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Face, palate, and craniofacial morphology in patients with a solitary median maxillary central incisor

Inger Kjær*, Karin Binner Becktor*, Jörg Lisson**, Charlotte Gormsen*** and Björn G. Russell****

Departments of Orthodontics, Universities of *Copenhagen, Denmark, and **Hannover, Germany, ***Private orthodontic practice, Warburg, Germany and ****Copenhagen County Dental Clinic for Handicapped Children, Gentofte, Denmark

SUMMARY The occurrence of a solitary median maxillary central incisor (SMMCI) is a very rare condition and might be a sign of a mild degree of holoprosencephaly. In this investigation, material from 10 patients, nine girls and one boy with a SMMCI (8–17 years of age) registered in orthodontic clinics was examined. The purpose was to evaluate the clinical characteristics and craniofacial morphology in this group of patients.

Oral photographs, study casts, profile radiographs, and orthopantomograms were analysed.

The study showed that this group of SMMCI patients were characterized by an indistinct philtrum, an arch-shaped upper lip, absence of the fraenulum of the upper lip, a complete or incomplete mid-palatal ridge, a SMMCI, and nasal obstruction or septum deviation. The craniofacial morphology of the nine girls, compared with normal standards for girls showed a short anterior cranial base, a short, retrognathic and posteriorly inclined maxilla, and a retrognathic and posteriorly inclined mandible. Furthermore, the sella turcica had a deviant morphology in five of the 10 subjects.

The results indicate that the presence of a SMMCI should not be considered as a simple dental anomaly, since it may be associated with other clinical characteristics and more complex craniofacial malformations. It is therefore suggested that the SMMCI condition in future studies is classified according to clinical symptoms and craniofacial morphology.

Introduction

Holoprosencephaly is a developmental defect affecting the forebrain (the proencephalon) and the face. The spectrum of holoprosencephaly has been classified into five different types:

(1) *cyclopia*, single eye or partially divided eyes in a single orbit (synophthalmia), with or without a proboscis above the eye;
(2) *ethmocephaly*, severe ocular hypotelorism with separate orbits and occasionally a proboscis between the eyes;
(3) *cebocephaly*, ocular hypotelorism with a single-nostril, blind-ended nose;
(4) *median cleft palate*, characterized by ocular hypotelorism, flat nose;
(5) *short upper lip*, the less severe dysmorphism with a prominent mid-palatal ridge and the presence of a solitary median maxillary central incisor (SMMCI; Berry *et al*., 1984; Cohen, 1989; Hall *et al*., 1997; Kjær *et al*., 1997).

The most severe cases of holoprosencephaly are not compatible with life and often appear as spontaneous abortions, while the less severe cases can be characterized by a SMMCI and therefore might be seen in the orthodontic clinic.

The frequency of postnatal holoprosencephaly is 1:16,000 live births, whereas prenatally it has

been recorded once in every 250 spontaneously aborted foetuses (Matsunaga and Shiota, 1977; Cohen, 1989).

All patients with holoprosencephaly have a SMMCI, but not all patients with a SMMCI have been diagnosed as holoprosencephalic. The appearance of a midfacial ridge has been associated with holoprosencenphaly (Kjær *et al*., 1997). The frequency of a SMMCI has been estimated as 1 to 50,000 (Hall *et al*., 1997). The boundaries between milder degrees of holoprosencephaly and a SMMCI have seemingly never been defined.

Genetically, deletions of chromosomes 18, 13, and 7 have been associated with holoprosencephaly and recently interest has focused on the *Sonic Hedgehog* (SSH) gene (Johnson, 1989; Frints *et al*., 1998). It is therefore important for the orthodontist to know if a patient with a SMMCI presents a mild degree of holoprosencephaly, as this might require genetic and paediatric consultation (Cohen, 1982; Berry *et al*., 1984; Arlis and Ward, 1992).

