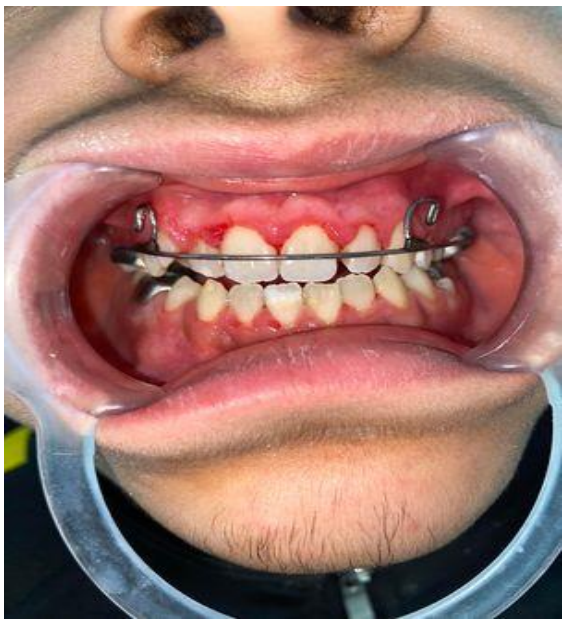

Figure 10 View of the anterior occlusion: Correction of the crossbite.

2.5 Outcomes and Follow-Up

By the end of 2022, the space maintainers had successfully facilitated the proper eruption of permanent incisors and molars. However, recurrent dental infections and enamel hypoplasia underscored ongoing challenges.

3. Discussion

XLHR is the most common form of inherited rickets [3]. When the clinical, biochemical, and radiographic findings suggest the diagnosis of XLH or another genetic disorder, genetic testing is recommended to confirm the diagnosis and for genetic counseling of the patient and the family members [9]. However, in our case, due to the lack of a genetic study, the diagnosis was mainly based on physical, biological, and radiographic exams.

The diagnosis was confirmed at the age of three based mainly on the family pedigree chart and the teeth features, which were pathognomonic of XLHR. Thus, dental characteristic manifestations are the formation of recurrent spontaneous abscesses, facial cellulite formation, poor dentin mineralization, and enamel hypoplasia [8].

Indeed, the underlying mechanism behind recurrent spontaneous dental abscesses in XLHR cases can be attributed to bacterial infiltration and the introduction of their toxins through micro-fissures within hard dental tissues. This process leads to pulp necrosis and the formation of spontaneous abscesses, even in the absence of any history of dental trauma or caries [10]. The disruption of phosphocalcic metabolism further exacerbates the invasion of bacteria into the pulp, even without dentin matrix destruction.

Radiographically, XLHR presents distinctive features, including widened pulp chambers with prominent horns extending to the enamel-dentin junction, reduced radiopacity of both enamel and dentin, short roots, and open apexes [8].

In XLHR, it’s commonly observed that the anterior teeth are more frequently impacted than the posterior ones, often resulting in early tooth loss for many patients [11]. This was evident in our case, where the patient experienced the loss of all primary incisors by the age of three. Consequently, prosthetic rehabilitation was necessary to address this spontaneous tooth loss, achieved through maxillary and mandibular fixed space maintainers.

The manifestations of rickets can vary significantly among patients due to several factors, including family history, the severity of hypophosphatemia, and the age at which systemic treatment is initiated.

This case highlights the critical importance of a comprehensive clinical and biochemical evaluation in differentiating XLHR from other causes of rickets, such as nutritional and vitamin D-dependent rickets. The chronological follow-up of this patient emphasized the progression of skeletal and dental manifestations characteristic of XLHR, underscoring the need for early diagnosis and intervention. Unlike nutritional rickets, which typically resolves with supplementation, and VDDR, which has distinct genetic and biochemical profiles, XLHR requires targeted treatment with phosphate supplements and active vitamin D analogs [12]. Emerging therapies like Burosumab have shown promise in addressing the underlying pathophysiology of XLHR by inhibiting FGF23, although access remains limited in resource-constrained settings [13]. This case underscores the need for heightened awareness and tailored management strategies to improve patient outcomes with XLHR.

While treatment doesn't offer a cure, its primary goal is to optimize growth patterns, reduce the severity of bone abnormalities and defects, and minimize limitations in activity [14].

Conventional management of XLHR typically involves multiple daily administrations of inorganic oral phosphate salts combined with active vitamin D analogs like calcitriol or Alfacalcidol [4]. Additional therapeutic strategies may include diuretics to enhance renal calcium reabsorption and promote remineralization, human growth hormone to elevate circulating phosphate levels and

enhance growth, and non-hypercalcemic vitamin D analogs to maximize skeletal benefits and suppress the onset of hyperparathyroidism [4]. Nonetheless, long-term care for XLHR patients poses potential complications, including hypervitaminosis, hyperparathyroidism, and soft tissue calcifications, particularly in renal tissues [15].

Some authors have indicated that the extraction of teeth that present periradicular abscesses is due to unsuccessful endodontic treatment [16]. These authors believe that success is not always obtained because endodontic and restorative treatment may not be able to maintain asepsis [17]. While managing the dental features in our patients, we prioritized preventive treatment. The endodontic treatment was realized on the necrotic teeth and aimed to reduce the consequences of pulp necrosis. We also covered the first permanent molars with preformed metal pedodontic crowns. Besides, the anterior hypoplastic tooth was restored with composite material. This therapeutic approach followed the protocol recommended in the literature. In cases of dentin exposure or enamel malformation, coronal coverage of anterior teeth (composite resin) and posterior teeth (metal crown) is indicated [18].

4. Conclusion

Acknowledgment of the dental characteristics is fundamental for performing a correct diagnosis and treatment management in patients with XLHR. Dental care consists of periodical examinations, topical fluoride application, and maintaining good oral hygiene, which is essential for improving dental alterations. As a pediatric dentist, besides managing dental features in both primary and permanent dentition, we suggest genetic testing for newborns ascending from a family with this condition.

Author Contributions

Soumaya Kachti: Conception and design, drafting the article. Manel Chalbi: Critical revision of the article. Soumaya Boussaid: Analysis and interpretation of data. Faten Awled Brahim: Acquisition of data. Mohamed Ali Chemli: Critical revision of the article. All the others aproved the article to be published.

Competing Interests

The authors have declared that no competing interests exist.

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