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CASE reports

A mild form of hypophosphatasia as a cause of premature exfoliation of primary teeth: report of two cases

Wa Sham Cheung, BA, DDS FRCD(C)

Abstract

Two clinical cases of a mild form of hypophosphatasia were reported. The patients presented with premature exfoliation of the primary incisors as their chief complaints. Phosphoethanolamine (PEA) was elevated in their urine specimens and their serum alkaline phosphatase (APase) was below normal level.

Hypophosphatasia (Rasmussen 1983) is a hereditary condition characterized by (1) decreased level of serum alkaline phosphatase (APase), (2) elevation of phosphoethanolamine (PEA) in urine, (3) premature loss of teeth, and (4) skeletal abnormalities. In severe cases, hypercalcemia and hypotonia may also be present (Poland et al. 1972). Four clinical types of hypophosphatasia have been recognized: newborn, infant, child, and adult. The classification is based on the time of diagnosis. The newborn group usually has the poorest prognosis. The majority of them die in the first few months of life. Most of the clinical cases of hypophosphatasia reported in the dental literature are of childhood type,[1] i.e., when the condition was first diagnosed in children after 6 months of age. In all of these reported cases, the patients' serum APase levels were at subnormal value or at the lower end of the normal range. The other consistent findings include the elevation of PEA in the urine and premature exfoliation of primary teeth. However, bony abnormality is only an occasional finding. Other dental abnormalities associated with the condition include enlarged pulp chambers, hypocementosis, and loss of alveolar bone.

The 2 reports presented in this article describe 2 unrelated patients having a condition that can be considered as a mild type of hypophosphatasia in which premature exfoliation of primary incisors was the dominant manifestation.

Case I

Patient AL, a 15-month-old, well developed, well nourished Caucasian female, was referred to the dental office with the chief complaint of premature exfoliation of her 2 primary mandibular central incisors. The mother recalled that 1 tooth exfoliated at 12 months of age, and the other about 14 months. She noticed that the teeth were becoming mobile a few weeks before they exfoliated. She did not recall that the patient had had any previous trauma to the face or the mouth region, nor did she recall any ulceration of the gingiva. The teeth were shed with minimal hemorrhage.

Clinical examination revealed that the 4 maxillary primary incisors and the 2 mandibular primary lateral incisors were present. No mobility was detected in any of the teeth. The gingiva was normal in color, contour, and texture. No sign of root resorption was noted on the exfoliated teeth. Radiographic examination did not reveal any obvious pathology.

The child's complete blood counts were within normal limits. Plasma analyses revealed a calcium level of 9.9 mg/dl (normal; 9–11 mg/dl); phosphorus level of 6.6 mg/dl (normal; 3–6 mg/dl); alkaline phosphatase of 93 u/l (normal female child; 123–502 u/l [Eastman and Bixler 1977]). Urine test for the presence of PEA was requested on 2 separate occasions which revealed 330 and 753 micromoles/g of creatinine (normal child; 43–146 micromoles/g creatinine [Eastman and Bixler 1980]). A tentative diagnosis of hypophosphatasia was made and the family was referred to the Clinical Genetic Unit, Faculty of Medicine, University of British Columbia for further investigation. The patient subsequently received a complete radiographic skeletal survey which was ob-

[1] Fung 1983; Brittain et al. 1976; Baer et al. 1964; Primstone et al. 1966; Bruckner 1962; McCormick and Ripa 1968; Houpt et al. 1970; Casson 1969; Album et al. 1969.

served to be normal, with the bone development age-appropriate. The parents' laboratory results showed that the mother's APase level was 22 u/l (normal adult; 30–100 u/l). The test for the mother's urine PEA was elevated. The father's urine laboratory tests were normal.

The mother was 4 months pregnant and an ultrasound scan showed a twin pregnancy. The twins were appropriately grown, and there was no evidence of severe lethal hypophosphatasia. The mother later gave birth to the twins, a boy and a girl. They were both healthy and showed no signs of hypophosphatasia, but no laboratory tests were conducted. The patient was observed regularly at the dental office for the subsequent year. All the other primary teeth erupted normally. Moderate mobility of her other incisors was noted when she was about 2 years of age.

The young patient in this case had been a very healthy child since birth. Her height and weight were within normal limits, and her developmental milestones were unremarkable. She was the first child of a young couple in their early twenties, unrelated to one another. They were both in good health, and recalled that they lost their primary teeth at school age.

The mother had 3 healthy siblings, and there was no history of premature exfoliation of the primary dentition. Her mother (the patient's maternal grandmother) also had a still birth for unexplained reasons, and 2 early spontaneous pregnancy miscarriages. A review of the family history did not reveal any other members with the likelihood of having hypophosphatasia. The father was the youngest of 7 in the family, with his elder siblings all in good health and no history of premature exfoliation of primary teeth or bony abnormalities.

Case II

Patient AF, a 21-month-old, well developed, well nourished Caucasian female presented to the dental office with an exfoliated mandibular central incisor. The mother noted that the tooth was slightly higher than the others, and gradually increased in height until it "fell out." As far as was known, the loss was not associated with any prior trauma. The exfoliated tooth showed no signs of root resorption and the rest of the primary dentition appeared to be normal. The gingiva was of normal color, contour, and texture.

The child's complete blood counts were within normal limits. Plasma analyses revealed a calcium level of 10.0 mg/dl, phosphorus level of 6.0 mg/dl, and an alkaline phosphatase level of 87 u/l. Urine test for the presence of PEA was requested on 2 separate occasions which revealed 675 and 700 micromoles/g creatinine.