Children with a SMMCI generally have a shorter stature and some have endocrinological deficiencies (Kocsis, 1990; Hall *et al*., 1997). In a recent study, 40 subjects with a SMMCI were investigated and it was found that 69 per cent had short stature, 48 per cent had growth hormone deficiencies or hypopituitarism, and 23 per cent had pituitary absence or hypoplasia (Lo *et al*., 1998).

Congenital nasal pyriform aperture stenosis (CNPAS), characterized by airway obstructions in newborns, is frequently reported in combination with a SMMCI (Arlis and Ward, 1992) and different degrees of mental retardation have also been described (Hall *et al*., 1997).

These genetic and endocrinological conditions all suggest that a SMMCI could be an expression of a mild form of holoprosencephaly and support the need for differential diagnostic criteria.

The purpose of the present investigation was to evaluate the clinical appearance and the craniofacial morphology in a sample of patients with a SMMCI in order to elucidate whether these conditions are applicable in the differential diagnosis between a SMMCI being associated or not associated with holoprosencephaly.

Subjects

The study included 10 patients, nine girls and one boy, with an age range of 8 to 17 years of age. The age distribution at the time of examination is shown in Table 1, where the patients are numbered from 1 to 10. Seven patients were from the community dental care system in Denmark, one from the Copenhagen County Dental Clinic for Handicapped Children, one from a private orthodontic clinic in Germany and one from a Public University Hospital in Germany.

All 10 patients had a SMMCI. Information from the case records showed that two individuals were mentally retarded, one had a chromosome deletion 13/18, one was a colostomy patient, and three subjects had a more or less pronounced nasal obstruction.

The material included facial and oral photographs of the dentition, and of the maxillary dental arch and palate from eight of the 10 patients, and photographs of study casts from two patients. Profile radiographs and orthopantomograms were available from all 10 individuals. For six patients intra-oral radiographs were also available.

Methods

For analysis of the clinical appearance, the morphology of the philtrum and of the lips was assessed from facial photographs (Table 1) and the palatal morphology, including the extension of a possible mid-palatal ridge, classified as complete or incomplete was assessed from palatal and study model photographs. A complete ridge extended posteriorly from the central incisor to the soft palate (Table 1 and Figure 1 a,b), while an incomplete ridge was located centrally in the palate (Table 1 and Figure 1 c). The dentition and the morphology of the nasal septum and nasal cavity were assessed from the orthopantomograms (Table 2).

The craniofacial morphology was investigated cephalometrically. Eight reference points (Figure 2) were marked directly on the cephalometric radiographs with a sharp soft pencil. Seven angular and three linear measurements (Table 3) were calculated and compared with

Table 1 Clinical appearance of 10 subjects with a SMMCI.

Pt.	Age (years)	Sex	Extra-oral	Intra-oral
1	17	Female	Indistinct philtrum Arch-shaped lip	–Fraenulum labii sup –Papilla incisiva Incomplete palatal ridge
2	9	Female	Indistinct philtrum Arch-shaped lip	–Fraenulum labii sup –Papilla incisiva Complete palatal ridge
3	11	Female	Indistinct philtrum	–Fraenulum labii sup –Papilla incisiva Complete palatal ridge
4	12	Female	Indistinct philtrum Arch-shaped lip	–Fraenulum labii sup –Papilla incisiva Complete palatal ridge
5	11	Female		–Fraenulum labii sup –Papilla incisiva Incomplete palatal ridge
6	13	Female	Indistinct philtrum Arch-shaped lip	–Fraenulum labii sup –Papilla incisiva Normal palate
7	11	Female	Indistinct philtrum Arch-shaped lip	–Fraenulum labii sup –Papilla incisiva Incomplete palatal ridge
8	8	Female	Indistinct philtrum	–Fraenulum labii sup –Papilla incisiva Incomplete palatal ridge
9	12	Male		–Fraenulum labii sup –Papilla incisiva Incomplete palatal ridge
10	12	Female	Indistinct philtrum Arch-shaped lip	– Fraenulum labii sup –Papilla incisiva Complete palatal ridge

–, Indicates absence.

standards from normally developed children (Björk, 1960; Riolo *et al*., 1974; Sarnäs and Solow, 1980). Differences in the means of the SMMCI and reference groups were assessed for the nine females by Student's *t*-test. The levels of significance were set at 5 and 1 per cent.

