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Solitary median maxillary central incisor and normal stature: a report of three cases

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Summary. Solitary median maxillary central incisor (SMMCI) is a rare finding. Growth deficiency or other systemic abnormalities may or may not be seen in children with this anomaly. Nevertheless, the growth and development of all children with SMMCI should be closely monitored. This article reports the dental findings of three Chinese girls with SMMCI, but no growth deficiency or other systemic involvement.

Introduction

Congenital absence of maxillary central incisors is rare [1]. The presence of a solitary median maxillary central incisor (SMMCI) is even rarer. According to Hall *et al*., the prevalence of SMMCI is about 1:50 000 live births [2]. This condition has been reported both as an isolated dental finding and also in association with holoprosencephaly (HPE), pituitary dysfunction and a large number of midline developmental defects.

Early in 1958, Scott reported SMMCI as an isolated dental finding in a girl [3]. Fulstow published another case of SMMCI in 1968, but the girl was also found to have short stature, congenital heart disease, microcephaly and scoliosis [4]. Pituitary dysfunction is one of the major midline developmental defects which can be associated with SMMCI. In 1976, Rappaport *et al*. noted the frequent association of short stature and SMMCI, and they named the condition 'mono-supero-incisivodontic dwarfism' [5]. These authors also published seven cases of SMMCI with short stature, five of whom showed growth hormone deficiencies [6].

Wesley *et al*. reported two cases of SMMCI with normal stature in 1978, and they also reviewed the 14 other cases of SMMCI which had been published at that time [7]. They commented that, although nine of the 14 cases had short stature, only five of them were proven to have growth hormone deficiency. Since then, more reports of SMMCI have appeared in the dental and medical literatures. Some of them had short stature with or without growth hormone deficiency [8,9] while others had normal stature [10–12]. In 1997, Hall *et al*. reported 21 cases of SMMCI treated over a 30-year period [2]. Among this group of patients, only six of them had short stature (below −2·0 standard deviations from the mean height) and only five children were found to have growth hormone deficiency.

Solitary median maxillary central incisor could be associated with various congenital nasal cavity anomalies such as choanal atresia, midnasal stenosis and nasal pyriform aperture stenosis [2]. Choanal atresia is a bony or membranous obstruction of the posterior nasal aperture caused by a failure of the oronasal membrane to disintegrate. Midnasal stenosis is a bony narrowing of the nasal cavity between the pyriform aperture and the posterior choanae. Congenital nasal pyriform aperture stenosis (CNPAS) is an anterior nasal cavity obstruction secondary to bony overgrowth of the nasal processes of the maxilla [13]. The clinical pictures of these conditions are similar and a computed tomography (CT) scan of the nasal cavity is often needed for the definitive diagnosis [14]. Arlis and Ward were the first authors who described a possible association of SMMCI and CNPAS [15]. They reported six patients with CNPAS in 1992, four of whom also had SMMCI. Lo *et al*. later reported two cases of SMMCI and

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CNPAS, and also reviewed the earlier case reports on these two conditions [14]. These authors found that 63% of those cases with CNPAS also presented with SMMCI. Among the 21 patients reported by Hall *et al*., all had histories of congenital nasal obstruction [2]. Choanal atresia and midnasal stenosis were confirmed in seven and eight children, respectively, yet there was no confirmed case of CNPAS in their series.

The significance of SMMCI lies in the fact that it may represent the mildest degree of HPE. This is a developmental field defect of impaired midline cleavage of the embryonic forebrain (prosencephalon) [16]. In its most severe form (alobar HPE), there is no interhemispheric fissure and only a single eye (cyclopia). Less severe forms of HPE can present with mild facial dysmorphism, such as hypotelorism, iris coloboma or SMMCI [17]. Most cases of HPE are sporadic, but familial forms have been described. There have also been case reports where holoprosencephalic children were born to parents with SMMCI and the condition might be transmitted in an autosomal dominant fashion [18,19]. At least 12 chromosome regions implicated in the pathogenesis of HPE have been identified and sonic hedgehog (*SHH*) at the long arm of chromosome 7 (7q36) was the first known gene to cause HPE in human beings [20,21]. The sonic hedgehog gene is expressed in the notochord, the floorplate, the brain and the gut during early human development [22]. However, the phenotypic expression of the *SHH* mutation is highly variable, and not all patients with *SHH* mutation have classic HPE [22–24]. Expressivity ranges from the classical phenotype with alobar HPE to very mild clinical signs, such as SMMCI. Nanni *et al*. suggested that the interactions of multiple gene products and/or environmental elements may determine the final phenotypic outcome for a given individual with HPE [17].

