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Solitary median maxillary central incisor syndrome occurring together with oromandibular-limb hypogenesis syndrome type 1: a case report of this previously unreported combination of syndromes

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Background. Solitary median maxillary central incisor syndrome is a unique developmental abnormality, involving the central incisor tooth germs, occurring with and without systemic involvement. This syndrome has been recorded in association with many other midline developmental anomalies and several known syndromes. Its presence, together with oromandibular-limb hypogenesis syndrome type 1, has not previously been reported.

Case report. A 3-year-old girl was presented with early childhood caries and a solitary median maxillary central incisor. She had a median submucosal cleft palate and severe micrognathia with hypoglossia. In addition, she had short stature, eating difficulty, and hearing and speech problems. Comprehensive dental treatment for severe early childhood caries was accomplished with a 3-month follow-up appointment to monitor the oral health. The multidisciplinary consultation important for further management has been established.

Conclusion. The results suggested that when a solitary median maxillary incisor tooth presents, a paediatrician and a geneticist should be asked to carefully examine the patient for other craniofacial malformations and especially midline systemic problems.

Introduction

The absence of upper central incisors was first reported by Scott[1] in 1958. In 1968, Fulstow[2] published a case of the congenital absence of an upper central incisor occurring together with short stature, congenital heart disease, microcephaly, and scoliosis. Rappaport *et al.*[3], in 1976, introduced the term 'monosuperocentroincisivodontic dwarfism' to describe the association between a single maxillary central incisor and isolated growth hormone deficiency. This association was later confirmed by Vanelli *et al.*[4] Other cases presented short stature, but normal growth hormone levels[5,6]. A single maxillary central incisor has also been reported as an isolated finding in association with normal growth[6–10].

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Among several names suggested by other authors[5–9], solitary median maxillary central incisor (SMMCI) syndrome (OMIM #147250) was originally suggested by Hall *et al.*[11] and has become the accepted term to describe the peculiarly formed symmetric incisor tooth occurring with and without other systemic involvement. The incidence of SMMCI is approximately 1 : 50 000 live births[11]. The aetiology remains uncertain although Nanni *et al.*[12] suggested that missense mutation in the *SHH* gene (I111F) at 7q36 may be associated with SMMCI. The defective process was estimated to occur at or before day 38–40 *in utero*[11]. The SMMCI has been found as a feature of holoprosencephaly, a midline defect of the brain and craniofacial structures which ranges from the gross malformation cyclopia, which is incompatible with life, to hypotelorism, nasomaxillary hypoplasia, and false median cleft lip and palate[13].

SMMCI may present as an isolated finding or in association with many other midline developmental anomalies including short stature[3–5,11], pituitary insufficiency[3,4], microcephaly[2,14],

congenital heart disease[2], choanal atresia[11], midnasal stenosis[11], and congenital nasal pyriform aperture stenosis[15]. Several known syndromes have been recorded in patients with the SMMCI, including CHARGE[11,16] and VACTERL[11] associations, velocardiofacial syndrome[11], autosomal dominant HPE[12], ectodermal dysplasia[17], and Duane retraction syndrome[18]. In addition, SMMCI can be found in association with specific chromosomal abnormalities such as 18p deletion[19], a ring chromosome 18[20], 7q terminal deletions[21], and deletion of 22q11.2[11] and triple-X syndrome[22]. A complete review of SMMCI syndrome has been published by Hall[23].

The congenital anomaly of extreme microglossia (hypoglossia or aglossia) is a rare condition. The most recent 'count' in the article by Weingarten *et al*.[24] was of 47 cases. Rosenthal[25] gave the term 'glossia congenital' for this anomaly in 1932. Hall[26] introduced the term 'hypoglossia' and linked this condition with hypodactylia, a frequently associating abnormality. Subsequently, Gorlin *et al*.[27] referred to this anomaly as the hypoglossia–hypodactylia syndrome, and classified it as one of the oromandibular-limb hypogenesis spectrum disorders (OMIM #103300). The classification is, however, complex as these abnormalities are sporadic in nature and involve the tongue, mandible and/or maxilla, and upper or lower limbs, all to a varying degree. Hall's classification in 1971 has been modified by Gorlin *et al*.[27] (Table 1). In type 1, limb involvement is absent.

Table 1. Syndromes of oromandibular-limb hypogenesis.