The morphology of the sella turcica was analysed and compared with that of a normal adolescent sella turcica, as described by Björk and Skieller (1983; Figure 3).

Results

Clinically

The extra-oral photographs from eight of the 10 patients revealed that six individuals had a characteristic, arch-shaped upper lip and all eight had an indistinct philtrum (Figure 4). The crown of the upper central incisor appeared symmetric (Figure 5).

Intra-orally, all patients lacked the fraenulum of the upper lip and the incisive papilla. In addition, nine of the patients had a characteristic ridge in the middle of the palate. In four subjects the ridge was complete (Table 1 and Figure 1 a,b) and in five patients it was incomplete (Table 1 and Figure 1c).

Nasal cavity and dentition described from the orthopantomograms

Narrow nasal cavities were recorded and also asymmetric nasal septa. In all 10 patients, abnormalities of the nasal cavity or of the nasal septum could be observed (Table 2 and Figure 6).

All 10 patients had a SMMCI in the permanent dentition. The crown of the central

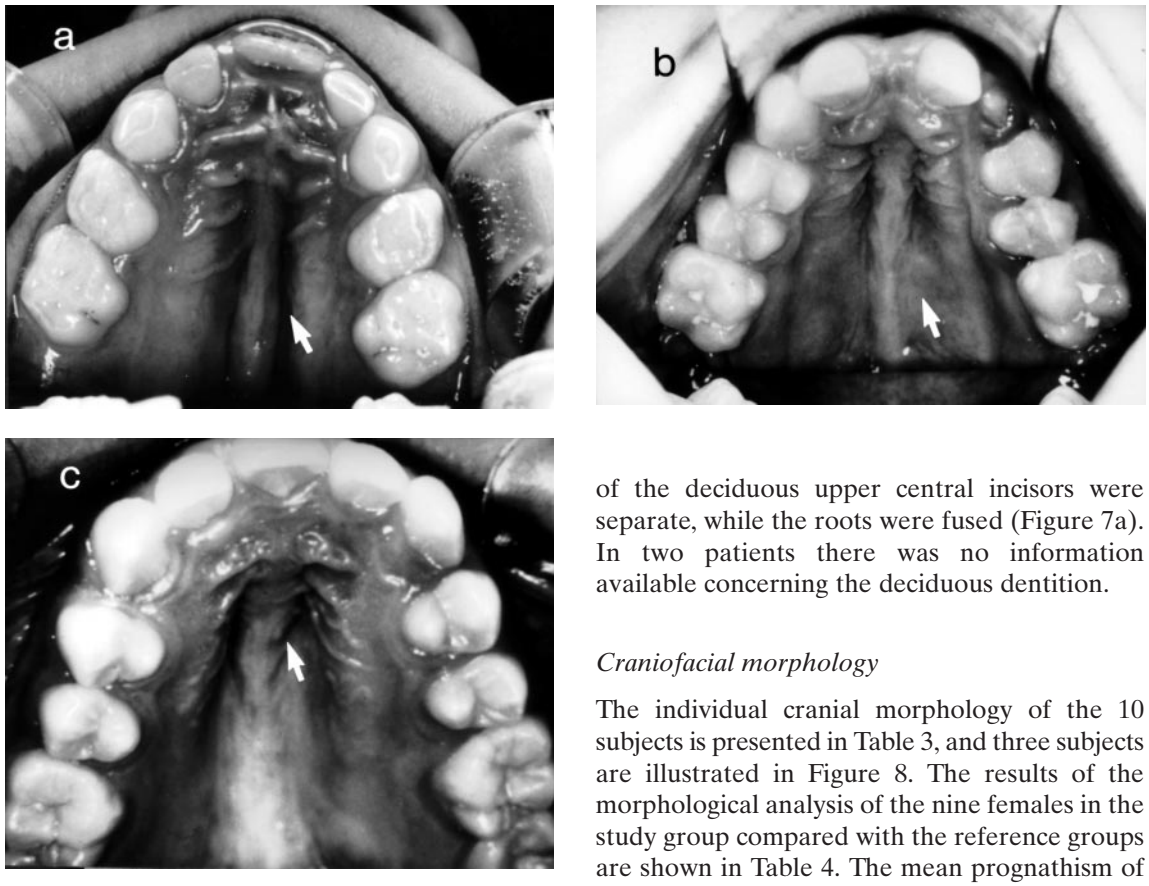

Figure 1 Occlusal view of the palate in three subjects with a SMMCI. (a) Complete palatal ridge (arrow) mid-sagittally in a child aged 9 years (case 2). Note the single central incisor in the maxilla and the absence of the incisive papilla. (b) Complete palatal ridge (arrow) mid-sagittally in a child aged 12 years (case 4). The single central incisor in the maxilla has been extracted. Note the absence of the incisive papilla. (c) Incomplete anterior palatal ridge (arrow) mid-sagittally in a child aged 11 years (case 7). Note the single central incisor in the maxilla and the absence of the incisive papilla.

incisor was symmetrical around the mid-axis (Figures 5–7). Thus, the central incisor did not present the morphology of a right or left central incisor. In one case, the pulp cavity did not appear symmetrical around the mid-axis (Figure 7a). The permanent central incisor appeared as a tooth consisting of the lateral parts of two central incisors. From the material available it could also be recorded that eight patients had a SMMCI in the deciduous dentition (Figure 7b). In one individual the crowns of the deciduous upper central incisors were separate, while the roots were fused (Figure 7a). In two patients there was no information available concerning the deciduous dentition.