Chromosomal defects have been detected in some children with SMMCI. Dolan *et al*. and Aughton *et al*. reported cases of del(18p) syndrome and SMMCI [25,26], while Masuno *et al*. described two unrelated cases of SMMCI with 7q terminal deletion [27]. Recently, Tubbs and Oakes also reported a case of SMMCI in a patient with a defect on chromosome 7q [28]. These two chromosomal regions are in fact loci containing HPE causing genes: *SHH* on 7q36 and *TGIF* on 18p11 [22]. Following the identification of the sonic hedgehog gene in patients with HPE, recent interest has focused on the role of this gene in patients with SMMCI. Nanni *et al*. performed a molecular study on SMMCI patients who did not have HPE and found a new missense mutation in *SHH* that may be specific for the SMMCI phenotype [29]. The same mutation had not been found in patients with HPE or in normal controls. The above authors suggested that SMMCI could result from different mechanisms, some of which may also cause HPE. Recently, Garavelli *et al*. found another *SHH* missense mutation in a patient with SMMCI, which gave further support to findings of Nanni *et al*. [30].

A large number of midline developmental defects such as hypotelorism and microcephaly have been reported in patients with SMMCI [29]. Besides HPE, SMMCI has been found as part of syndromes or associations with more severe midline anomalies, including the CHARGE association (colobomata, heart defects, atresia choanae, retarded growth, genital hypoplasia and ear abnormalities) [2,31], the VACTERL association (vertebral anomalies, anal atresia, cardiac malformations, tracheoesophageal fistula, renal anomalies and limb anomalies) [2,7] and velocardiofacial syndrome [2]. Solitary median maxillary central incisor has also been found in patients with triple-X syndrome [32] and ectodermal dysplasia [33]. Comparatively fewer cases of SMMCI as an apparently isolated defect have been reported [3,7,10–12,34–36]. This article presents three cases of SMMCI with normal stature and no other congenital abnormalities.

Case reports

Case 1

Case 1 was a 7-year-old Chinese girl. She was the only child in her family and had no previous dental history. There was no history of hereditary disease in her family. The girl's birth history was unremarkable, but her mother reported that she had had breathing difficulties in the neonatal period and was put under observation. No abnormality was found and no treatment/follow-up was done. Her weight and height at the time of dental consultation were between the fiftieth and seventy-fifth percentiles.

On examination, this case had a Class I skeletal relationship and there was no sign of nose block or mouth-breathing. The philtrum of her upper lip was indistinct. Intraorally, the maxillary labial fraenum was absent. Case 1 was in the early mixed dentition

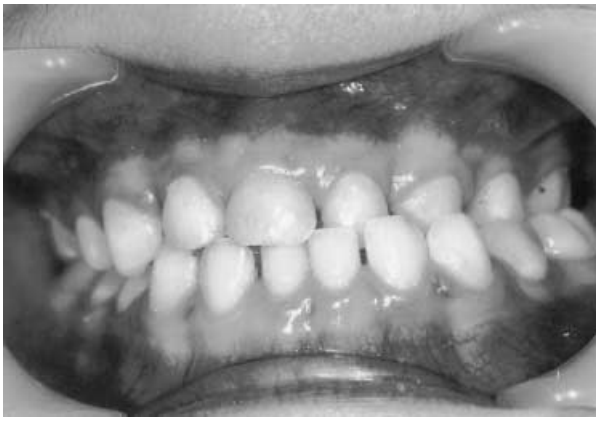

Fig. 1. Frontal view of case 1 showing a solitary maxillary primary central incisor.

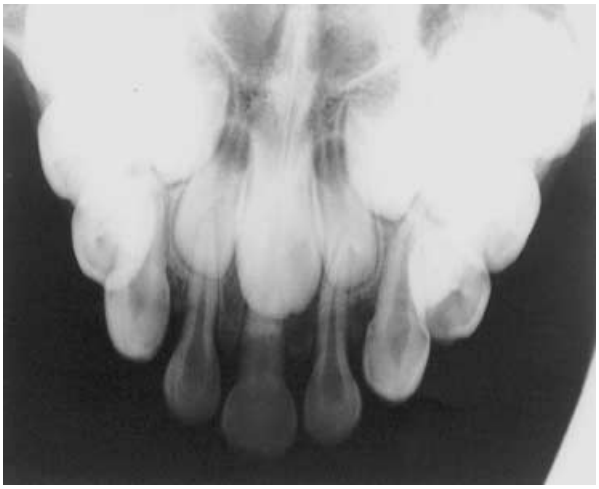

Fig. 2. Maxillary occlusal radiograph of case 1 showing a developing solitary maxillary permanent central incisor.

with the first permanent molars erupting. A solitary maxillary primary central incisor was seen (Fig. 1). The maxillary arch was V-shaped and mild prominence of the midpalatal ridge was seen. There was a unilateral cross-bite on the left side with no mandibular shift.

