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Case Report

Sotos syndrome with oligodontia: Case report

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Abstract We present a case of Sotos syndrome. A 2-year-1-month-old Japanese boy diagnosed with Sotos syndrome was referred to our clinic for an oral examination. His growth from birth to the age of 4 years 11 months was pronounced above the 97th percentile. The primary teeth erupted extremely early, with the lower central incisors appearing at the age of 5 months, and all the primary teeth except the lower lateral incisors erupted by the age of 2 years 1 month. In addition, the lower permanent first molar erupted at the age of 4 years 6 months. However, mean dental age did not advance with chronological age. The tooth morphology appeared to be normal, however, the primary teeth were easily degraded by attrition, suggesting the poor calcification. A radiographic examination showed congenital missing of the lower primary and permanent lateral incisors, second premolars, and upper first premolars. In addition, the roots of the primary molars were extremely long and the ration of root length to crown length shown in panoramic radiographs was high.

Key words
Oligodontia,
Sotos syndrome

Introduction

Sotos syndrome, first reported by Sotos *et al.*[1], is a type of cerebral gigantism that appears in childhood. Its characteristic clinical features are overgrowth in childhood, a prominent forehead, advanced bone age, mild mental retardation, and delayed motor and social development. The syndrome is especially characterized by pre- and post-natal overgrowth, resulting in higher birth height and weight above the 97th percentile. Growth during the first few years is particularly pronounced, with height in the 2nd and 6th years of life, still above the 97th percentile, whereas the final height in adults is within a normal range, though in a high percentile[2,3]. These patients with Sotos syndrome commonly show facial features such as frontal bossing, a high hair line, a prominent jaw, and palpebral fissures[4]. The bone age of patients with Sotos syndrome is also advanced above the 97th percentile for age[2]. It was recently reported that the syndrome is caused by a mutation in the gene for the nuclear receptor-binding SET domain-containing protein (NSD1)[5].

There are few studies regarding oral manifestations associated with Sotos syndrome. Callanan *et al.*[6] reported a patient with Class 1 malocclusion with lower anterior crowding and severe dental caries in the primary molars. Further, congenital missing was found for all premolars, all third molars, the upper lateral incisors, and the lower left second molar in the permanent dentition. In another study, Inokuchi *et al.*[7] found enamel hypoplasia in all the primary canines and molars, and congenital missing of the upper first and second premolars, though no dental caries were observed. In the present report, the dental manifestations of a patient with Sotos syndrome are presented.