Craniofacial morphology

The individual cranial morphology of the 10 subjects is presented in Table 3, and three subjects are illustrated in Figure 8. The results of the morphological analysis of the nine females in the study group compared with the reference groups are shown in Table 4. The mean prognathism of the maxilla (s–n–ss) was 5.9 degrees smaller in the SMMCI group and differed significantly from the reference groups ($P < 0.01$). The mean mandibular prognathism (s–n–pg) was 5.1 degrees less than the reference groups ($P < 0.05$). The mean vertical inclination of the palate (NSL/NL) was 3.1 degrees smaller and the mean vertical inclination of the mandible (NSL/ML) 9 degrees larger in the SMMCI group than the reference groups. The jaw inclinations differed significantly from the reference groups ($P < 0.01$). The mean cranial base angle (n–s–ba) was significantly larger in the SMMCI group ($P < 0.05$) than in the reference groups. For the linear measurements the mean length of the anterior cranial base and also the length of the maxilla was significantly smaller in the SMMCI group than that of the reference groups ($P < 0.01$, $P < 0.05$), respectively. The large difference in variations for the n–s–pg angles between the SMMCI group and the reference groups, might be

Table 2 Orthopantomographic analysis in 10 subjects with a SMMCI.

Pt.	Orthopantomogram Nasal cavity morphology	Orthopantomogram Dentition
1	Narrow nasal cavity	Solitary deciduous upper central incisor SMMCI
2	Narrow and asymmetric nasal cavity	Solitary deciduous upper central incisor (crowns separate) SMMCI
3	Narrow and asymmetric nasal cavity Septum nasi malformation	Solitary deciduous upper central incisor SMMCI
4	Narrow nasal cavity Septum nasi asymmetry	No information concerning deciduous upper central incisor SMMCI
5	Narrow nasal cavity	Solitary deciduous upper central incisor SMMCI
6	Narrow nasal cavity	Solitary deciduous upper central incisor SMMCI
7	Narrow nasal cavity	No information concerning deciduous upper central incisor SMMCI
8	Nasal cavity structures unclear.	Solitary deciduous upper central incisor SMMCI Agenesis lower second molars
9	Narrow nasal cavity	Solitary deciduous upper central incisor SMMCI
10	Narrow nasal cavity	Solitary deciduous upper central incisor SMMCI

