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Oral Expression of Hypophosphatasia: Case Report and Clinical Management

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Abstract :

Introduction: Hypophosphatasia (HPP) is a rare genetic disease of bone metabolism linked to a non-tissue specific alkaline phosphatase deficiency. It causes an alteration of bone and dental mineralization. Oral and dental manifestations can constitute an early revealing sign, particularly in children, and need a specific and multidisciplinary dental care.

Observation : We report the case of a 10-year-old female patient referred to the Pediatric Dentistry Clinic of Monastir for pain in the maxillary left first permanent molar (#26). Clinical examination revealed short stature, intermittent bone pain, and delayed motor development. Oral findings included premature exfoliation of primary teeth without physiological root resorption, generalized enamel hypoplasia, increased tooth mobility, and carious lesions. The association of systemic and dental findings strongly supported the suspicion of hypophosphatasia. The radiological examination revealed bone and dental hypomineralization. The diagnosis of HPP was confirmed by laboratory tests showing a marked drop in serum alkaline phosphatase level, in line with the general clinical context.

Discussion : Premature loss of fully rooted primary teeth is pathognomonic and dental manifestations may represent the earliest and persistent expression of the disease, extending into permanent dentition. In this case, characteristic periodontal destruction related to cementum defects resulted in early tooth loss. In the absence of enzyme replacement therapy, dental management remains preventive and supportive, emphasizing preservation of dentition, growth-adapted rehabilitation, and long-term pediatric dental follow-up.

Keywords : Hypophosphatasia, Alkaline phosphatase, mineralization defect, Early tooth loss, dental prosthesis

Introduction

Hypophosphatasia (HPP) is a rare inherited metabolic disorder caused by mutations in the *ALPL* gene, resulting in deficient activity of tissue non-specific alkaline phosphatase (TNSALP). This enzyme defect leads to defective bone and dental mineralization (1). In children, oral manifestations may be the first clinical signs, including premature loss of teeth, enamel hypoplasia, and hypomineralized alveolar bone (2). Early recognition by pediatric dentists is crucial, as dental findings often precede systemic symptoms.

The prevalence of severe forms of the disease has been estimated at 1/100 000 (3). According to Orphanet and Duffus.S et al 2018 (4), in North and West Europe, the birth prevalence of severe forms of the disease (perinatal lethal and infantile forms) has been estimated to be 1/300 000. Because of possible dominant autosomal inheritance, moderate forms of HPP are expected to be more frequent and are estimated to have a prevalence of 1/6300.

The aim of the study is to highlight oral and dental manifestations of hypophosphatasia and to underscore the role of the dentist in the early detection and management of this condition.

Observation

A 10-year-old female patient was referred to the Pediatric Dentistry Clinic of Monastir with pain localized to the maxillary left first permanent molar (#26).

General examination revealed short stature. The medical history was notable for intermittent bone pain and delayed motor development, suggestive of an underlying skeletal disorder.

According to the parents, the patient had experienced premature exfoliation of primary teeth—predominantly incisors—occurring in the absence of physiological root resorption, as well as unexplained tooth mobility and defective enamel quality.

Intraoral examination showed that the permanent incisors, canines, and first molars had erupted, all presenting generalized enamel hypoplasia. The first permanent molars were positioned at a markedly reduced occlusal level, resulting in the absence of posterior occlusal contact and subsequent anterior traumatic occlusion associated with lateral tongue interposition.

Periodontal evaluation revealed deep periodontal pockets and severe mobility, including grade III mobility of the maxillary left first permanent molar (#26) and grade II mobility of the maxillary left central incisor (#21). Carious lesions were observed in the maxillary left first permanent molar (#26) and the mandibular left first permanent molar (#36).

The coexistence of systemic skeletal findings and characteristic dental abnormalities strongly supported the suspicion of hypophosphatasia.