Type I
Hypoglossia
Aglossia
Type II
Hypoglossia–hypodactylia
Hypoglossia–hypomelia
Type III
Glossopalatine ankylosis
With hypoglossia
With hypoglossia–hypodactylia
With hypoglossia–hypomelia
With hypoglossia–hypodactylomelia
Type IV
Intraoral bands and fusion
With hypoglossia
With hypoglossia–hypodactylia
With hypoglossia–hypomelia
With hypoglossia–hypodactylomelia
Type V
Hanhart syndrome
Charles M. syndrome
Robin syndrome
Moebius syndrome
Amnionic rupture sequence

Case report

The patient was a 3-year-old Thai girl (Fig. 1). She attended the Pediatric Dentistry Clinic, Faculty of Dentistry, Khon Kaen University, Thailand because of early childhood caries. The information collected from the parents; medical history; and physical, oral, and radiographic examinations was investigated. Both parents and her younger brother were of normal stature and were healthy. There was no history of hereditary disease in her family. Her weight (12 kg) and her height (86 cm) were below the fifth percentile of the standard weight and height of Thai children. Her head circumference (49 cm) was, however, within average. She had normal limbs and digits. Although she could

Fig. 1. Three-year-old girl with solitary median maxillary central incisor syndrome.

speak only a few words, her intellectual ability seemed at this stage to be average.

The medical history revealed that she was born at 32 weeks gestation with a weight of 2100 g. Her father was 35 and her mother was 34 years of age at her birth. In the neonatal period, she was treated with oxygen supplementation for 2 weeks because of pneumonia. Apart from that, she also had congenital sensorineural hearing loss, submucosal cleft palate, and micrognathia with hypoglossia. She, therefore, had suckling difficulty and later eating difficulty which have continued to the present. She could not chew because the maxillary teeth did not occluded well with the mandibular teeth. Feeding advice is still being given by a paediatrician to increase the body weight. She has also received ongoing treatment by an otorhinolaryngologist and a speech therapist. Hearing aids were placed when she was 2 years of age.

The dental history revealed that the patient was first seen by a dentist at the age of 1 year and 10 months because of severe dental caries. There was no history of trauma to the upper anterior segment. Because of her inability to cooperate, only an occlusal view of the upper anterior teeth could be taken which revealed a solitary maxillary primary central incisor with extensive carious lesions and the left lateral incisor with lingual talon cusp (Fig. 2).

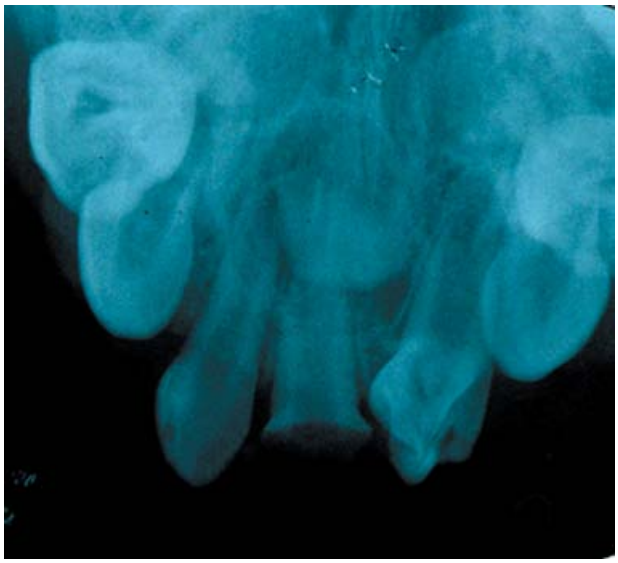

Fig. 2. Maxillary topographic radiograph: a carious primary solitary median maxillary central incisor and left lateral incisor with lingual talon cusp.

Fig. 3. Lateral profile of the girl.

All carious teeth have now been treated in the dental chair (at the parents' request) but with difficulty, because of the patient's limited ability to cooperate.

Recent examination, after complete dental treatment, showed that the patient had convex facial profile with severe mandibular retrognathism (Fig. 3). The upper lip had an arched shape with an indistinct philtrum. There was no sign of nasal obstruction. Intraorally, maxillary, and mandibular frenula, and the incisive papilla were absent (Figs 4 and 5a). She was in the primary dentition stage, with the second primary molars erupting. Although the patient had previously received complete dental treatment, all new erupting molars were now carious. The parent reported that the patient could eat only soft food and brushing her teeth was very difficult. The mandible was collapsed inwards, being extremely small and narrow (Fig. 6a,b). This, in addition to the hypoglossia, resulted in a deep posterior overbite (Fig. 4) and eating difficulty. Radiographic examination also revealed a developing permanent SMMCI (Fig. 5b). Interestingly, both mandibular central incisors and associated alveolar and basal bone were also absent (Fig. 6b).

