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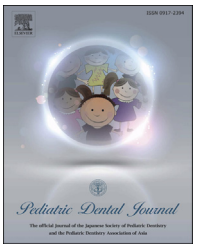

Case Report

Oral findings in patient with lethal hypophosphatasia treated with enzyme replacement therapy

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ABSTRACT

Hypophosphatasia (HPP) is a skeletal disorder, with hypocalcification of bone and early exfoliation of primary teeth displayed in affected individuals. We report here a 3-year-old female diagnosed with perinatal HPP who had received enzyme replacement therapy starting from 1 day after birth. Oral and radiographic examinations revealed deep periodontal pockets, severe mobility, and dentinogenesis imperfecta with root formation defects, especially in the mandibular primary second molars, while the tooth germs of permanent teeth except for the first molars were unclear. Dental manifestations of lethal HPP following treatment with enzyme replacement therapy were markedly different from those of mild HPP.

1. Introduction

Hypophosphatasia (HPP), an inherited skeletal disorder caused by mutations in the *ALPL* gene encoding tissue nonspecific alkaline phosphatase (TNSALP), is characterized by impaired bone mineralization [1–4]. The disorder is classified into 6 clinical forms (perinatal lethal, perinatal benign, infantile, childhood, adult, odonto-hypophosphatasia) based on age at diagnosis, as well as severity of the associated signs and symptoms [1,2,4]. HPP frequency is estimated to be 1 per 100,000 newborns [4]. Dental manifestations include early exfoliation of primary teeth caused by disturbed cementum formation [5], while early exfoliation of primary teeth sometimes leads to diagnosis in mild cases [6]. Until recently, no effective treatment modalities for this disease were available,

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and patients with severe forms often died at or soon after birth due to respiration failure [1–3]. However, enzyme replacement therapy using recombinant TNSALP has been introduced and recent reports have noted positive outcomes [1–3]. Here, we present dental findings of a patient with perinatal lethal HPP who had been treated with enzyme replacement therapy soon after birth.

2. Case report

A Japanese girl was referred to the Pediatric Dentistry Clinic of Osaka University Dental Hospital by the Osaka Medical Center and Research Institute for Maternal and Child Health for consultation regarding severe mobility of primary teeth. A provisional diagnosis of perinatal HPP had been made at 28 weeks of gestation based on fetal 3-dimensional computed tomography findings and the patient was delivered at 37 weeks of gestation by caesarean section. Serum ALP activity was low (2 IU/L, normal reference range for 0–1 month of age 530–1610 IU/L) and severe hypomineralization of bone throughout the body confirmed the diagnosis of HPP. Enzyme replacement therapy using the recombinant ALP drug asfotase alfa (ENB-0040; Alexion Pharmaceuticals, Cheshire, CT) was started at 1 day after birth (2 mg/kg of body weight, 3 times per week, subcutaneous injection). Thoracic and pulmonary hypoplasia were also recognized, and the patient was intubated and ventilated because of respiratory failure. Fortunately, bone mineralization and respiratory function improved with treatment, and the patient was referred to our dental clinic at the age of 3 years 5 months.

Her height was 85.2 cm (−3.0 SD) and weight was 9.75 kg (−2.7 SD), and she could walk with simple assistance. Skeletal and craniofacial bone growth had improved to a normal level, though hearing loss was also observed. The Kyoto Scale of Psychological Development test indicated that at the age of 3 years 6 months, the development status of the patient corresponded to 1 year 2 months. Her mother fed her thickened food in small portions, similar to that given a child after weaning. In addition, she brushed her teeth every night, though the patient was unable to fully open her mouth.

Our initial intraoral examination revealed that all primary teeth had erupted, though the left maxillary primary canine was located in an unusually low position (Fig. 1a–c). Both maxillary primary central incisors showed enamel hypoplasia, with pulp of the maxillary bilateral primary first molars visible through the thin enamel and dentin (Fig. 1a). Excessive dental calculus was attached to the occlusal surface of the primary molars and lingual side of the mandibular primary incisors. A periodontal examination showed deep pockets and severe mobility, especially for the mandibular primary second molars (Fig. 2), while swelling was noted in the buccal gingiva of the left mandibular primary second molar (Fig. 1d). An orthopantomograph revealed thin roots and wide pulp chambers caused by dentinogenesis imperfecta, along with root formation defects, especially for the right and left mandibular second molars (Fig. 3). The tooth germs of the permanent teeth except for the first molars were unclear and their formation appeared to be delayed. In addition, the germs of the second molar were not completely visible.

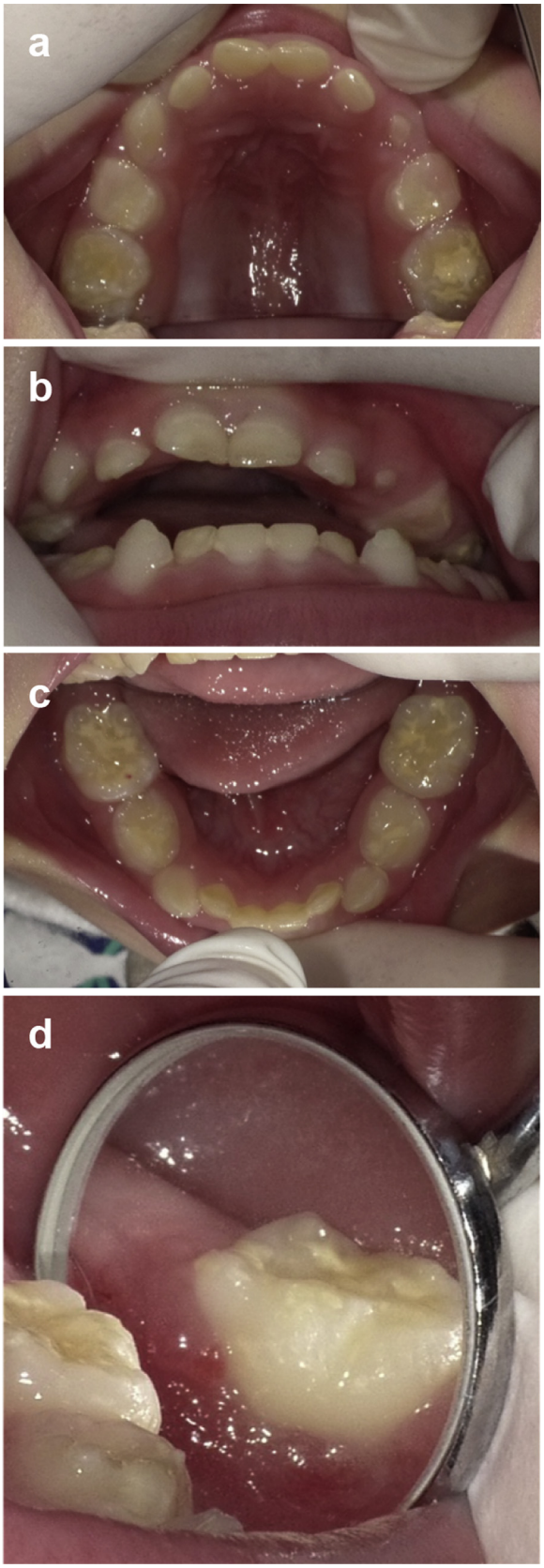

Fig. 1 – Oral photographs obtained at the initial examination (patient age 3 years 5 months). a. Maxillary occlusal view. b. Frontal view. c. Mandibular occlusal view. d. Mirror image of buccal gingiva of mandibular left primary second molar.

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