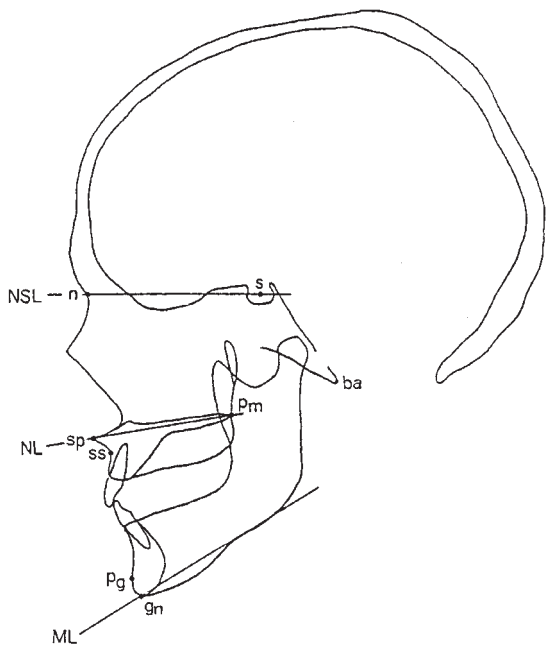

Figure 2 Skeletal reference points and lines. For definitions, see Solow (1966).

because subject 3 had a very prognathic mandible (Table 3) compared with the other eight female subjects.

Five individuals had malformations of the sella turcica: subjects 2 and 4 had a sella turcica bridge (Figure 9 a,b), subjects 3 and 8 had a very deep sella turcica (Figure 9 c,d), and subject 10 had a small, narrow sella turcica.

Discussion

Whilst diagnosis of the presence of a SMMCI is easy, it is difficult to understand the pathogenesis behind this type of agenesis, although it is obvious that a genetic inheritance exits. Johnson (1989) has shown the relationship between a SMMCI and holoprosencephaly. She described two unrelated families, in which four children were born with holoprosencephaly. In the first family, the mother of a child with holoprosencephaly and a sister of the proposita had a SMMCI. In the second family, a father with a SMMCI and hypotelorism had two children with holoprosencephaly. His sister also had a SMMCI and she had a holoprosencephalic daughter, born at term, described as having cyclopia associated

Table 3 Craniofacial morphology in 10 subjects with a SMMCI.

Pt.	N-S (mm) linear (mean)	S-Ba (mm) linear (mean)	Sp-Pm (mm) linear (mean)	Cranial base angle (°) n-s-ba	Variable	Angle (°)	SD	Variable	Angle (°)	SD	Sella turcica morphology
1	66/(77)	40/(45)	45/(57)	131	s-n-ss:	75	1½SD	NSL/NL:	3	1½SD	
					s-n-pg:	69	3SD	NSL/ML:	52	3SD	
					ss-n-pg:	7	2SD	NL/ML:	49	4SD	
2	72/(73)	48/(41)	35/(51)	137	s-n-ss:	68	4SD	NSL/NL:	11	1SD	
					s-n-pg:	68	3½SD	NSL/ML:	46	2SD	
					ss-n-pg:	0	½SD	NL/ML:	35	1½SD	
3	62/(74)	41/(44)	48(54)	130	s-n-ss:	82		NSL/NL:	0	2SD	
					s-n-pg	86	1½SD	NSL/ML:	28	½SD	
					ss-n-pg	-4	2SD	NL/ML:	28		
4	67/(75)	39/(44)	45/(54)	142	s-n-ss:	72	2½SD	NSL/NL:	5	1SD	
					s-n-pg:	73	2SD	NSL/ML:	38	1SD	
					ss-n-pg	-1	1SD	NL/ML:	33	1SD	
5	66/(74)	41/(44)	49/(54)	138	s-n-ss:	72	2½SD	NSL/NL:	8		
					s-n-pg:	68	3SD	NSL/ML:	52	3SD	
					ss-n-pg:	4	½SD	NL/ML:	44	3SD	
6	71/(76)	49/(46)	49/(55)	132	s-n-ss:	76	1½SD	NSL/NL:	4	1SD	
					s-n-pg:	76	1SD	NSL/ML:	37	½SD	
					ss-n-pg:	0	½SD	NL/ML:	33	1SD	
7	63/(74)	47(44)	45/(54)	133	s-n-ss:	81		NSL/NL:	5	1SD	
					s-n-pg:	77	1SD	NSL/ML:	42	1½SD	
					ss-n-pg:	4	½SD	NL/ML:	37	2SD	
8	64/(72)	50/(41)	43/(51)	131	s-n-ss:	75	2SD	NSL/NL:	4		
					s-n-pg: not measured			NSL/ML: not measured			
					ss-n-pg: not measured			NL/ML: not measured			
9	64/(78)	39/(47)	42(57)	136	s-n-ss:	79	½SD	NSL/NL:	5	1SD	
					s-n-pg:	80		NSL/ML:	35	½SD	
					ss-n-pg:	-1	1½SD	NL/ML:	30	1SD	
10	60/(75)	40/(44)	47/(54)	136	s-n-ss:	79	½SD	NSL/NL:	7		
					s-n-pg:	70	2½SD	NSL/ML:	50	2½SD	
					ss-n-pg:	9	2½SD	NL/ML:	43	3SD	