Radiographic examination revealed a solitary maxillary permanent central incisor (Fig. 2). The orthopantomogram showed that all other permanent teeth except the third molars were developing normally.

Case 1 was subsequently referred to a paediatrician to assess her physical condition and for further investigation. Nothing abnormal was detected clinically, and the brain CT scan prescribed by the paediatrician revealed normal structure. She has been followed in the author's clinic to monitor her dental and physical growth. The maxillary permanent central incisor recently erupted when she was 8 years of age (Fig. 3). Arrangements were being made for specialist orthodontic management of her malocclusion.

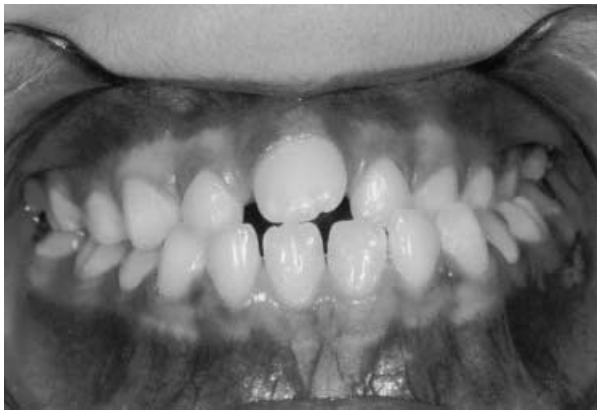

Fig. 3. Frontal view of case 1 taken at 8 years of age showing a solitary maxillary permanent central incisor.

Case 2

Case 2 was an 8-year-old Chinese girl. She was the third child in her family, and her two elder sisters were both healthy with unremarkable medical histories. There was no history of hereditary disease in her family. The girl was born as a full-term baby and found to have breathing difficulties during oral feeding. Surgery was carried out to remove soft tissues from her throat when she was about 1 year old, but her mother could not recall the detailed history. Neither the surgeon nor the paediatrician could be contacted for details. According to the mother's description, the authors speculated that the surgical procedure was an adenoidectomy. Case 2 still had difficulty in nose breathing after the surgery, but she had not been followed up by the paediatrician. Her height was at the fiftieth percentile at the time of the dental consultation and her weight was slightly below the fiftieth percentile.

On examination, she showed a slightly hypoplastic midface with no hypotelorism. The philtrum of the upper lip was indistinct and she was a mouth-breather. Intraorally, the maxillary labial fraenum was missing. Case 2 was in the mixed dentition with a solitary maxillary permanent central incisor; her mandibular permanent incisors and first molars had erupted (Fig. 4). An occlusal radiograph taken by her previous dentist showed that she also had a

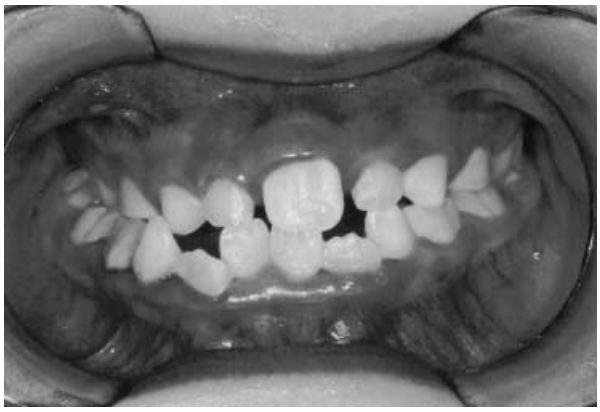

Fig. 4. Frontal view of case 2 showing a solitary maxillary permanent central incisor.

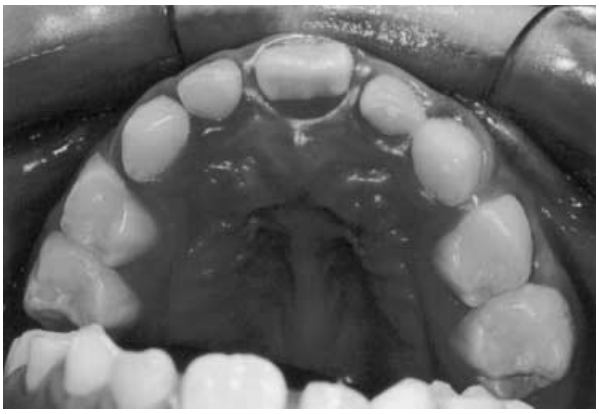

Fig. 6. Occlusal view of case 2 showing the prominent midpalatal ridge.