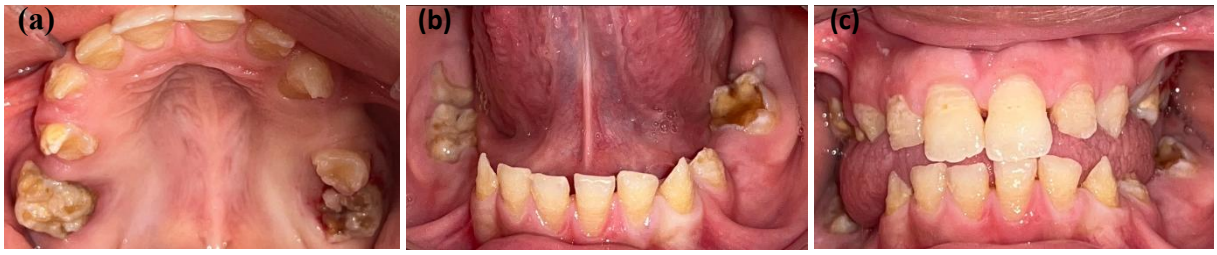

Figure 1: (a) Intraoral view of the maxillary ; (b) Intraoral view of the mandibular arch ; (c) intraoral view of the occlusion

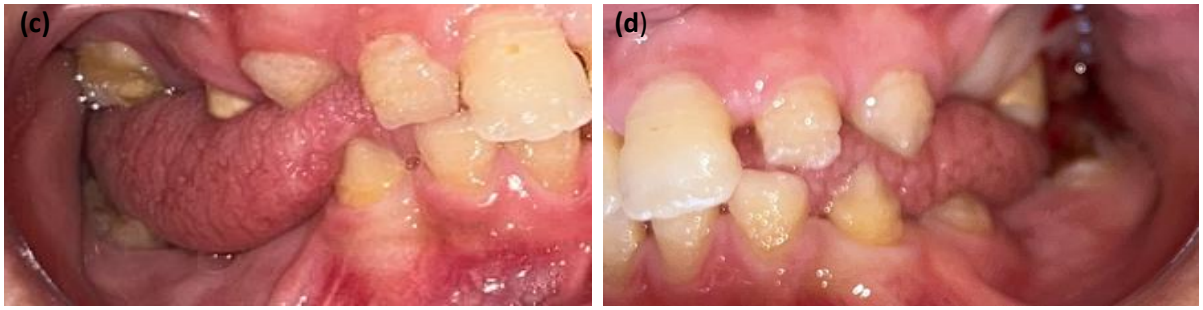

Figure 2: (c) intraoral view of right occlusion ; (d) intraoral view of left occlusion

Figure 3: Statutes of the patient

In an orthopantomographic examination (Figure 4) demonstrated hypomineralized alveolar bone and reduced bone density. Concerning the mineralized tissues of teeth, we noticed an enamel alterations, thin and hypomineralized dentin, widened pulp chambers, and tooth root malformations and carious cavity in #26 and #36. We also noted an external root resorption on the right maxillary first molar #16 related to adjacent tooth #15 eruption due to insufficient space.

