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Case report

Characteristics and dental considerations of patients with Sotos syndrome

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Sotos syndrome, also called cerebral gigantism, is a rare genetic disease characterized by large height, increased bone age, large head size, characteristic facial morphology which is a long and inverted triangle face, and learning disabilities. Common oral findings include premature eruption of teeth, high and arched palate, and rarely prognathism. Also, congenital missing of the second premolar is often observed. A 7-year-old patient with Sotos syndrome visited the Department of Pediatric Dentistry, Yonsei University Dental Hospital with ectopic-eruption of the maxillary right first molar. In periapical radiograph, tooth germ of maxillary right second premolar was not observed, so maxillary right primary second molar was early extracted and the mesial shift of the maxillary right first molar was induced considering the possibility of congenital missing of the second premolar, a characteristic finding of Sotos syndrome. The second patient was a 10-year-old boy, and visited for dental examination. The patient cooperation was good, and in the panoramic radiography, early loss of the deciduous teeth, congenital missing of mandibular left second premolar and delayed root development of mandibular right canine teeth were found. Patients with Sotos syndrome have dental characteristics and dentists should understand these characteristics and strive to provide better care for the patients. **[Int J Dis Oral Health Vol.16, No.2: 80-84, December 2020]**

Key words: Sotos syndrome, Dental anomaly, Hypodontia

Introduction

Although consideration in oral care for the disabled is increasing, the dental management environment for the disabled is still insufficient. It is generally acknowledged that their dental health is poorer, and their dental needs are greater than for persons without disabilities. Dental treatment for the disabled should take into account the characteristics of the type of disability, and factors such as lack of cooperation or underlying diseases that patients have make dental treatment difficult.[1] Among patients with disabilities, some are familiar to us and some are not. Patients with cerebral palsy or epilepsy are relatively familiar, so we know the characteristics of patients and can keep in mind the precautions in dental treatment.[2,3] Among the many syndromes, Down syndrome is one of the syndromes with well-known dental characteristics.[4] On the other hand, in the case of a syndrome that is not easily seen due to its extremely low prevalence, most of us are not aware of the syndrome itself and do not know the characteristics to be considered for dental treatment. Sotos syndrome is one such syndrome. Sotos syndrome, also called cerebral gigantism, is a rare genetic disease characterized by large height, increased bone age,

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large head size due to over-development of the body during the first to two years of life, characteristic facial morphology, and learning disabilities. Although the exact incidence has not been reported, it is thought to be a frequency of 1/15,000 which is to occur less frequently than the incidence of other hyperdevelopmental diseases. Characteristic facial morphology include long and narrow faces, high forehead, flushed cheeks, small and pointed chin, and outside corners of the eyes may point downward. In addition, common oral findings include premature eruption of teeth, high and arched palate, and rarely prognathism. Also, congenital missing of the second premolar is often observed.[5-8]

Case report

1. Case 1

A 7-year-old patient with Sotos syndrome visited the Department of Pediatric Dentistry, Yonsei University Dental Hospital with ectopic-eruption of the maxillary right first molar. He was diagnosed with Sotos syndrome and had a history of heart surgery with total anomalous pulmonary venous return. Currently, he was prescribed a medication at Ajou University Hospital to control epilepsy. When looking at the results of the clinical genetic test conducted at Ajou University Hospital, a loss of about 2.0 Mb was observed at the site of 5q35.2q35.3, and the deletion of the site contained the NSD1 gene, the cause of Sotos syndrome inherited by autosomal dominance. Figure 1 shows the characteristic facial shape of a patient, long and narrow face, high forehead, small and pointed chin. As a result of the examination, the maxillary right first molar was locked under the distal edge of a primary second molar. In the periapical radiograph taken on the day of visit, the maxillary right first molar was severely locked to maxillary right primary second molar, and it was judged that there is no possibility of natural resolution (Fig. 2). A panoramic radiograph was attempted, but failed due to problems with cooperation. If the maxillary first molar is locked like this patient, early loss of primary molar may occur due to the root resorption, and a considerable amount of space may be lost due to the mesial shift of first molar. When the degree of locking is mild, O-ring can be considered, and when the degree of locking is moderate or severe, aggressive treatment such as Halterman appliance is required. However, in this case, it was judged that the use of the Halterman appliance would be difficult due to lack of cooperation. In the end, it seems that the loss of space due to mesial shifting of the maxillary right first molar cannot be avoided. However, considering that the tooth germ of maxillary

Fig. 1. Frontal photo of the 7-year-old patient diagnosed with sotos syndrome shows a long face, a narrow pointed chin, and an inverted triangle face.