Multidisciplinary consultation for further management has been established. It included a neurologist, a nutritionist, an endocrinologist, a geneticist, an orthodontist, an oral and maxillofacial surgeon, and a prosthodontist.

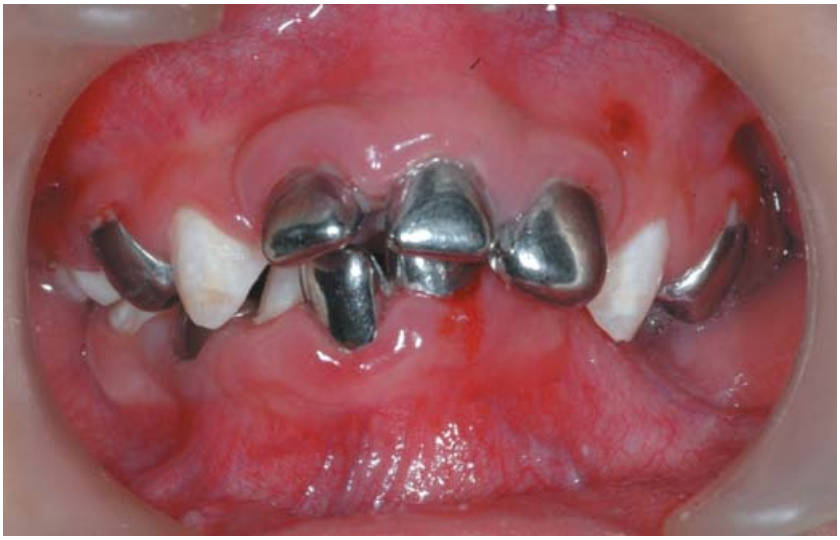

Fig. 4. Absence of maxillary and mandibular frenula and deep posterior overbite.

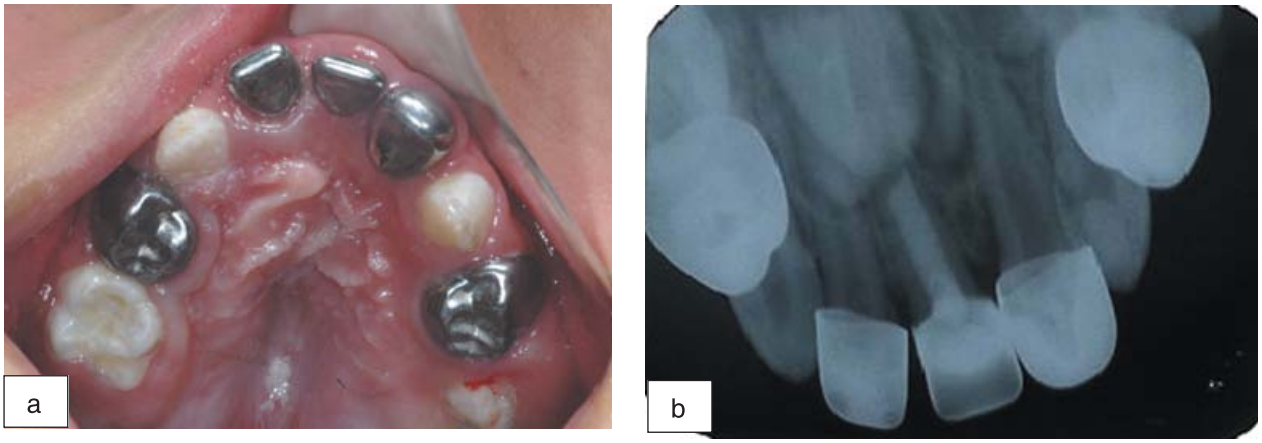

Fig. 5. (a) Absent incisive papilla. (b) Maxillary topographic radiograph: a restored primary solitary median maxillary central incisor (SMMCI) and a developing permanent SMMCI.

