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Case report

A case of Costello syndrome with delayed eruption of primary teeth☆

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ABSTRACT

Costello syndrome is very rare and a multiple malformation syndrome that includes characteristic craniofacial features, skin abnormality, severe failure to thrive, congenital cardiac abnormalities including hypertrophic cardiomyopathy, predisposition of papillomas and malignant tumors, and neurologic abnormalities. We report on the oral manifestation of a 27-month-old Japanese boy with this syndrome associated with delayed eruption of primary teeth. The oral characteristics of our patient included thick lips, high-arched palate, and macroglossia, but abnormal tooth morphology and missing were not observed. The data on the mesiodistal diameter of the primary teeth and the dental arch were similar to the mean values of Japanese infants aged 3–4 years old, except that the mesiodistal diameter of the lower primary canines and distance between the buccal cusp tips of the primary first molars of the mandible was smaller.

Costello syndrome is a multiple malformation syndrome that was first reported in 1971 by Costello. The syndrome includes characteristic craniofacial features, skin abnormality, severe failure to thrive, congenital cardiac abnormalities including hypertrophic cardiomyopathy, predisposition of papillomas and malignant tumors, and neurologic abnormalities such as developmental delay and mental retardation [1]. Costello syndrome used to be diagnosed based on these features, but genetic diagnosis is now widely used since Aoki et al. identified the association of the disease with a mutation in the Harvey-RAS (HRAS) gene in 2005 [2,3]. There are over 100 cases of Costello syndrome reported in the literature. However, the disease is relatively rare, with the number of patients estimated to be approximately 200–300, although the exact incidence is unknown [4]. There are no detailed reports on Costello syndrome in the oral cavity. Here, we report a case of an oral manifestation of this syndrome associated with delayed eruption of primary teeth.

1. Case report

The patient was a 27-month-old Japanese boy who was referred to the Department of Dentistry and Oral Surgery from the NICU of the National Hospital Organization Mie Chuo Medical Center for a close examination of delayed eruption of primary teeth and appropriate oral management. His family history included Hashimoto's disease in his mother. The patient was born as one of dizygotic twins and delivered by Cesarean section due to polyhydramnios (33 weeks and 6 days of gestation; 2504 g; Apgar score 5 points (1 min), 7 points (5 min); second twin). Macrocephaly was present at birth (36 cm). The patient was intubated until Day 11 after birth for control of respiration due to diagnosis of respiratory distress syndrome. Phenobarbital for sedation was administered at a starting dose of 11 mg/kg/day, and was subsequently reduced and continued until Day 699 after birth.

On Day 6 after birth, patent ductus arteriosus ligation was performed for treatment of heart failure and pulmonary hemorrhage caused by patent ductus arteriosus. Thereafter, respiratory insufficiency worsened and the patient was intubated again on Day 60 after birth. Tracheobronchomalacia was diagnosed and tracheostomy was performed on Day 97 after birth, but artificial respiration control was required from Day 125 after birth due to ventilatory defect. Swallowing training was started from Day 200 after birth, but the patient repeatedly developed aphagia and aspiration pneumonia. In addition, he frequently vomited milk-like contents from around Day 410 after birth. Therefore, gastrostomy

☆ AsianAOMS: Asian Association of Oral and Maxillofacial Surgeons; ASOMP: Asian Society of Oral and Maxillofacial Pathology; JSOP: Japanese Society of Oral Pathology; JSOMS: Japanese Society of Oral and Maxillofacial Surgeons; JSOM: Japanese Society of Oral Medicine; JAMI: Japanese Academy of Maxillofacial Implants.

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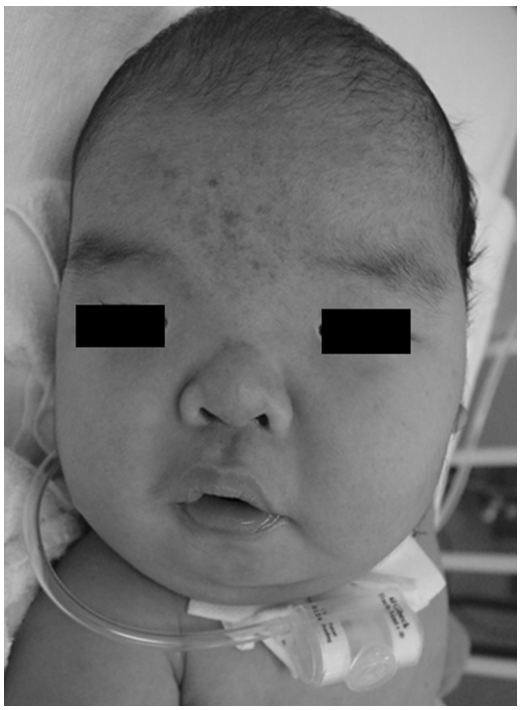

Fig. 1. The findings at the initial examination. Macrocephaly, high and broad forehead, short neck, thin hair (slightly curly hair), low-set ears, hypertelorism, blepharophimosis, and depressed nasal bridge were observed.

and a Nissen operation were performed to start tube feeding on Day 659 after birth. Oral findings included delayed eruption of primary incisors and canines, while the primary molars had started to erupt from around 18 months old.