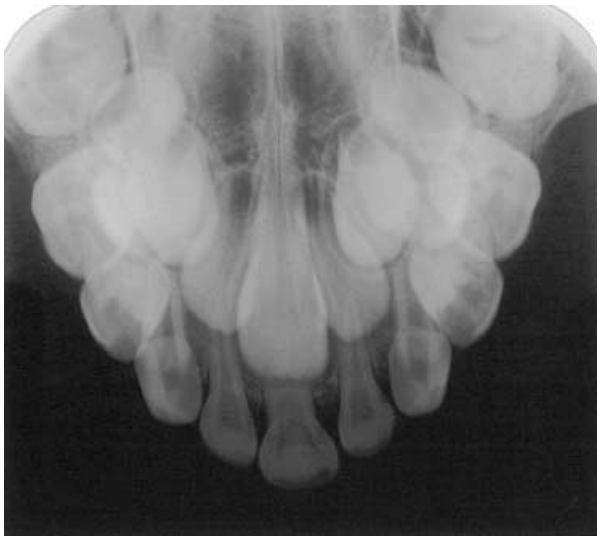

Fig. 5. Maxillary occlusal radiograph of case 2 taken at 6 years of age showing the presence of solitary maxillary primary and permanent central incisors.

solitary maxillary primary central incisor (Fig. 5). She had a unilateral cross-bite on the right side with a mandibular shift. The maxillary arch was V-shaped and a prominent mid-palatal ridge was also seen (Fig. 6). The orthopantomogram showed that all other permanent teeth were developing normally except for the third molars.

Case 2 was referred to a paediatrician to assess her nasal status as well as her overall physical condition. An overnight oxygen saturation test was performed and no abnormality was found. The rest of her development was found to be normal. She is continuing to be followed up by the paediatrician. No definitive treatment has been offered for her nose blockage at this stage. She will be followed up in the author's clinic to monitor her growth and development. Arrangements were being made for specialist orthodontic treatment of her malocclusion.

Case 3

Case 3 was an 11-year-old Chinese girl who was the only child in her family. There was no family history of hereditary disease and the birth history was unremarkable. Her mother reported that the girl had had breathing difficulty in the neonatal period and was put on observation. No abnormality was found and no treatment/follow-up was undertaken. Her weight and height were above the ninety-seventh percentile at the time of the dental consultation.

On examination, case 3 showed a Class I skeletal relationship. No sign of nose block or mouth-breathing were seen, and the philtrum of her upper lip was indistinct. Intraorally, her maxillary labial fraenum was missing. A solitary maxillary permanent central incisor and all the other permanent teeth were erupted except for the third molars (Fig. 7). All teeth were in acceptable alignment except that mild spacing was seen distal to the maxillary lateral incisors. The maxillary arch was U-shaped and mild prominence of the midpalatal ridge was seen. Paediatric assessment revealed nothing of note. A brain CT scan was found to be normal.

Case 3 was satisfied with the appearance of her teeth and no further treatment has been planned for her occlusion.

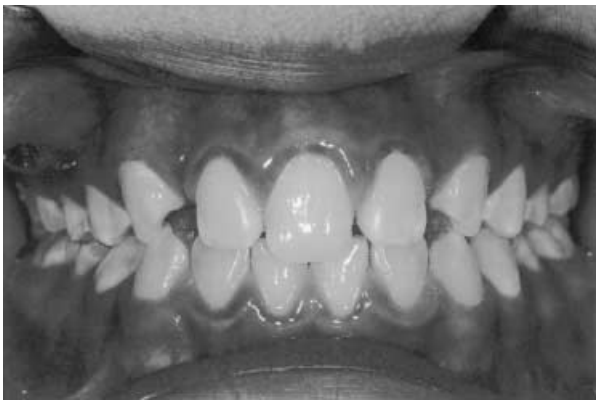

Fig. 7. Frontal view of case 3 showing a solitary maxillary permanent central incisor.

Discussion

Over 70 systemic anomalies have been reported in patients with SMMCI without a recognized syndrome [29]. Among those, short stature, pituitary dysfunction, microcephaly, hypotelorism and CNPAS were more commonly reported [2,29]. Comparatively fewer cases of SMMCI as an apparently isolated anomaly have been published [3,7,10–12,34–36]. However, this may be because patients with SMMCI and major systemic abnormalities have been reported by both medical and dental professionals, whereas isolated cases of SMMCI have mainly been reported by dentists. Nevertheless, it is generally agreed that SMMCI represent the mildest degree of HPE [14,17–21,24].