Linear mean values according to Riolo *et al.* (1974).
SD, standard deviation from angular mean values according to Björk (1960).

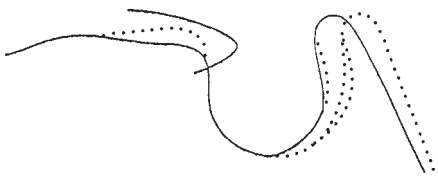

Figure 3 Contour of a normal sella turcica morphology, analysed from profile radiographs (anterior to the left), from childhood (solid line) to adulthood (dotted line). The figure shows that the upper contour of the anterior wall of the sella turcica is perpendicular and unchanged during the normal course of development. The increasing size of the sella turcica under normal conditions is a result of resorption and apposition processes on the dorsum sella (Björk and Skieller, 1983).

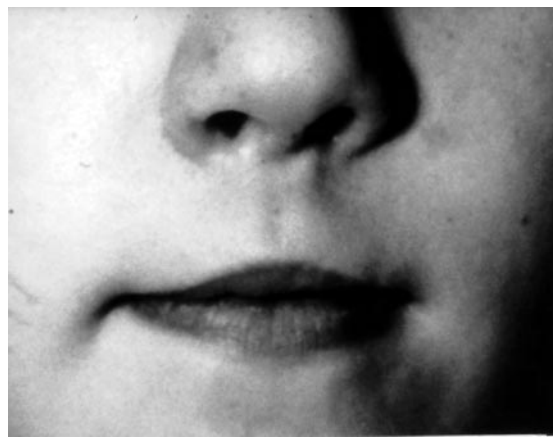

Figure 4 Contour of the lips in a child aged 11 years with a SMMCI (case 7). Note the prolabium of the upper lip without curved contours and the indistinct philtrum.

with a prosboscis. The child died a few hours after birth. A SMMCI has been reported as very common in holoprosencephaly (Cohen, 1989). It must be remembered, however, that a SMMCI has also been reported in conditions not associated with holoprosencephaly (Wesley *et al.*, 1978), although detailed information on the differential diagnostic criteria distinguishing mild degrees of holoprosencephaly from non-holoprosencephaly has never been given.

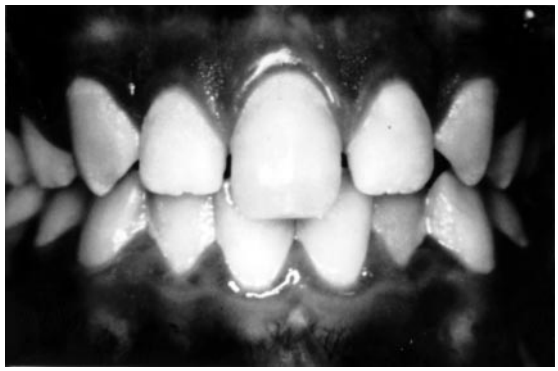

Figure 5 Dentition in a subject with a SMMCI (case 7) showing a permanent single central incisor, symmetrical around the mid-axis.