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Case Report

A 2-year-1-month-old Japanese boy diagnosed with

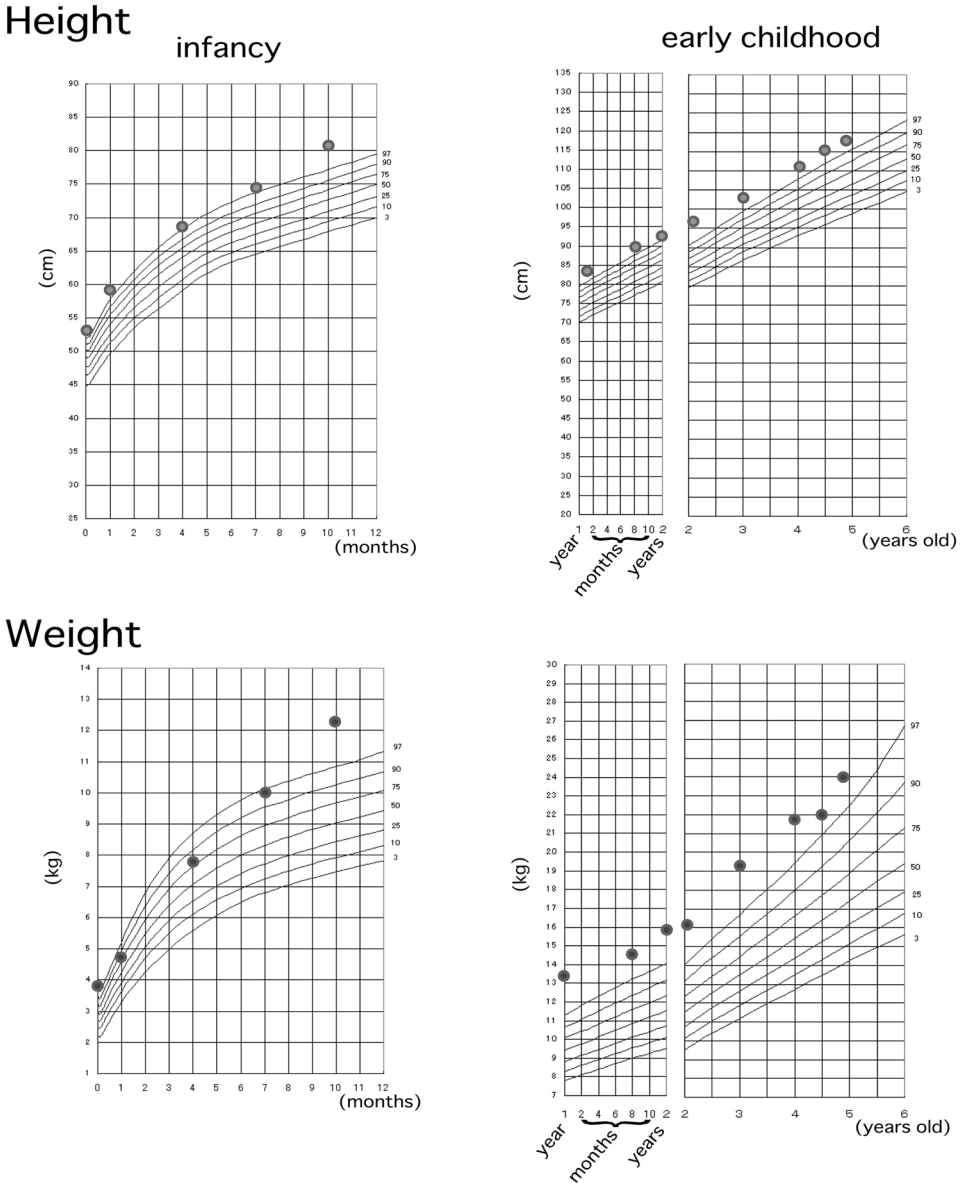

Fig. 1 Growth curve of the patient

As compared the standard curve of Japanese boys, the patient values were greater than the 97th percentile.

Sotos syndrome was referred to the Pedodontic Clinic of Osaka University Dental Hospital for an oral examination by his pediatrician at Osaka University Medical Hospital. His parents are not related and he was born at normal term, though birth weight and height were 3,890 g and 52.8 cm, respectively, both above the 97th percentiles (Fig. 1). Thereafter, the patient grew at a rate that kept him above the 97th percentile for height, and at the age of 2 years 1 month he weighed 16 kg and was 95.5 cm in height. Further, at the age of 4 years 6 months, his weight and height were 22 kg and 115.2 cm, respectively.

An oral examination at the age of 2 years and 1 month showed that all primary teeth except for the lower primary lateral incisors, which were thought to be congenitally missing, had already erupted. His mother later told us that the lower primary central incisors had erupted at the age of 5 months. The lower first permanent molars erupted at the age of 4 years 6 months. The color of the primary teeth at the age of 4 years 11 months appeared to be normal, though a bit whitish and the heights of the tooth