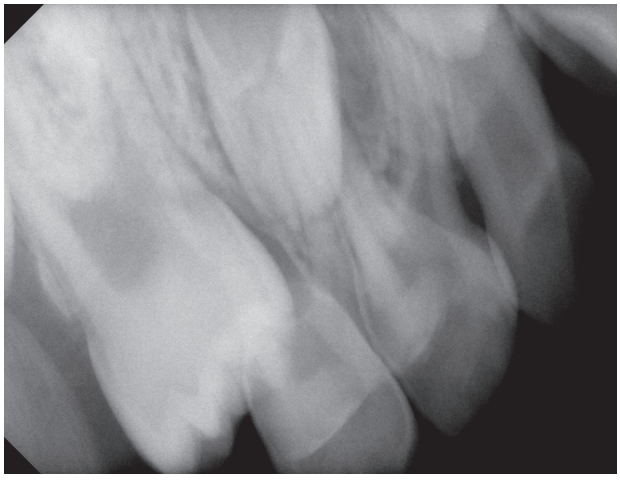

Fig. 2. Periapical view. The maxillary right first molar was severely locked to maxillary right primary second molar and the tooth germ of maxillary right second premolar was not observed.

right second premolar was not observed on the periapical radiograph, and the possibility of congenital missing of the second premolar was high in the case of Sotos syndrome patients, the mesial shift of the first molar rather can be a way to solve the spacing problem caused by missing of premolar. In the case of this patient, the primary second molar was extracted under protective stability and is being followed up continuously.

2. Case 2

A 10-year-old patient with Sotos syndrome visited the Department of Pediatric Dentistry, Yonsei University Dental Hospital for dental examination requested by the Department of Clinical Genetics at Severance Hospital. This patient was referred to Severance Hospital for delayed development and macrocephaly at a local pediatric clinic and was diagnosed with Sotos syndrome. Physically, the growth rate was too fast, at the age of 3 years and 10 months, it was 110.1 cm tall and weighed 21.7 kg, which was included in the top 3% of growth evaluation. Figure 3 is a frontal picture of this patient at 5-year-old. In the pictures, long and narrow face, high forehead, small and pointed chin, which are characteristic facial morphology of children with Sotos syndrome, are observed. As a result of clinical genetic testing, c.5893-6T>G mutation was found in intron18 of the NSD1 gene, which is known to cause Sotos syndrome. As a result of dental examination, there is early loss of many primary molars and a transpalatal arch in the maxilla and a lingual arch in the mandible were placed for space maintenance. In the panoramic radiograph, a congenital missing of mandibular left second premolar and delayed development of mandibular right canine were additionally found (Fig. 4).

Discussion

Sotos syndrome is a rare genetic disorder known to be caused by mutations in the NSD1 gene. There are two types of mutations that cause NSD1 haploinsufficiency: mutations within the NSD1 gene (mutation type) and a 5q35 submicroscopic deletion encompassing the entire NSD1 gene (deletion type).[9] Nagai et al. clinically compared two types of Sotos syndrome patients, and reported that major anomalies such as central nervous, cardiovascular, and urinogenital abnormalities were more common in the deletion-type.[10] In this report, it can be seen that the first patient is the deletion type and the second patient is the mutation type. The NSD1 gene plays a role in directing the production of proteins related to normal growth and development, but the function of this protein is not known exactly.[11] Sotos syndrome is an autosomal dominant inheritance. When a child has Sotos

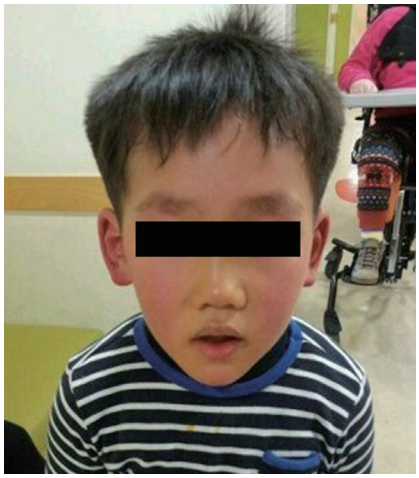

Fig. 3. Frontal photo of the 5-year-old patient diagnosed with sotos syndrome shows a long face, a narrow pointed chin, and an inverted triangle face.