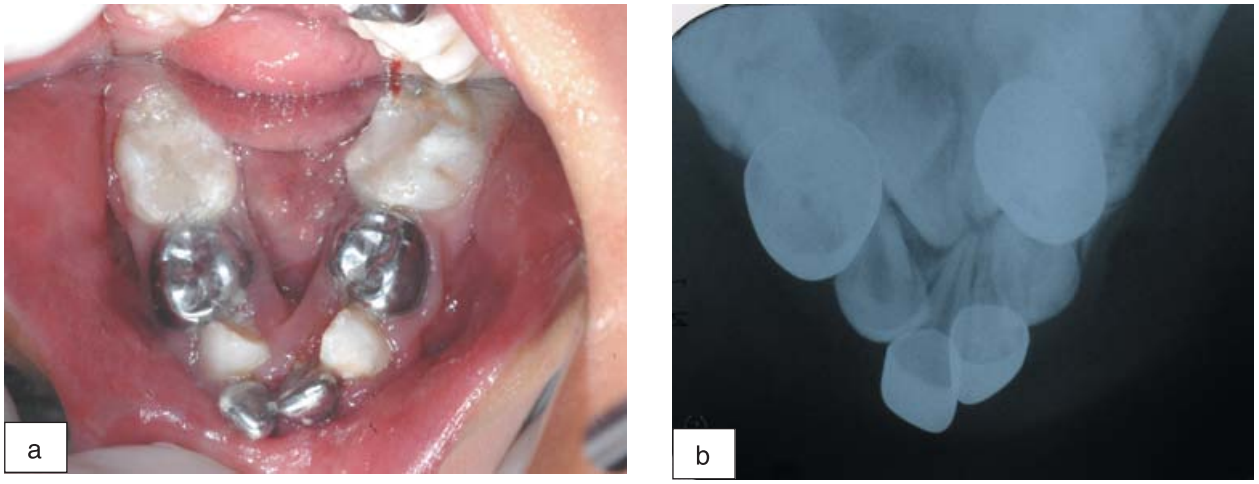

Fig. 6. (a) Small and narrow, tapered mandible with absence of central incisor teeth. (b) Mandibular topographic radiograph: absence of mandibular central incisors and associated alveolar and basal bone.

Discussion

The SMMCI tooth is unique in that both crown and root are symmetrical[23]. It develops precisely in the midline and is the sole central incisor present with the crown and root size the same as that of a normal central incisor[17]. The clinical and radiographic findings and absence of any history of trauma confirmed that this patient had an SMMCI tooth. The mechanism leading to the formation of an SMMCI tooth is unknown, although Hall *et al.*[11] have postulated that a critical absence of, or reduction in, lateral growth from the midline, on or about gestation day 37 or 38, results in premature fusion of the epithelial dental lamina, thus preventing the formation of two complete and separate central incisor teeth. Instead, one tooth consisting of two normal distal halves of the central incisors develops from the fused enamel knots and subadjacent mesenchyme of these tooth germs.

Apart from SMMCI, the patient also had short stature and other midline anomalies, including submucosal median cleft palate, hypoglossia, and congenital absence of mandibular midline structures. These may all result from a delay in or temporary lack of lateral growth at days 35–38 of gestation. Our patient also has oromandibular-limb hypogenesis syndrome type I (hypoglossia and mandibular defects without limb or digital abnormalities). The aetiology of oromandibular-limb hypogenesis syndrome is unknown. There are three main theories[27], the first being drug usage during gestation and a number of drugs including Tigan, meclizine, imipramine, diazepam, and chlorpromazine have been suggested. In our patient, there was no history of any of these drugs being taken during pregnancy. The second theory is that of gestation hyperthermia and has been postulated in those patients with Moebius syndrome; third, genetic theories of either multifactorial inheritance or autosomal dominant transmission with variable genetic expression. This case may be sporadic because there was no evidence of consanguinity or of any other defects in siblings or family members.

The failure of midline mandibular basal bone and central incisor teeth to form is an unusual anomaly which has previously only been reported in mandibulo-acral dysplasia (MAD), previously described as craniomandibular dermatodysostosis (OMIM #248370) by Danks *et al.*[28], the orofacial features being described by Hall[29]. In MAD, the mandibular midline dysplasia is associated with clavicular, thoracic, cranial suture, limb, and digital abnormalities; calcification of atrophic skin ulcers; and focal segmental glomerulosclerosis[30]. Although the mandibular midline dysplasia in this patient appears almost identical to that in author Hall's case of MAD[28,29], there are no other features of MAD in this case, and to date SMMCI has not been reported in a case of MAD.

Early diagnosis of SMMCI is important as it may be a sign of other severe congenital or developmental abnormalities. Referral to a paediatrician for further investigation is crucial. Comprehensive dental management for the patient should be tailored to suit the patient's need. Preventive care, orthodontic treatment, and aesthetic restorative dentistry are important in long-term dental management.

What this paper adds

- This is the first case of which we are aware where oromandibular-limb hypogenesis syndrome type 1 has been associated with SMMCI syndrome.

Why this paper is important to paediatric dentists

- When an SMMCI tooth is present, the possibility of the presence of an additional syndrome should always be considered.
- The child with SMMCI syndrome may require long-term comprehensive care by a multidisciplinary team which includes several specialists working in close collaboration.

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