The Role of Dentist in Early diagnosis of Odontohypophosphatatasia - A Clinical Case Report

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Abstract: Hypophosphatasia is a genetic disorder that happens very rarely. It affects the way bones and teeth mineralize and is accompanied by a lack of tissue-nonspecific alkaline phosphatase activity in both serum and bone tissues. The estimated prevalence of severe manifestations of the disease is 1 in every 100,000 individuals. Individuals who exhibit dental manifestations characterized by the premature loss of primary teeth without any accompanying systemic symptoms are categorized as having odontohypophosphatasia. This case report will outline the presentation of a three-year-old male patient who sought treatment at our clinic due to premature loss of primary teeth.

Keywords: Hypophosphatasia, Odontohypophosphatasia, OdontoHPP, Alkaline phosphatase, TNSAP

1. Introduction

Hypophosphatasia (HPP) is a hereditary metabolic bone disorder characterized by compromised bone mineralization and related complications due to a deficiency of tissue-nonspecific alkaline phosphatase enzyme (TNSALP), which is one of the three isoforms of alkaline phosphatase enzyme (1,2,3). The estimated prevalence of severe manifestations of the disease is 1 in every 100,000 individuals.

The primary means of diagnosing and confirming HPP is through genetic testing. However, a significant indication of the disease is a decrease in the activity of the alkaline phosphatase (ALP) enzyme, which can be measured by analyzing a blood sample.

HPP is characterized by six distinct classifications that are determined by the timing of symptom onset. These classifications include perinatal, prenatal, benign, infantile, childhood, adult, and odonto-type HPP1–5. Among the different types, perinatal hypophosphatasia (HPP) is generally thought to be the worst. It has clear clinical signs like short and bent limbs, an underdeveloped thoracic cage, and chest deformities. Moreover, specific pregnancies have the potential to culminate in stillbirth. The neonate's lifespan is brief because of respiratory insufficiency.

The diagnosis of adult-onset HPP commonly occurs when skeletal symptoms manifest during middle adulthood. Often though, these individuals recall atypical instances of tooth loss during their early childhood (4) or on the accounts provided by their parents or possess a childhood medical record indicating a history of fractures or persistent muscular discomfort. Clinicians may first think that a person has odontohypophosphatasia (odontoHPP) if they have dental symptoms but no bone disease in the early stages of life (5).

Odonto HPP, is characterized by early loss of primary teeth, severe dental caries, premature exfoliation of permanent teeth, and frequently, dental abscesses (7, 8, 9).

Commonly observed dental abnormalities include irregular development of cementum and enamel, enlarged pulp spaces, and premature shedding of fully rooted primary teeth prior to the age of 5 years, often affecting permanent teeth as well. (12,13), only deciduous teeth are lost prematurely in certain cases, with the anterior teeth being the most affected and lost first, with no evidence of bone disease (14). Sometimes it may be associated with radiographic findings like reduced alveolar bone and an enlarged pulp chamber (14). It is important for clinicians to recognize odontoHPP clinical features to diagnose patients early and manage their dental and bone health (15, 9).

The purpose of this case presentation is to highlight the distinctive features of this hereditary condition and discuss the dental intervention that was undertaken to address the patient’s oral health issues and improve their overall quality of life.

2. Case Description

A male patient, aged 3 years, was brought to the pediatric dental clinic at Princess Haya Bint Al Hussein Hospital in Jordan by his mother. The reason for the visit was the premature loss of the patient's upper right primary central incisor (Figure 1).
During the dental examination, the patient exhibited varying degrees of mobility in their primary teeth.

The patient under consideration is the eldest male sibling within a two-son family unit. The parents, who are not biologically related, have a documented history of six terminated pregnancies.

The mother stated that, to her knowledge, there is no recorded occurrence of atypical tooth shedding among other relatives in the extended family.

Medical history: Thus far, he has exhibited a state of physical well-being in accordance with medical standards.

Extraoral examination: No abnormalities were detected in his nose, eyes, or temporomandibular joint (TMJ), no facial asymmetry, no signs of child abuse or trauma, and no lymphadenopathy.

Intraoral examination: The patient had poor oral hygiene, with signs of mild gingivitis, localized gum recession in the upper left central incisor, and no periodontal involvement with the other teeth. All primary teeth are present, except the upper right primary central incisor, which was exfoliated early and has no history of dental trauma.

Radiographic investigations: A panoramic radiograph (figure 2), periapical radiographs (figure 3), and a hand-wrist radiograph (figure 4) were taken.

No abnormalities were detected, and all permanent teeth are present, with average bone age.

Blood investigations: A complete blood count (CBC), kidney function test, liver function test, and biochemical analysis were done (Table 1).