All three cases described in this report showed normal stature and development, and no complex anomalies had been identified. Wesley *et al*. recommended growth hormone evaluation when the patient's height is two standard deviations below the mean [7]. However, as reported by Parker and Vann, progressive deterioration from the normal curve could occur despite the presence of normal levels of growth hormone [9]. Stanhope *et al*. further commented that children with midline defects may have an evolving endocrinopathy that only appears in later childhood [37]. Therefore, regular follow-up and close monitoring of the growth and development of patients with SMMCI is important. All three cases in this report also presented with a history of neonatal nasal airway obstruction, which concurs with the findings of Hall *et al*. [2]. In their study, all 21 patients had histories of congenital nasal obstruction. Choanal atresia and midnasal stenosis were confirmed in seven and eight children, respectively. Diagnoses were uncertain in the remaining six cases. Kjaer *et al*. identified 10 cases of SMMCI in their orthodontic clinics and all these patients were found to have narrow nasal cavities on radiographic examination [38]. However, only three of them showed pronounced nasal blockage clinically. Therefore, the authors suspected that all of the three cases described in this report might also have some degree of nasal deformity since they all had histories of nasal obstruction in the neonatal period. However, this could not be confirmed without specialist otolaryngological assessment.

All cases described in this report showed prominent midpalatal ridges, the absence of labial fraena and indistinct lip philtra, which have been typically reported in other patients with SMMCI [2,38]. Case 2 showed the most prominent midpalatal ridge and presented with severe nasal block. This concurs with the findings of Kjaer *et al*., who showed that the degree of palatal malformation had a direct relationship with that of the nasal cavity [39]. They demonstrated that a prominent midpalatal ridge is also a consistent finding in patients with HPE, and found a close relationship between facial and palatal malformation. They also suggested that these palatal ridges may be of great diagnostic value in HPE, and may be the result of fusion of excess tissue from the normal palatal shelves during the formation of the narrow palate. Kjaer *et al*. also analysed the craniofacial morphology of nine girls with SMMCI and compared the data with the normal standards for girls [38]. These authors demonstrated that those with SMMCI have a shorter anterior cranial base, short, retrognathic and posteriorly inclined maxillas, and also retrognathic and posteriorly inclined mandibles. They suggested that SMMCI should not be considered as a simple dental anomaly since it may be associated with more complex craniofacial malformations. Becktor *et al*. reviewed the radiographs of 11 patients with SMMCI, finding that the central incisor erupted within the normal age interval in all cases, and that there was evidence of normal horizontal and vertical growth of the maxilla in these patients [40]. They suspected that transverse growth of the maxilla may be defective in patients with SMMCI, but this could not be assessed in their study. The maxillas of the first two cases in this report were constricted, but only case 2 presented with mouth-breathing. It is not known if the constricted maxilla in case 2 was caused by a transverse

growth defect or was consequent to the mouth-breathing habit.

All the cases described in this report are female. Suthers *et al*. reviewed the literatures and found a skewed sex ratio among the transmitting parents with the *SHH* mutation, with more females having this chromosomal defect [41]. They also reviewed the reports of patients with isolated SMMCI and no other congenital malformations, and found that significantly more females were affected. Similar findings were also seen among the cases presented by Kjaer *et al*. [38]. In their study, eight of the subjects with SMMCI had no histories of congenital abnormalities, and all except one were female. In comparison, the sex ratio was found to be about 1:1 among the cases seen by Hall *et al*. where most of their patients also had other congenital abnormalities in addition to SMMCI [2].

Early diagnosis of SMMCI is important because it may be a sign of more severe congenital malformations. Referral to a paediatrician for further investigation is important. The dental management of the cases in this report was preventive and orthodontic. The problem of chronic mouth-breathing in case 2 was being investigated by her paediatrician. Long-term dental management for the first two cases may involve orthodontic expansion of the upper arch, movement of the solitary incisor to one side, with the creation of space for an implant or prosthesis [42]. Therefore, specialist orthodontic care will be needed and has been planned for the first two cases.

What this paper adds

- There is evidence that more females than males are affected by apparently isolated SMMCI with no systemic involvement.

Why this paper is important for paediatric dentists

- Paediatric dentists may play an important role in diagnosing serious malformations in young patients with SMMCI.

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