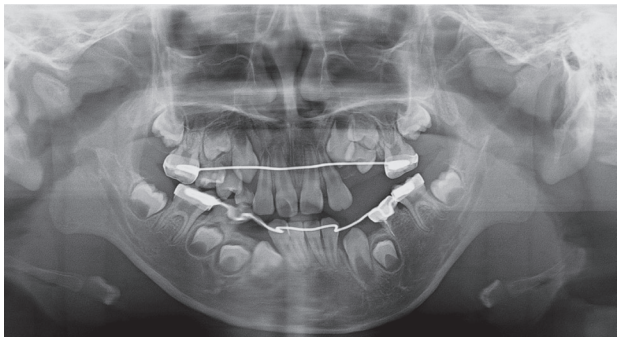

Fig. 4. Panoramic view. Early loss of primary molars, congenital missing of mandibular left second premolar and delayed development of mandibular right canine were observed.

syndrome, the probability of recurrence in the next child is very low, around 1:15,000, but the probability of the patient's child becoming Sotos syndrome is 50%. Sotos syndrome has a characteristic appearance and clinical symptoms, so it is used for diagnosis. Before it was found that the cause of Sotos syndrome was a mutation in the NSD1 gene, the diagnosis of Sotos syndrome was followed by clinical symptoms, characteristic abnormalities found by MRI of the brain, and increased bone age. However, in 20% of patients with Sotos syndrome, bone age is normal or delayed, and only 80% of brain imaging findings are abnormal. If there is no abnormality in the NSD1 gene even though the body is overgrown, learning disabilities, or a peculiar face shape is shown, other diseases should be suspected.[12]

In the first case, maxillary right primary second molar was extracted early, and it was expected that the spacing problem due to the congenital missing of second premolar would be solved through the mesial shift of the first molar. In general, Halterman appliance can be considered for more than moderate locking.[13,14] If there was a healthy child in the same situation or the case of good cooperation, the first consideration would be to eliminate locking through the Halterman appliance. However, in the case of the patient, it was difficult to consider because the cooperation was so poor that the panoramic radiograph could not be taken. In the periapical radiograph, the tooth germ of second premolar was not observed. The initiation of hard tissue formation in the maxillary second premolar begins around 2 - 2 years of age, and the completion period of enamel development is around 6 - 7 years old. The age of the patient was 7 years and 6 months, and it was judged that the possibility of congenital missing was high. Of course, the second premolar may develop at a later age, but it was also considered that congenital missing of premolar frequently appear in patients with Sotos syndrome. Early extraction of maxillary right primary second molar and induction of mesial shift of the first molar is considered appropriate treatment plan.

Even in patients with the same systemic disease, the degree of cooperation differs depending on the severity of the disease or whether there are additional diseases.[15] The patient in the second case had good cooperation, unlike the patient in the first case. Before visiting the Department of Pediatric Dentistry, Yonsei University Dental Hospital, the patient received treatments such as root canal treatment, extraction, and space maintainer at a local dental clinic. Sotos syndrome is often known to have intellectual impairment and autistic trait. In addition, attention deficit hyperactivity disorder (ADHD), phobias, obsessive compulsive disorder, tantrums, and impulsive behaviors are also frequent behavioral impairments.[8,16] However, these characteristics should not be simplified and considered as common to all children with Sotos syndrome. Of course, it is important to know the general characteristics of the disease, but it is necessary to establish a treatment plan with in mind that individual characteristics are different even within the same disease.

Sotos syndrome is an unfamiliar genetic disorder, rarely encountered in the dental office. However, it has a characteristic appearance and dentally significant characteristics, dentists must be able to contribute to improving the quality of life of patients through understanding this syndrome.

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