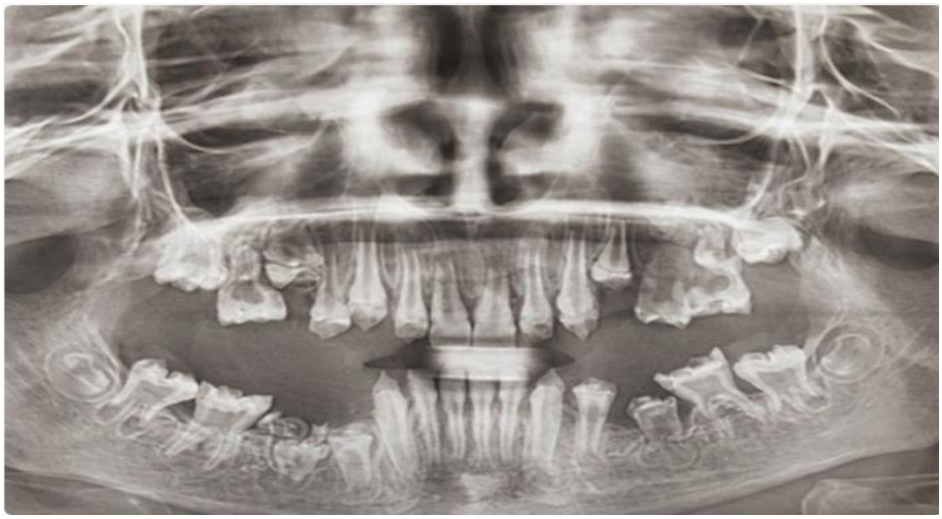

Figure 4: orthopantomographicradiography

Bone metabolism tests revealed the low serum alkaline phosphatase (ALP) levels of 20 U/L (reference range: 156-460 U/L) however, blood calcium level was 2.34 mmol/L (reference range: 2.1-2.57 mmol/L) and blood phosphorus level was 1.71 mmol/L (reference range 0.81-1.45 mmol/L), as shown in Table 1, confirming the diagnosis of hypophosphatasia. Results are shown in Table 1.

	Reference values	Patient's values
PASL	156-460	<20 U/I ↓
CALCIUM	2,1-2,57	2,34 mmol/l
PHOSPHORE	0,81-1,45	1,71 mmol/l

Table 1: Biochemical parameters

The referral letter of her doctor mentioned that the patient has hypophosphatasia with associated spinal deformity (scoliosis), managed with a spinal orthosis (corset) in physical medicine and she is under nonsteroidal anti-inflammatory drug as a symptomatic treatment.

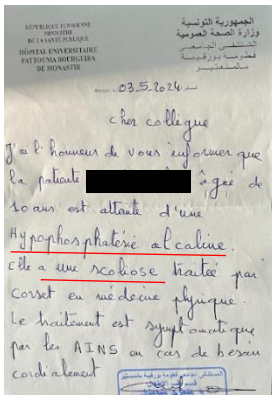

Figure 5: Referral letter from the patient's doctor

The dental diagnosis revealed extensive carious involvement of teeth 25 and 26, associated with root resorption and grade III mobility, in the context of hypophosphatasia. =>The tooth #26 was extracted with the tooth #25 based on clinical and radiographic findings indicating a non-restorable tooth, and a preventive obturation was done on the #36 using composite resin.

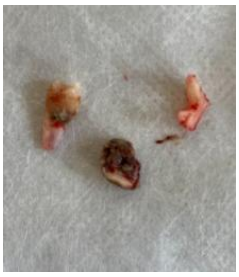

Figure 6: The extracted tooth

The patient was absent for more than a year, she came back with a mobility 3° of her first left permanent incisor #21. A retroalveolar radiography was done showing a tooth root malformation with a periodontal disease. She was referred to a periodontist to control the mobility. We make a rigid contention with a bonded dental splint regarding the number of her teeth and a defective enamel quality which altered the bond.

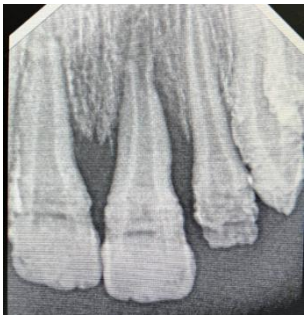

Figure 7: Periapical radiograph of the #21

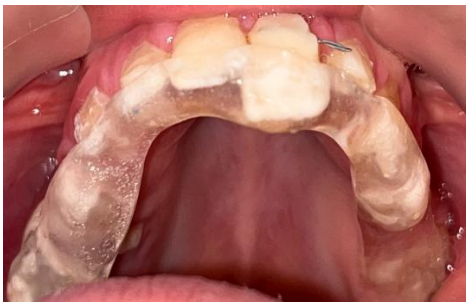

Figure 8: intraoral view with the dental splint

After 3 months she lost her incisor with the dental splint and a removable dental prosthesis replaced the #21 and #26.