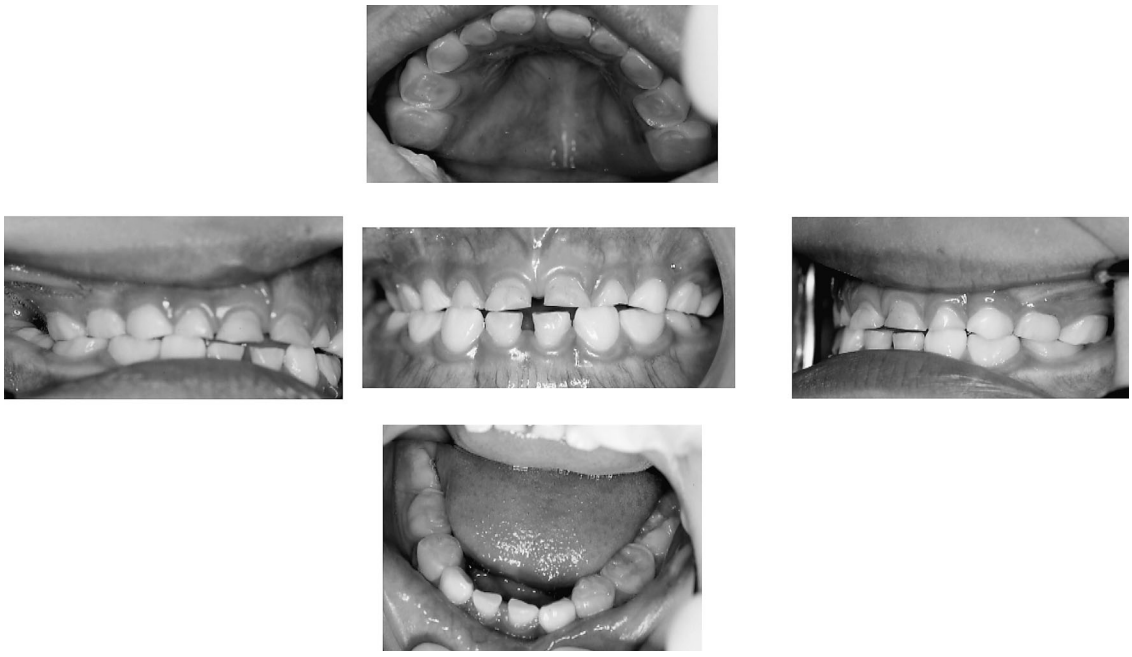

Fig. 2 Oral photographs taken at the age of 4 years 11 months

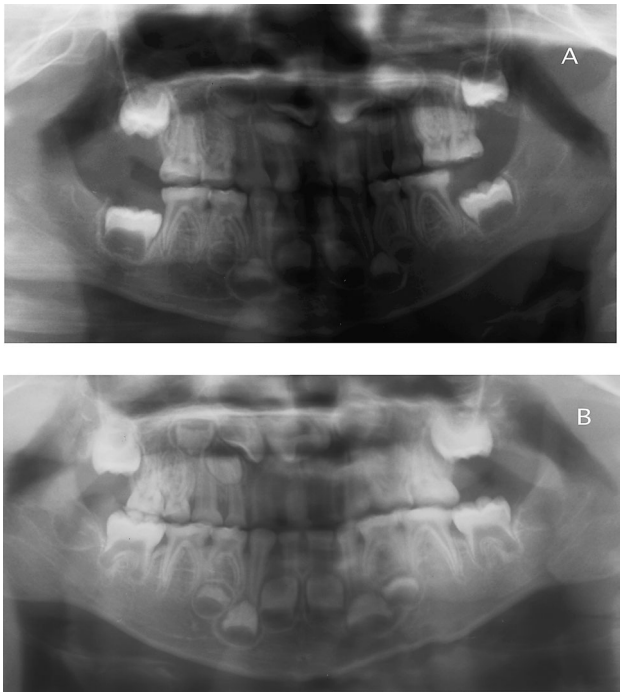

Fig. 3 Panoramic radiographs of the patient
(A) 3 years 8 months of age, (B) 4 years 11 months of age

crowns seemed to become gradually shorter from attrition, which suggested poor calcification (Fig. 2).