A preoperative cardiac echo test showed mild myocardial hyperplasia and arrhythmia. Costello syndrome was suspected based on the presence of myocardial hyperplasia, development of postoperative impaired glucose tolerance (dumping syndrome), and appearances that manifested during the course (macrocephaly, high and broad forehead, hypertelorism, blepharophimosis, depressed nasal bridge, low-set ears, thin hair (slightly curly hair), thick lips, high-arched palate, short neck, short stature, loose skin, and limitation of elbow/knee extension). Respiratory distress syndrome, tracheobronchomalacia and patent ductus arteriosus are not major symptoms of this syndrome, but aphagia occur at high frequency. The diagnosis of Costello syndrome was confirmed by detection of a HRAS mutation (c. 34 g >a, G12S) in a genetic test.

The findings at our initial examination were macrocephaly, high and broad forehead, short neck, thin hair (slightly curly hair), low-set ears, hypertelorism, blepharophimosis, and depressed nasal bridge (Fig. 1). Oral findings included thick lips, high-arched palate, hyperplasia of the palatal gingiva, open bite and macroglossia. In the mandible, the primary central and lateral incisor, primary canine and primary first molars had already erupted on both sides. However, in the maxilla, the right primary first molar alone had erupted and eruption of the right primary lateral incisor and canine and the left primary canine and first molar was in progress. The upper primary central incisors and the upper left primary lateral incisor had not to erupt (Fig. 2). Neither abnormal tooth morphology nor odontodysplasia was observed. X-ray findings showed the presence of crowns for the upper and lower second primary molars, permanent first molars, central incisors, and lateral incisors, and there were no missing teeth on the images (Fig. 3).

Tooth brushing alone was performed for oral hygiene without gingivectomy, and the upper primary central incisors started to erupt 2 months after the initial examination (Fig. 4). The patient was discharged, and under treatment at home at this point. According to his parents, the upper left primary lateral incisor erupted 1 month later. Unfortunately, the patient died of heart failure when he was 30 months old.

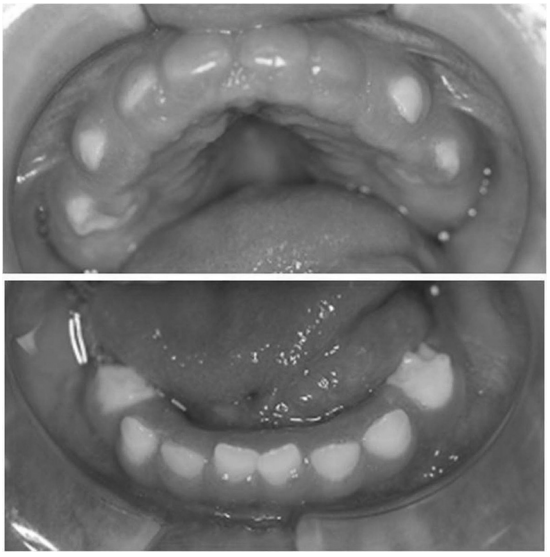

Fig. 2. Oral findings at the initial examination. High-arched palate, hyperplasia of the palatal gingiva, and macroglossia were observed. In the mandible, the primary central and lateral incisor, primary canine and primary first molars had already erupted on both sides. In the maxilla, the right primary first molar alone had erupted and eruption of the right primary lateral incisor and canine and the left primary canine and first molar was in progress.

1.1. Sizes of the primary tooth crown and primary dental arch

Maxilla and mandible dentition models were made at the initial examination to evaluate the sizes of the primary tooth crowns and dental arch. Evaluation of the size of the primary tooth crowns was

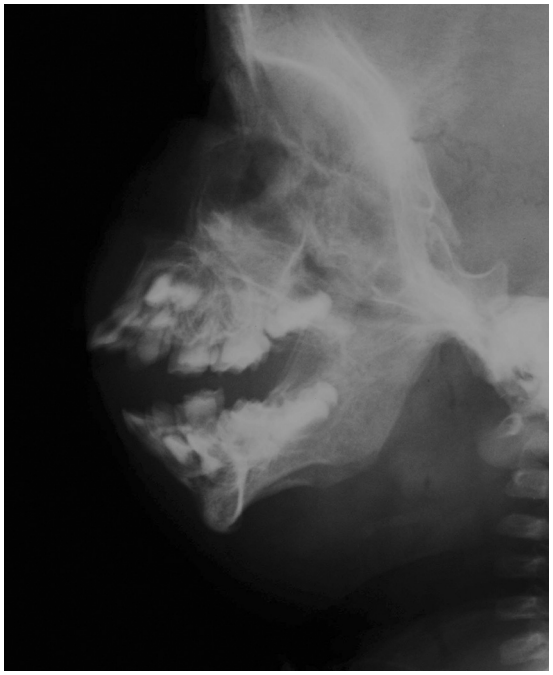

Fig. 3. X-ray findings showed the presence of crowns for the upper and lower second primary molars, permanent first molars, central incisors, and lateral incisors.