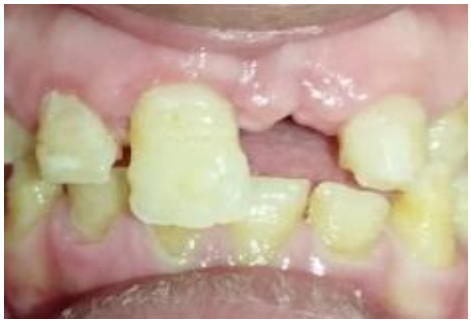

Figure 9: intraoral view after loosing her

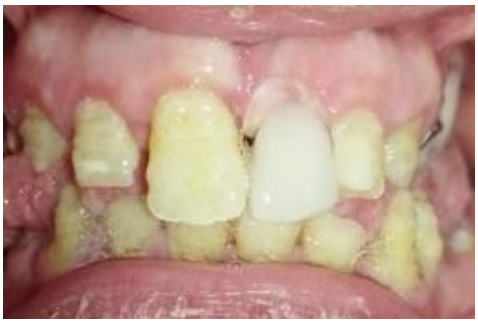

Figure 10: intraoral view with the removable dental prosthesis

After one month the #16 also became painful and mobile because of the resorption caused by the eruption of the adjacent tooth the first right premolar #15 due to lack of space, so it was extracted.

She is still under hygiene control.

Written informed consent for both treatment and case publication was obtained from the parents of the three patients.

Discussion

Mutations in the ALPL gene cause hypophosphatasia, a rare inherited metabolic condition that impairs the mineralization of bone and dental tissues and results in a lack of tissue-nonspecific alkaline phosphatase. The most common general presentation was scoliosis, a spine deformity that is commonly seen in hypophosphatasia patients. (5)

Premature loss of fully rooted deciduous teeth is pathognomonic for HPP, and loss of permanent teeth in adulthood can also occur. Here, the term "fully rooted" indicates substantial remaining root structure teeth are lost due to defective periodontal ligament-cementum attachment. (2) (6)

Dental manifestations may represent the primary clinical expression of the disease and can persist into the permanent dentition, as observed in the present case (7).

This patient, already diagnosed with hypophosphatasia and referred to pediatric dentistry during the permanent dentition stage, exhibited premature loss of a maxillary first molar and a maxillary first incisor. These findings are consistent with the characteristic dental phenotype of hypophosphatasia, which is mainly related to defective cementum formation, gingival recession and the development of periodontal pockets; spaces that develop between tooth root surfaces and gingival tissues, can be made more likely by compromised cementum and bone. These pockets can lead to the buildup of bacteria, an increase in inflammation, and the development of periodontitis, an inflammatory and destructive condition that compromises the periodontal tissues and explains the early loss of teeth (2) (6) (11). All of this was described in Figure 11, compared with a healthy tooth.

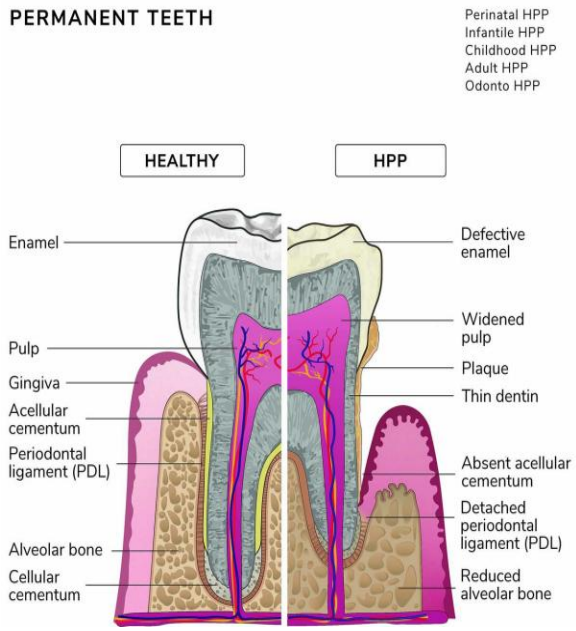

Figure 11: Dental impact of HPP. These schematics of permanent teeth contrast health (left side) and potential effects of HPP (right side), In HPP, permanent teeth can exhibit enamel defects, thin dentin, enlarged pulp chambers, short roots, reduced or absent acellular cementum, periodontal ligament detachment, and reduced alveolar bone. (2)

Other common characteristics include enlarged pulp chambers and enamel hypoplasia. Tooth eruption disorders, such as late tooth eruption and ankylosis of primary teeth, can also be observed (9).

