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Article

Hypophosphatasia: oral cavity and dental disorders

Hypophosphatasie : atteintes buccale et dentaire

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Summary

Dental anomalies exist in every subtype of hypophosphatasia (HPP), from the most severe to the most moderate, called odontohypophosphatasia. The forms are defined by the age at onset of the initial symptoms. These anomalies affect all dental mineralized tissues from enamel, dentin and cementum to alveolar bone in a gradient proportional to the severity of the disease. Early loss of the deciduous teeth, before 3 years of age, and then possibly of the permanent teeth, is due to an abnormality of the cementum, the tissue attaching the teeth to alveolar bone, and is the most frequent abnormality. Tooth loss is a very important diagnostic sign and needs to be recognized. Patients with HPP need specialized oral and dental care in coordination with the reference and expert centers. The oral and dental signs and their treatment remain poorly known. The recording of the abnormalities and their treatment in a registry is indispensable in order to enhance patient management and oral and dental health.

Résumé

Les anomalies dentaires sont présentes dans toutes les formes de l'hypophosphatasie (HPP), de la plus sévère à la plus modérée dite « odontohypophosphatasie ». Elles sont définies par l'âge d'apparition des premiers symptômes. Ces anomalies touchent tous les tissus minéralisés de la dent, à savoir : l'émail, la dentine, le cément et l'os alvéolaire selon un gradient proportionnel à la sévérité de la maladie. La perte précoce de dents temporaires avant l'âge de 3 ans, puis éventuellement de dents permanentes, liée à une anomalie du cément, tissu permettant l'attachement de la dent à l'os alvéolaire, est l'anomalie la plus fréquente. Cette perte des dents est un signe diagnostique très important à reconnaître. Les patients atteints d'HPP nécessitent une prise en charge bucco-dentaire adaptée en coordination avec les centres de référence et de compétence. Ces signes bucco-dentaires et leur prise en charge sont encore mal connus ; le recensement de ces anomalies et leur traitement dans un registre sont indispensables à une amélioration de la prise en charge et de la santé bucco-dentaire des patients.

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1. Introduction

HPP is a genetic disease due to a deficiency in Tissue-Nonspecific Alkaline Phosphatase (TNSALP), an enzyme coded for by the gene *Alkaline Phosphatase, Liver/Bone/Kidney* (*ALPL*), which is important for the mineralization of the skeleton and hard tissues of the teeth and periodontium, namely the enamel, dentin, cementum and alveolar bone [1]. The disease has a wide range of clinical presentations, from the most severe, perinatal, resulting in death *in utero* to the most moderate, known as odontological HPP. The latter presents as dental abnormalities without any other clinical manifestations. The oral/dental features consist in the early and spontaneous loss of the lacteal teeth before age 3 years and, possibly, loss of the permanent teeth. These orodental signs have long been known [2,3] and were reported when the disease was first described [4]. Early deciduous tooth loss may be the first sign of the disease, emerging as of age 6 months and before age 3 years. All the forms of HPP include dental development abnormalities in the clinical picture [5-8]. The various dental tissues referred to in this article are defined and their locations shown in figure 1.

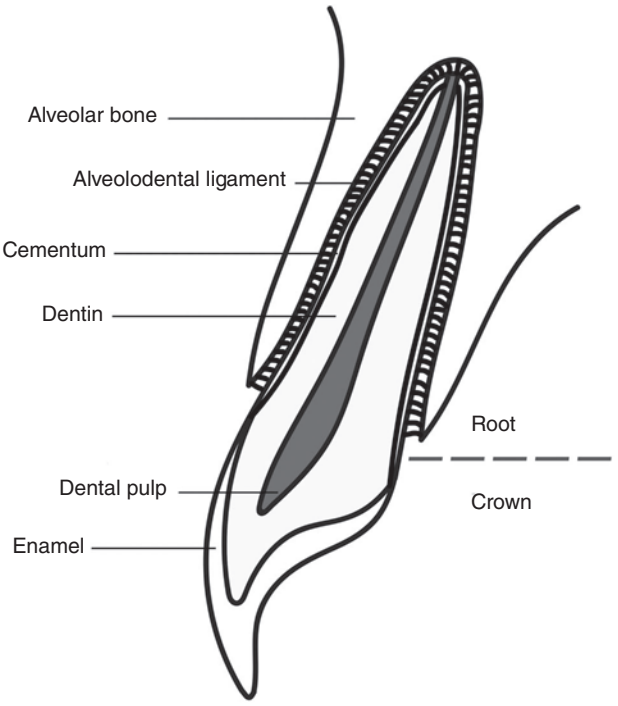

Figure 1. Dental tissues.
The teeth consist of four tissues which are distinct but have strong functional or biological links. Dentin, a tissue like bone, accounts for the majority of the organ. The coronal dentin is covered by enamel and the radicular dentin by a very thin layer of cementum. The dental pulp retains its odontogenesis properties throughout its life. The teeth are connected to alveolar bone by the alveolodental (or periodontal) ligament.

2. Literature review

The oral cavity and, in particular, diet play an important role in HPP. Feeding and weight gain difficulties during childhood are frequently mentioned by patients and their parents (38% of patients and 81% of those in whom the disease is expressed before age 1 year) [9]. Alkaline phosphatase is involved in dental development and the mineralization of the enamel, dentin, cementum and alveolar bone [10-12]. Animal models have been used to simulate the dental abnormalities encountered in human HPP [13,14]. The proposed treatments, enzyme replacement [15-17] or gene therapy [18], alleviate the orodental manifestations in those models.

2.1. Etiology

The accumulation of inorganic pyrophosphate, the substrate of alkaline phosphatase, in the extracellular matrix, underlies the disorders of mineralization of hard dental tissues and, in particular, premature tooth loss [19] due to defective development of the non-cellular cementum [20].

2.2. Clinical aspects

The orodental manifestations affect all the mineralized tissues and appear proportional to the severity of the alkaline phosphatase deficiency.

The cementum, the tissue that anchors a tooth to alveolar bone via the periodontal ligament, seems particularly vulnerable to the accumulation of inorganic pyrophosphate, a substrate not degraded by the defective enzyme and a potent inhibitor of mineralization [21]. Thus, defective cementum underlies the early tooth loss observed in all forms of HPP [22,23]. Early tooth loss is considered as a significant diagnostic sign of the disease, particularly for moderate forms diagnosed during childhood [8]. The teeth become loose and gradually fall out with an intact root in the absence of any infectious or inflammatory context. The dental abnormalities of HPP are listed in table 1 and illustrated in figure 2 [6]. The deciduous dentition seems to be more strongly affected than the permanent teeth [24,25]. Thus, premature loss of the deciduous teeth is not always followed by loss of the permanent teeth. Some patients with adult onset HPP report a history of tooth loss in infancy [26]. It is thus of great importance to question patients about early loss of the lacteal teeth and to determine whether there is a family history of tooth loss. Feeding difficulties and high caries activity evidenced by the presence of numerous caries or dental restorations should also be noted.