Case report

Case of osteopetrosis with multiple impacted primary and permanent teeth diagnosed at eight years old

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Running title: Case of osteopetrosis with multiple impacted teeth

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Abstract

Background Osteopetrosis is a rare skeletal disease characterized by increased bone density caused by a malfunction of osteoclasts.

Case Presentation An 8-year-4-month-old girl with multiple primary and permanent tooth impaction was diagnosed with osteopetrosis. In spite of typical manifestations of osteopetrosis in early childhood, including visual and hearing impairments, short stature, and dental abnormalities, diagnosis was severely delayed.

Conclusion Multiple impacted teeth may indicate a possible diagnosis of osteopetrosis. Dentists should perform an orthopantomography examination when eruption disturbances are encountered and systemic disease should also be suspected, with referral to a pediatrician when necessary.

1. Introduction

Osteopetrosis, an inherited skeletal disorder initially reported by a German radiologist in 1904 [1], is characterized by increased bone density due to a defect in remodeling caused by malfunction of osteoclasts [2]. Based on its inheritance form and clinical severity, osteopetrosis is classified into three distinct types; (1) severe/malignant infantile type with autosomal recessive inheritance, (2) intermediate type with dominant or autosomal recessive inheritance, and (3) mild/late onset/adult type with autosomal dominant inheritance [3, 4]. As for the main systemic manifestations, bone osteosclerosis develops, resulting in a short stature and likelihood of bone fractures [5]. Osteosclerosis in the skull base causes narrowing of the neural foramen, which leads to cranial nerve damage, as well as vision and hearing loss [3]. Furthermore, deficiency in all types of blood cells due to reduced bone marrow space has been reported to lead to anemia, hemorrhage, and immunodeficiency [6, 7].

Dental manifestations in patients with osteopetrosis include missing teeth, delayed tooth eruption, ankylosed teeth, impacted teeth, crown and root abnormalities, enamel hypoplasia, periodontal membrane defects, narrowing of dental pulp chambers, and mandibular prognathism [8-10]. In addition, disruption of the calcium-phosphorus ratio, enamel defects, and crown abnormalities have been reported to increase retention of dental plaque, making the patient more susceptible to dental caries [11]. In addition, a jawbone affected by osteosclerosis is highly susceptible to fracture [12]. Due to compromised vascular supply, osteomyelitis can occur as a complication of tooth extraction, dental caries, and periodontitis [13]. Jawbone fractures and osteomyelitis are generally treated with symptomatic therapy, thus it is very important for osteopetrosis patients to maintain good oral hygiene for preventing these complications [13, 14].

The incidence of autosomal recessive manner type has been reported to be 1 per 250,000 and autosomal dominant manner type 1 per 20,000 births [15]. While at least 10 genes have been identified as causative factors in humans, gene mutations described thus far only account for approximately 70% of all reported cases and the search continues for genes responsible for the remainder [15]. Since the causative genes are diverse, osteopetrosis has a variety of phenotypes ranging from asymptomatic to fatal [16]. Diagnosis of patients with an asymptomatic or mild condition is often delayed until late adolescence or early adulthood, and sometimes initially revealed by an examination for an accidental bone fracture, or radiograph findings of the hands or legs [17].

Early diagnosis and management of patients with osteopetrosis can improve their quality of life and possibly life expectancy, thus it is important for pediatric dentists to recognize oral manifestations in affected children, and establish effective methods for diagnosis and management. Here, we report a case of osteopetrosis in a patient with multiple impacted primary and permanent teeth diagnosed at the age of 8 years. Informed consent was obtained from the guardians for publication of this case report and the accompanying images.

2. Case report

An 8-year-4-month (8Y4M)-old Japanese girl was referred to the Pediatric Dentistry Clinic of Osaka University Dental Hospital from the pediatric clinic of a children's hospital for prosthetic treatment with dentures to improve masticatory function.

The patient was delivered by cesarean section due to arrest of labor, and had normal height (50 cm) and weight (3114 g) at birth, after which height remained at -2 standard deviation (SD) and weight within ±1 SD thereafter (Figure 1). At the age of 8Y4M, height and weight were 114 cm and 23 kg, respectively. She had visited ophthalmologists and otolaryngologists due to strabismus, visual impairment, and hearing impairment from the age of 1 year. Visual acuity in the right eye was approximately 20/200 (0.01), while the left eye was only able to perceive light and nearly invisible due to bilateral optic nerve hypoplasia. A tube had been placed in the right ear due to otitis media with effusion, while adenoid removal was performed at the same time. The tympanic membrane did not completely close after the tube was removed, resulting in mild hearing loss in the right ear. However, there was no experience with bone fracture.

Primary teeth emerged into the oral cavity from the mandibular primary central incisors at the age of 6 months and the patient started regular dental visits from the age of 3 years for oral management including caries control. The dentist only pointed out the low number of teeth and there was no experience with dental caries. Furthermore, in previous consultations regarding the delayed eruption of primary teeth, the guardians were advised to continue observations. At 8Y0M old, the patient complained of discomfort in the toes and an orthopedic clinic was consulted, with X-ray findings of the toes revealing extremely high bone density. Skeletal disease was suspected and the patient was referred to a specialized hospital, where she was finally diagnosed with osteopetrosis

based on clinical symptoms. Genetic testing was performed, though no known mutation could be identified. Her guardians initially consulted with a doctor regarding masticatory disability caused by permanent successors that had not erupted after primary incisors had exfoliated and they were referred to our clinic.

