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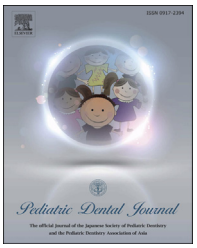

Case Report

Early exfoliation of permanent tooth in patient with hypophosphatasia

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ABSTRACT

Background: Hypophosphatasia (HPP) is a rare inherited skeletal disorder caused by mutations in the *ALPL* gene encoding tissue-nonspecific alkaline phosphatase, with early exfoliation of primary teeth due to disturbed formation of cementum often recognized as a major dental manifestation. However, reports regarding permanent teeth in HPP cases are scant.

Case report: An 11-year-old boy diagnosed with childhood type HPP was referred to our hospital for exfoliation of the maxillary right central incisor. Micro-computed tomography findings of the affected tooth revealed external root resorption, enamel hypoplasia, thin dentin, and a wide pulp chamber, while disturbed cementum formation, enamel hypoplasia, dentin hypo-mineralization, and scant cementum around the enamel junction were observed by scanning electron microscopy.

Conclusion: Permanent teeth may have a risk of early exfoliation as well as other structural abnormalities in HPP patients, thus longitudinal dental follow-up examinations of affected patients are required.

1. Introduction

Hypophosphatasia (HPP), an inherited skeletal disorder caused by mutations of the *ALPL* gene encoding tissue nonspecific alkaline phosphatase is characterized by defective bone mineralization and classified into 6 clinical types (perinatal, benign prenatal, infantile, childhood, adult, odonto) based on age at diagnosis, as well as severity of associated signs and symptoms [1–5]. The frequency of the severe type in newborns is estimated to be 1 per 100,000 [3]. Early exfoliation of primary teeth due to disturbed formation of cementum is known to be a major feature of affected teeth in HPP patients [6–8]. In mild cases, such as childhood and odonto type, dental manifestations found by a dentist can occasionally lead to early diagnosis of HPP [7]. The site of early exfoliation is

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often the anterior primary teeth before the age of 4 years [6], while early exfoliation of permanent teeth is considered to be rare. In the present report, we describe a patient with HPP who showed early exfoliation of a permanent incisor and focus on the morphological features of the affected tooth. Informed consent was obtained from the patient for publication of this case report and accompanying images.

2. Case report

An 11-year-6-month-old Japanese boy was referred to the Pediatric Dentistry Clinic of Osaka University Dental Hospital by pediatricians of the Pediatric Clinic of Osaka University Medical Hospital for consultation regarding mobility of permanent teeth. He had been diagnosed with childhood type hypophosphatasia at the age of 2Y2M due to a low serum alkaline phosphatase (ALP) level (66 IU/l), and radiological examination findings of the lower extremities and hands, which revealed the metaphyseal irregularity of rickets. According to his parents, 2 mandibular primary incisors had spontaneously exfoliated at 2Y2M, and 6 incisors and 2 canines were spontaneously lost by 3Y3M. An intraoral examination demonstrated that all incisors and canines, as well as the first molar had emerged into the oral cavity, each of which showed enamel hypoplasia, while all first molars were located in a prominently lower position (Fig. 1). In addition, the mandibular left primary and bilateral second molars showed internal root resorption. Since the maxillary and mandibular molars did not contact when biting, traumatic occlusion was thought to have occurred in the incisors region. Furthermore, a periodontal examination revealed deep pockets and severe mobility in the maxillary right central incisor and mandibular left central incisor regions (Fig. 2). However, gingival inflammation was mild. In an orthopantomographic examination, all permanent teeth except for the mandibular left second premolar were identified, however, permanent tooth root formation was delayed, and the mandible and maxilla bone appeared to be thin (Fig. 3). In addition, a calcified area sized 6.5 mm in diameter was observed close to the mesial root of the mandibular right first molar. A periapical radiographic examination showed severe absorption of the alveolar bone in the regions of the maxillary right central incisor and mandibular left central incisor (Fig. 4). We considered that it would be difficult to preserve the maxillary right and mandibular left central incisors, though requested a local general dental practitioner to follow the patient and maintain his periodontal condition for preservation of the teeth for as long as possible.

Unfortunately, the maxillary right central incisor was exfoliated due to a traumatic injury caused by striking with his knee at the age of 11Y11M (Fig. 5a and b). The exfoliated tooth showed enamel hypoplasia and external root resorption, and the apex of the root was incompletely closed. After fixing in 10% neutral buffered formalin, the tooth was analyzed using a small-animal micro-computed (CT) tomography device (R_mCT2; Rigaku®, Tokyo, Japan) to assess the morphology of the enamel and dentin (Fig. 5c–e). Those results revealed thin dentin and a wide pulp chamber. External root resorption and enamel hypoplasia were also detected in three-dimensional images generated by reconstruction of the CT data (Fig. 5f and g).

Following the micro-CT analysis, the tooth was hemi-sectioned, half of which was subjected to histological analysis. The hemi-sectioned tooth was demineralized with 0.5 M EDTA at 4 °C, conventionally processed for paraffin embedding, cut into 5-μm-thick sagittal sections, and mounted on silane-coated slides, then subjected to hematoxylin and eosin (H-E) staining. Histopathological findings revealed disturbed cementum formation and incomplete cementum was observed near the enamel region, though that was not detected along the dentin of the root (Fig. 6a–d). The

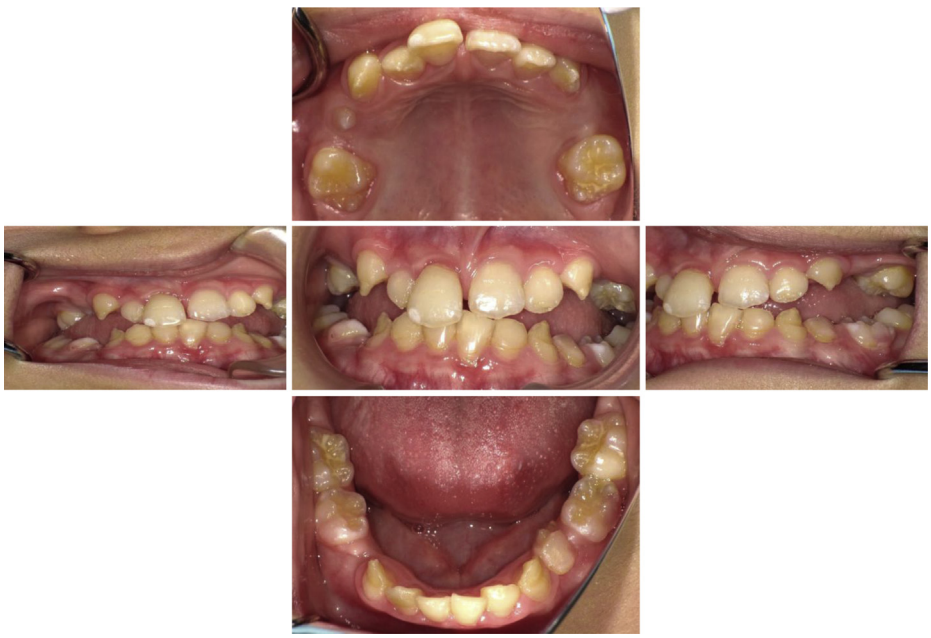

Fig. 1 – Oral photographs obtained at initial examination (patient age 11 years 5 months).

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