A panoramic radiograph taken at the age of 3 years 8 months showed the presence of permanent tooth germs of the central incisors, canines, first molars, upper lateral incisors, and lower first premolars (Fig. 3A), whereas the permanent tooth germs of the second molars, upper first and second

Table 1 Comparison of the crown heights of primary teeth in the patient

mean value of Japanese children	5.62	5.76	6.5	5.78	6.12	6.12	5.78	6.5	5.76	5.62
4 years old 11 months	3.87	3.88	3.84	3.15	3.97	3.92	3.2	4.34	3.69	4.01
4 years old 0 month	4.24	4.35	4.56	3.64	4.13	4.11	3.29	4.48	4.4	4.34
	E	D	C	B	A	A	B	C	D	E
	E	D	C	B	A	A	B	C	D	E
4 years old 0 month	2.95	3.84	6.04	×	4.08	4.09	×	6.05	3.78	2.97
4 years old 11 months	2.93	3.85	5.3	×	4.07	4.06	×	5.54	3.76	2.95
mean value of Japanese children	5.61	6.41	6.94	5.84	5.38	5.38	5.84	6.94	6.41	5.61

Crown height (mm) of the primary teeth in the patient was measured on dental cast models, while their mean value was shown by measuring normal primary teeth extracted from Japanese children.

premolars, lower lateral incisors and lower second premolars were not observed. Further, the lengths of the primary tooth roots appeared to be long, as compared to the height of the respective tooth crown. The ratio of the root length to the crown length (root length/crown length) of the lower second primary molar was 4.55, which is much higher than the mean value (1.86) of normal primary teeth extracted from Japanese children[8]. A panoramic radiograph taken at the age of 4 years 11 months showed the presence of permanent tooth germs of the lower second molars, however, permanent tooth germs of the upper second molars, upper first and second premolars, lower lateral incisors, and lower second premolars were not observed (Fig. 3B).

The dental age of the patient was evaluated using panoramic radiographs taken at the age of 3 years 8 months and 4 years 11 months by the method of Moorrees *et al.*[9], and used to compare with their chronological age. The mean dental age at the age of 3 years 8 months was 3 years 6 months, while that at the age of 4 years 11 months was 5 years 0 month.

Dental casts were taken at the age of 4 years 0 month and 4 years 11 months, and used to compare the crown heights of the primary teeth (Table 1). The crown heights of all primary teeth at the age of 4 years 11 months were shorter than those at the age of 4 years 0 month, and much shorter than the mean values of those of normal primary teeth extracted from Japanese children[8].

Discussion

In the present Sotos syndrome patient, characteristic clinical features such as overgrowth and prominent forehead were recognized, however mental retardation and congenital cardiac anomaly were not observed. In particular, height overgrowth was pronounced, and maintained above the 97th percentile from birth to 4 years 11 months old.

The congenital absence of permanent teeth in Sotos syndrome patients, especially premolars, has been reported in the previous studies[6,7]. We confirmed the congenital absence of primary lower lateral incisors is confirmed, and the permanent tooth germs of the second premolars, upper first premolars, and lower lateral incisors were not observed in the panoramic radiograph images taken at the age of 4 years 11 months. All reports concerning Sotos syndrome show oligodontia in the permanent dentition, which should be considered as a characteristics of oral manifestations in afflicted individuals. In addition, the lengths of the primary tooth roots in our patient were quite long in the dental radiographs, as shown in the previous report[7], which may be another characteristic oral manifestation of Sotos syndrome.

Haploinsufficiency of NSD1, which is essential for post-implantation development, is the major cause of this syndrome[5]. It is considered that the NSD1 protein acts as a nuclear receptor co-repressor and co-activator by interacting with the ligand-binding domain of nuclear hormone receptors. Haploinsufficiency of NSD1 in Sotos syndrome may imply that NSD1 acts as a co-repressor of genes that promote growth. Functional data for this protein in regard to tooth development has not been reported, though enriched *NSD1* expression was detected in the tooth buds of mouse[10]. Further, homozygous mutant *NSD1* mouse embryos show no expression of sonic hedgehog (*Shh*), which is a member of the hedgehog gene family that plays a key role during

embryogenesis and organogenesis. It has also been shown that Shh signaling is necessary for the tooth bud initiation and development[11]. During the later bell stage during tooth development, *Shh* expression is downregulated in differentiating ameloblasts as they mature into a secretory population. Therefore, it is likely that NSD1 insufficiency causes oligodontia and enamel hypoplasia by itself and/or via Shh signaling.

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