Our initial examination showed that the maxillary and mandibular bilateral primary canines, and first molar, mandibular right primary second molar, and mandibular bilateral lateral incisors had erupted (Figure 2). Furthermore, the bilateral lateral incisors were twisted. At approximately 5 years old, the maxillary primary central incisors had exfoliated, while exfoliation of the mandibular primary central incisors occurred at around the age of 6 years (Figure 3). Morphological examinations of the crowns of exfoliated primary teeth showed dental calculus accumulation. Root resorption of the teeth caused by spontaneous exfoliation was also observed.

Other examination findings showed irregular enamel and poor oral hygiene, while there was also no history of caries treatment. Gingival recession of the mandibular primary canine was recognized, though mobility of the primary teeth was within the physiological range. Abnormal percussion sounds suggesting ankylosis were not recognized. Orthopantomography and cone beam computed tomography findings revealed multiple impacted primary and permanent teeth, crown and root malformations, and congenital absence of the maxillary bilateral second premolar (Figure 4, 5). No significant abnormalities were observed regarding vertical growth of alveolar bone in the maxillary molar region. We consulted with orthodontists regarding alignment and occlusion, and the patient was classified as having skeletal class III malocclusion with both maxilla and mandibula hypogrowth. Treatments for control of oral hygiene to prevent caries and periodontitis were planned, as well as periodical observations to note

replacement of primary with permanent teeth and growth monitoring of the jaw bone. It was also noted that extraction of primary teeth may be necessary in the future. Three months following the first visit to our clinic, the maxillary permanent central incisor was recognized in the oral cavity.

3. Discussion

Dental abnormalities caused by osteopetrosis are secondary to increased bone density and include delayed tooth eruption, congenital missing teeth, crown and root malformations, and enamel defects [8-11]. In the present case, delayed primary and permanent tooth eruption, as well as crown and root malformations of permanent teeth, and congenitally missing permanent teeth were also recognized. Pulpal necrosis and tooth extraction are primary factors related to osteomyelitis, especially in the mandible of patients affected by osteopetrosis [18]. For the present case, oral hygiene treatments are planned to prevent inflammation spreading to the jaw bone, along with observations to note replacement of primary with permanent teeth and monitoring of jaw bone growth. Following observation of tooth movement, whether to perform surgical or prosthetic treatment was considered.

Based on clinical symptoms, the patient was diagnosed with intermediate type osteopetrosis. Diagnosis of this disease is usually deceived because of increased bone density revealed by findings obtained from radiography performed due to a fracture [19]. Affected patients are sometimes show a short stature, cranial nerve deficits, sensorineural hearing loss, mild or moderately severe anemia, and impacted teeth from early childhood [15]. In spite of visual and hearing impairments, short stature, and dental abnormalities, the present patient was not diagnosed until 8 years old. Dental examination results can sometimes lead to diagnosis of osteopetrosis [5, 20-22], especially those showing

osteomyelitis of the jaw [5, 21, 22]. Fortunately, the intraoral condition of the present patient was found to be good and no factors related to spread of inflammation to the jawbone were noted.

Primary dentition is normally completed at approximately the age of 3 years, while mixed dentition starts at around 6 years old [23]. Pediatric dentists must focus on eruption disturbances of primary teeth, with most of those caused by a local problem such as odontoma [24]. However, multiple eruption disturbances of primary teeth sometimes accompany systemic disease, especially a skeletal disease such as in the present patient. When delayed eruption is noted after the age of 3 years, panoramic radiography should be performed to assess tooth eruption. Early detection by a pediatric dentist can lead to early diagnosis by a pediatrician, which allows for management of growth and development with pediatric examinations and treatments. On the other hand, early intervention by a pediatric dentist is also possible when the disease is known. Collaboration between medical and dental clinics for diagnosis and management is important, especially in cases of skeletal disease.

4. Conclusion

Even though the present patient underwent various examinations at ophthalmology, otolaryngology, and dental clinics, a definitive diagnosis of osteopetrosis was not reached for several years, likely because of its rarity. As for the field of dentistry, if teeth have not erupted in accordance with chronological age at the time of an examination, a check of tooth formation by use of panoramic X-ray imaging may lead to early detection of systemic disease in some cases. In the future, it will be important to establish a system for early diagnosis of children with characteristic dental findings of rare diseases,

including osteopetrosis.

Conflicts of interest

The authors hereby confirm that there are no known conflicts of interest associated with this publication and no significant financial support has been received for this work that could have influenced the findings presented.

Figure legends

Figure 1. Growth curves for height and body weight from 0 to 8 years old.

Figure 2. Intraoral photograph taken at 8Y4M.

Figure 3. Exfoliated primary teeth. **(A)** Upper left primary central incisor. **(B)** Lower right primary central incisor.

Figure 4. (A) Orthopantomogram obtained at hospital examination at 8Y1M and later brought to our clinic. **(B)** Orthopantomogram with estimated number of teeth.

Figure 5. Cone beam computed tomography (CBCT) findings obtained at hospital examination at 8Y1M and later brought to our clinic. **(A)** Three-dimensional construction of CBCT findings without bone. **(B)** Three-dimensional construction of CBCT findings with bone.

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