<table>
<thead>
<tr>
<th>Blood test</th>
<th>Result</th>
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<tbody>
<tr>
<td>Hb</td>
<td>9.6</td>
</tr>
<tr>
<td>WBC</td>
<td>6.01</td>
</tr>
<tr>
<td>RBC</td>
<td>3.83</td>
</tr>
<tr>
<td>MCV</td>
<td>74.2</td>
</tr>
<tr>
<td>PLT</td>
<td>319</td>
</tr>
<tr>
<td>Calcium</td>
<td>10.51</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>6.55</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>49</td>
</tr>
</tbody>
</table>

The patient was anemic with low hemoglobin (Hb) and mean corpuscular volume (MCV) levels.

The biochemical analysis revealed that Ca+ levels are within the normal range, with low alkaline phosphatase and high phosphorus levels. We referred the patient to the endocrine clinic as a case of odontoHPP.

Follow up: After 6 months, the patient showed up to our clinic with further early exfoliated teeth, including lower anterior primary teeth, gum recession of multiple teeth, and different grades of mobility of teeth (Figure 5)
3. Discussion

There is a consensus that the severity of HPP increases with earlier disease onset, leading to a correspondingly worse prognosis. While it is true that certain symptoms may be alleviated naturally in mild cases, the management of these symptoms is still being actively researched (16).

Surgical intervention has the potential to ameliorate bone deformities (17). Phosphate preparations with a high phosphate content, like neutral sodium phosphate or bisphosphonates, can raise serum phosphate levels and increase the amount of inorganic pyrophosphate (PPi) that is passed out of the body through urine (18). The utilization of bone marrow transplantation has demonstrated efficacy in mitigating respiratory complications and skeletal abnormalities in individuals afflicted by perinatal conditions (19). The potential efficacy of mitigating symptoms associated with the infantile form of hypophosphatasia (HPP) in TNSALP-null mice can be observed through the administration of enzyme replacement therapy; this therapy involves the high-dose subcutaneous injection of a mineral-targeting human TNSALP known as sALP-FcD10 (20). In addition, it is important to highlight that asfotase alfa (Strensiq™, Alexion Pharmaceuticals Inc., New Haven, CT, USA), an enzyme replacement therapy, has exhibited substantial therapeutic advantages. This therapy involves the use of a recombinant human tissue-nonspecific alkaline phosphatase (TNSALP). Significant improvements have been observed in skeletal manifestations, pulmonary function, and growth in individuals diagnosed with perinatal or infantile forms of hypophosphatasia (HPP) (21). Recently, regulatory agencies in the United States, Canada, Europe, and Japan have authorized the use of asfotase alfa for the treatment of perinatal/infantile- and juvenile-onset hypophosphatasia (HPP) (22). Another intriguing field of research revolves around the potential application of genetic therapy. Previous studies have demonstrated that the introduction of a viral vector carrying the TNSALP gene into mice results in the maintenance of increased serum TNSALP levels and the alleviation of related symptoms. The intervention described exhibits promising qualities that may have implications for future therapeutic approaches in the treatment of HPP (23).

Patients and their families necessitate suitable education and regular follow-up to address bone and other secondary complications. With the recent approval of enzyme replacement therapy using recombinant human TNSALP, there is a chance that this group of people could benefit from early detection and quick action.

Previous studies on odontoHPPhave provided evidence suggesting that individuals who initially exhibit dental symptoms of HPP during childhood may later develop either the adult or childhood forms of the disease. Therefore, one could posit that odontoHPP should be conceptualized as a disease manifestation that is commonly observed in individuals with HPP during their early developmental stages, rather than being regarded as a separate diagnostic category. This is especially relevant in situations where premature tooth loss is the primary symptom (24).

It is recommended that individuals who experience premature primary tooth loss or notable dental irregularities, particularly in conjunction with low ALP levels relative to their age, undergo an assessment to determine if they have HPP. It is imperative to closely monitor these individuals for additional presentations of HPP, such as delays in development, decreased muscle tone, irregularities in the skeletal structure, elevated levels of calcium in the blood, persistent pain and fatigue, as well as fractures resulting from pathological conditions.

Based on the empirical evidence gathered, we posit that the designation odontoHPP is appropriate for denoting the dental manifestations associated with the disease. Furthermore, we recommend reserving its application as a diagnostic category until a later stage in life, specifically when there is a lack of discernible extra-dental manifestations following an extended period of observation.

Within the scope of our investigation, it has been observed that odontoHPP represents a distinct subtype of hypophosphatasia with autosomal recessive or autosomal dominant inheritance patterns, primarily characterized by its manifestation in the dental phenotype. The diagnosis of this particular form remains a subject of controversy.

4. Conclusion

Many systemic diseases have oral manifestations, and a dentist who specializes in oral and dental health could be the first to diagnose it. The dentist must consider that some dental problems could be alarming signs of systemic disease. So proper dental examination combined with knowledge of systemic diseases is the cornerstone of dentistry.

References