This child also was referred to the same Clinical Genetic Unit for further investigation. The patient's radiographic skeletal survey was observed to be within normal limits. Her mother's laboratory results showed that the alkaline phosphatase level was 27 u/l, and her urine PEA was elevated while the laboratory results of the father and the patient's older brother were all within normal limits.

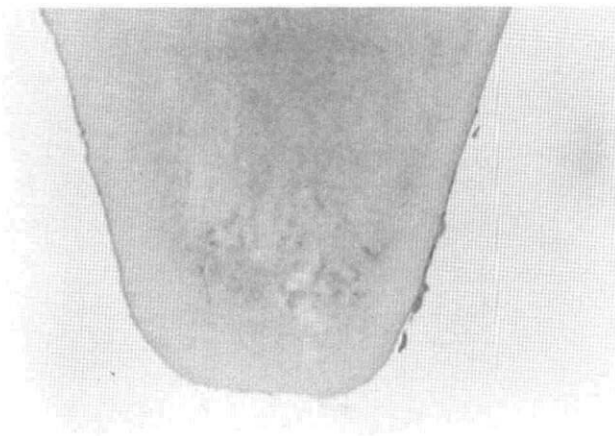

FIG 1. Histological section of the root of the exfoliated tooth. Notice the hypocementosis of the root surface (H&E).

The patient was born to a 25-year-old mother and 30-year-old father. The parents were nonconsanguinous and were in good health. The patient had no major health problems, and her developmental milestones were unremarkable. She had a 4-year-old brother who was in good health. His dental condition was normal. No exfoliation or mobility of any of his teeth was noted.

Microscopic Examination

The exfoliated tooth of patient AF was sent to the histological laboratory for microscopic examination. The decalcified section of the root of the mandibular incisor showed normal dentin, but most of the root was devoid of normal cementum (Fig 1).

Discussion

The 2 cases described in the present article have many similarities. Both patients presented with premature exfoliation of unresorbed primary teeth. They both had elevated levels of PEA in their urine, and the serum APase levels were below normal range. The condition appeared to be a mild form of the hereditary disorder of hypophosphatasia.

It was once agreed that hypophosphatasia is inherited as an autosomal recessive trait (Rasmussen 1983). In the present 2 cases, both patients' mothers could be considered as heterozygous carriers of the condition. They had subnormal levels of serum APase and their urine showed elevation of PEA. Silverman (1962), however, has reported a pedigree strongly

suggesting the condition inherited as an autosomal dominant trait. Recently, Eastman and Bixler (1983) reported detailed clinical and laboratory investigations of 6 hypophosphatasia kindreds. The clinical and biochemical phenotypes were subjected to the segregation analysis. They concluded that the genetic disorder of hypophosphatasia was best described as an autosomal dominant disorder with 85% penetrance and homozygous lethality. In the present 2 cases, especially the first 1, it can be said that the condition was inherited in an autosomal dominant manner with various degrees of penetrance.

Brittain et al. (1976) suggested the term of odontohypophosphatasia to describe mild cases of hypophosphatasia in which premature exfoliation of primary dentition was the dominant clinical manifestation of the condition. In fact both odontohypophosphatasia and hypophosphatasia are the same genetic condition represented as varying phenotypes related to gene dosage (Eastman and Bixler 1983). It is more appropriate to refer to the conditions as hypophosphatasia with or without premature exfoliation of teeth.

In most reported cases of hypophosphatasia there was premature exfoliation of teeth, with hypoplasia or aplasia of the cementum.[2] Since the stability and retention of the teeth depend on the attachment of the periodontal fibers from the cementum to alveolar bone, the irregular deposition or the absence of the cementum probably accounts for the premature loss of teeth (Primstone et al. 1966). Bruckner et al. (1962) suggested that normal cementogenesis may not be able to take place in these affected patients. Whether the abnormality of the cementum matrix formation is directly due to the deficiency of the enzyme APase is not clear.

Due to the mild nature of this form of hypophosphatasia, the detection of it may not be easy. It is possible that many such cases may have been overlooked and never been diagnosed. Thus it is important to test the quantity of PEA in the urine and the level of serum APase when hypophosphatasia is suspected. If PEA is elevated in the urine, the family members should also be tested for hypophosphatasia, or, preferably, they should be referred to the genetic clinic for further investigation. The elevation of PEA in the urine alone, however, may not be a clear indication of the disease. Patients with a variety of metabolic bone diseases and different endocrine disorders may also excrete a considerable amount of PEA in the urine (Licatta et al. 1978).

Different approaches have been used to improve the condition of severe cases of hypophosphatasia where bony abnormality is of major concern. These approaches include a supplement of vitamin D, phosphate, or combination of vitamin D and fluoride (Rasmussen 1983). Unfortunately none of these approaches have proven to be consistently successful. In mild types of the condition where the primary teeth are exfoliating prematurely, the major concern is to maintain the arch length until the permanent dentition erupts.

In view of the cases presented here and the other reported cases, routine complete skeletal radiographic examination does not seem to be indicated. If the possibility of a skeletal dysplasia is suspected, radiographs of hand, wrist, and knee should be evaluated before a complete radiographic survey is ordered.

Unexplained premature loss of primary teeth of young patients always causes anxiety and frustration to the concerned parents. As there are many causes for this phenomenon (Straffon et al. 1985; McDonald and Avery 1983), the dentist should carefully determine the exact cause of the problem. As prudently pointed out by Straffon et al. (1985), a "child who experiences the premature loss of primary teeth may be presenting an early, and diagnostically significant, sign of a more complicated disease." A chief complaint of such should not be taken lightly.

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Dr. Cheung is in private practice, pediatric dentistry. Reprint requests should be sent to Dr. Wa Sham Cheung, 3020 Lincoln Ave.—Suite 103, Coquitlam, B.C. V3B 6B4, Canada.

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