Hypophosphatasia is a rare inherited skeletal disorder characterized by defective bone mineralization and tissue non-specific alkaline phosphatase (TNSALP) deficiency, with mutations in the gene encoding the TNSALP isozyme the cause. As for dental manifestations, premature loss of primary teeth due to disturbed cementum formation is well known and tooth roots in affected patients are not able to adequately attach to absorbed alveolar bone due to malformed cementum. We report spontaneous early exfoliation along with mild to severe mobility of primary anterior teeth in 2 child patients referred to pediatric dentists from a general dental practitioner. Case 1 was a 1-year-7-month-old boy with 3 mandibular incisors exfoliated, while Case 2 was a 3-year-3-month-old girl with 1 mandibular central incisor exfoliated. The possibility of hypophosphatasia was considered and the patients were referred to the Pediatric Clinic of Osaka University Medical Hospital, where each was diagnosed with hypophosphatasia (odontotype). We performed repeated periodontal treatments and applied removable partial dentures in both cases, which solved esthetic and functional problems. Although the incidence is quite low, it is important to diagnose hypophosphatasia as early as possible for planning general and dental preventive approaches. In patients with mild forms, such as odonto and childhood types, early exfoliation of primary teeth identified in a dental examination can occasionally lead to early diagnosis of hypophosphatasia. In addition, dental findings obtained by a dentist are useful to identify patients with a risk of hypophosphatasia, who can then be immediately referred to a pediatrician for more detailed systemic examinations. Thus, a cooperative relationship between pediatricians and pediatric dentists should be regarded as necessary. This is the first known report to describe cases of hypophosphatasia diagnosed after referral from a pediatric dentist because of typical dental findings for the disorder.
in stature (-2.5 SD) and TNSALP gene sequencing demonstrated a heterozygous c.550C>T (p.Arg184Trp) mutation.

At 2Y11M, the mandibular primary right lateral incisor was exfoliated and orthopantomograph findings obtained at the age of 3Y5M showed mild absorption of the alveolar bone at the corresponding location (Figure 1f). Thereafter, the patient gradually responded to various dental procedures and we began to manufacture removable partial dentures (Figure 1g), which were applied at the age of 3Y11M (Figure 1h). At 4Y1M, the maxillary primary left central incisors were spontaneously exfoliated (Figure 1i), even though the roots were not resorbed (Figure 1j). A histopathological examination at that time revealed disturbed cementum formation (Figure 1k). Finally, we produced a maxillary partial denture and applied it for the patient (Figures 1l and 1m).

Case 2

Female: An intraoral examination at the first visit demonstrated that 1 mandibular primary central incisor was already exfoliated.
(Figure 2a), while orthopantomograph findings showed mild absorption of alveolar bone at the corresponding location (Figure 2b). According to the mother of the patient, the mandibular primary left central incisor had spontaneously exfoliated at the age of 3Y0M. Periapical radiography showed severe absorption of the alveolar bone (Figures 2c-2e). Furthermore, the other 4 incisors demonstrated prominent mobility (Table 1). Although her mother did not report any systemic problems, we suspected that the patient might be complicated with a systemic disease such as hypophosphatasia and referred her to the Pediatric Clinic of Osaka University Hospital for consultation. Low serum
ALP (254 IU/I) was found and a diagnosis of hypophosphatasia (odontodysplasia type) was made. Radiological examinations of the lower extremities and hands at 3Y5M did not show any signs of rickets (Figures 2f and 2g). The mandibular primary right central incisor was extracted at the age of 3Y6M due to severe mobility. The root of the extracted tooth was not absorbed (Figure 2h) and histopathological findings revealed a

![Figure 2f: Radiograph of lower extremities (3Y5M).](image)

![Figure 2g: Radiograph of right hand (3Y5M).](image)

![Figure 2h: Exfoliated primary teeth.](image)

![Figure 2i: Histopathological appearance of roots of primary teeth.](image)

![Figure 2j: Intraoral photograph before application of partial denture (3Y8M).](image)

![Figure 2k: Partial denture.](image)

![Figure 2l: Intraoral photograph after application of partial denture (3Y8M).](image)
near total lack of cementum (Figure 2i). We applied removable partial dentures at the age of 3Y8M (Figures 2-2j) and then refashioned them at 4Y11M because of incompatibility due to mandible growth.

Discussion

This is the first known report to describe cases of hypophosphatasia diagnosed following referral from a dentist based on findings of spontaneous early exfoliation of primary teeth. In normal individuals, the tooth root surface is covered with cementum tissue, which attaches to alveolar bone via the periodontal ligament. However, in those with hypophosphatasia, the root is not able to adequately attach to absorbed alveolar bone due to disturbed cementum, leading to spontaneous early exfoliation of the affected tooth [5-8]. Dentists can screen for possible cases of hypophosphatasia if they have such knowledge and then refer the suspected patient to a pediatrician for more detailed examinations.

In both of the present cases, exfoliation of primary anterior teeth had started before the age of 4 years and the roots of those teeth appeared to have not undergone resorption, both of which should be regarded as typical dental findings in hypophosphatasia cases. Our patients were ultimately diagnosed with odonto type and no treatments were performed by the attending pediatricians. Mild forms of hypophosphatasia, such as odonto type, are thought to occur most often, with a frequency of 37% reported [9]. Although no medical approaches for cases with odonto type have been reported, affected patients may develop possible problems in the jaw bones. Thus, we consider it necessary to develop some options for improvement of the condition and its associated symptoms by accumulation of similar case reports. In addition, communication between pediatric dentists and pediatricians is important to better treat patients with hypophosphatasia.

Although the present patients were diagnosed as odonto type and no treatment was performed by their respective pediatricians, it is possible that dentists will encounter other mild cases, such as childhood and adult types, which will require medical intervention as soon as possible. Thus, it is important to find patients with a risk of hypophosphatasia based on dental findings by a dentist, who can then immediately refer them to pediatricians for more detailed examinations. A cooperative relationship between pediatricians and pediatric dentists is also necessary for such cases.

As for dental treatment for hypophosphatasia patients, periodontal therapy is important for teeth with mobility. Although that may not recover a healthy condition, it can maintain the stability of the current condition, thus enabling preservation of affected teeth as long as possible. In addition, application of a partial denture is a useful treatment modality for cases with tooth loss, as that can solve not only esthetic but also functional problems, such as mastication and speech. We were able to adequately perform those treatments for the present cases. For patients referred by a pediatrician, it often takes time to initiate such treatment, thus pediatricians should also refer these patients to pediatric dentists if their condition is adequate to undergo dental examinations.

References


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