In the same line, Foster BL, 2012 (8) underlines that dental tissue is more sensitive to changes in serum ALP levels than bone tissue,which may explain the most common manifestations of HPP.

Radiographic changes such as alveolar bone hypomineralization, decreased trabecular density, and poorly defined lamina dura further support the diagnosis. However, these findings may vary depending on the severity of the systemic condition (2) (6).

Although, oral signs may appear before any skeletal abnormalities, positioning pediatric dentists as key clinicians for the early detection of HPP like a premature loss of primary teeth which is considered to be the most typical dental sign of this disease (2) (6).

Therapeutically, the introduction of enzyme replacement therapy (asfotase alfa) (10) has significantly improved the prognosis in severe pediatric cases, leading to better skeletal mineralization and improved quality of life which wasn't administered in our case.

The patient was not getting enzyme replacement therapy at the time of dental care; instead, systemic management consisted solely of non-steroidal anti-inflammatory medications. Since there was no systemic treatment that targeted mineralization, this emphasizes the significance of dental-centered preventive and conservative therapies. As a result, our priorities must be growth-compatible functional rehabilitation, avoiding more tooth loss, and preservation of the remaining dentition.

This case emphasizes the essential role of pediatric dentists in the long-term follow-up of patients with hypophosphatasia, particularly in permanent dentition. Early identification of dental complications, implementation of individualized preventive protocols, and coordination within a multidisciplinary care model are fundamental to improve oral function, esthetics, and quality of life in these patients as shown in Table 2.

Manifestations	Clinical Description	Pediatric Relevance
Premature exfoliation of primary teeth (6)	Early loss of incisors/molars without physiological root resorption	Pathognomonic sign in children (2)
Cementum defects and attachment loss(2)	Hypoplastic or absent acellular cementum creating a non-inflammatory periodontal destruction (2)	Early mobility compromising oral functions
Enamel hypoplasia and enamel hypomineralization(2) (9) (11)	Thin, porous enamel (9) (2) (11)	High caries risk (2)(11)
High caries susceptibility(11)	Rapid lesion progression (11)	Preventive priority (11)
Reduced bone density (2) (6)	Hypomineralized alveolar bone(2) (6)	Altered alveolar support
Esthetic impairment	Early tooth loss (2) (6) (11)	Psychosocial effect
Phonetic alteration	Due to anterior tooth loss (2)	Developmental implication
Early rehabilitation (13)	Need for space maintainers/prostheses (13)	Management adapted to craniofacial growth (13)

Table 2: Clinical oral manifestations of hypophosphatasia and pediatric implications

From a clinical management standpoint, dental treatment is mainly preventive and supportive. The goals are to preserve oral function and esthetics, maintain arch integrity, and prevent psychological impact. This may include the use of space maintainers, removable prostheses for anterior esthetics, and reinforcement of oral hygiene measures to minimize gingival inflammation around mobile teeth. (11) (12) (13)

Conclusion

Hypophosphatasia is a rare metabolic disorder in which oral manifestations may constitute key diagnostic indicators which was highlighted by Lira Dos Santos EJ et al. 2025 (2) Pediatric dental intervention remains essential to guide diagnosis, implement preventive and supportive management, ensure arch integrity, and address functional, esthetic, and psychosocial consequences during growth. Early referral, long-term follow-up, and multidisciplinary collaboration are therefore critical to optimise oral health outcomes in children with hypophosphatasia. (7) Patients with hypophosphatasia need multidisciplinary management. Indeed, dental followup starts from an early age and interim removable prosthesis seems to be the best transitional solution until reaching the age of the definitive prosthesis. (13)

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