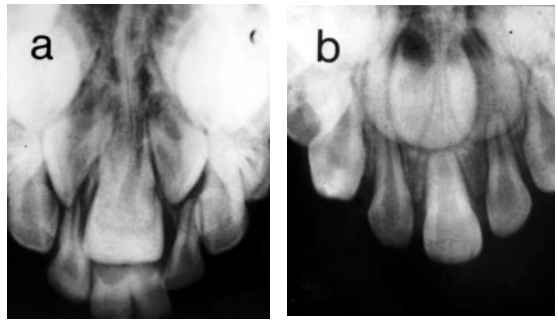

Figure 7 Dental radiographs illustrating upper deciduous incisors from two SMMCI patients. (a) Case 2 showing fused roots and separated crowns of the decidious upper central maxillary incisor. (b) Case 8 showing a deciduous central maxillary incisor with almost normal morphology.

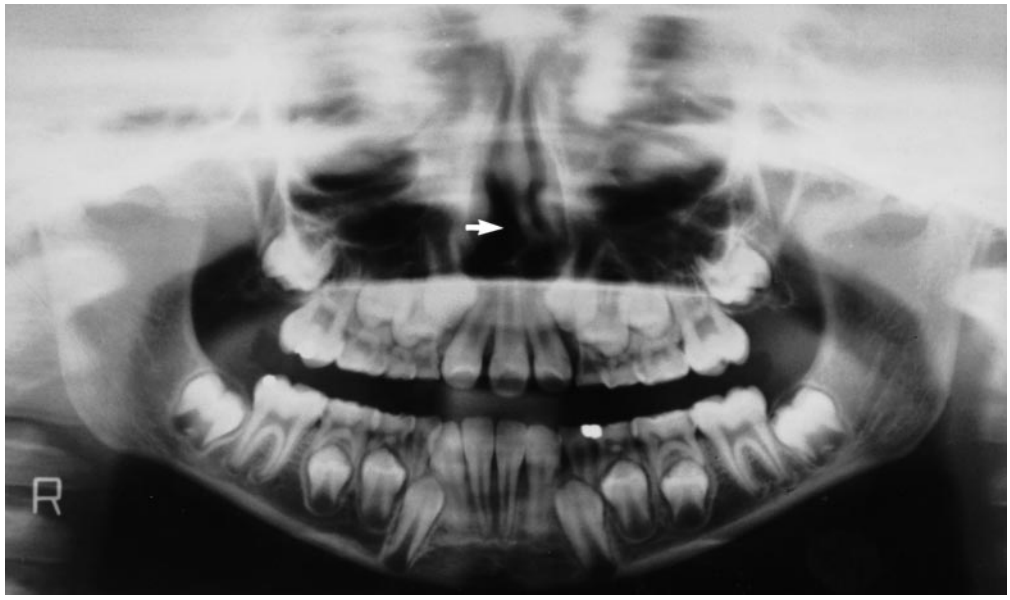

Figure 6 Orthopantomogram from a child aged 11 years (case 3). Note the symmetrical single maxillary central incisor and the asymmetric septum deviated to the left (arrow).

The prenatal craniofacial morphology in holoprosencephaly has previously been described (Kjær *et al*., 1991). This study showed that the degree of malformation in the craniofacial skeleton reflected the facial abnormalities. Connections between the degree of facial malformation in holoprosencephaly and the degree of cerebral malformation have been elucidated neurologically (Siebert *et al*., 1990). In a histological study on foetuses with holoprosencephaly, sella turcica and pituitary gland malformations have been reported (Kjær and Fischer-Hansen, 1995). In a comparative investigation, where the prenatal malformation of the palate in holoprosencephalic foetuses was compared with postnatal palate malformations, it was also demonstrated that abnormalities in the palate were correlated to facial abnormalities (Kjær *et al*., 1997).

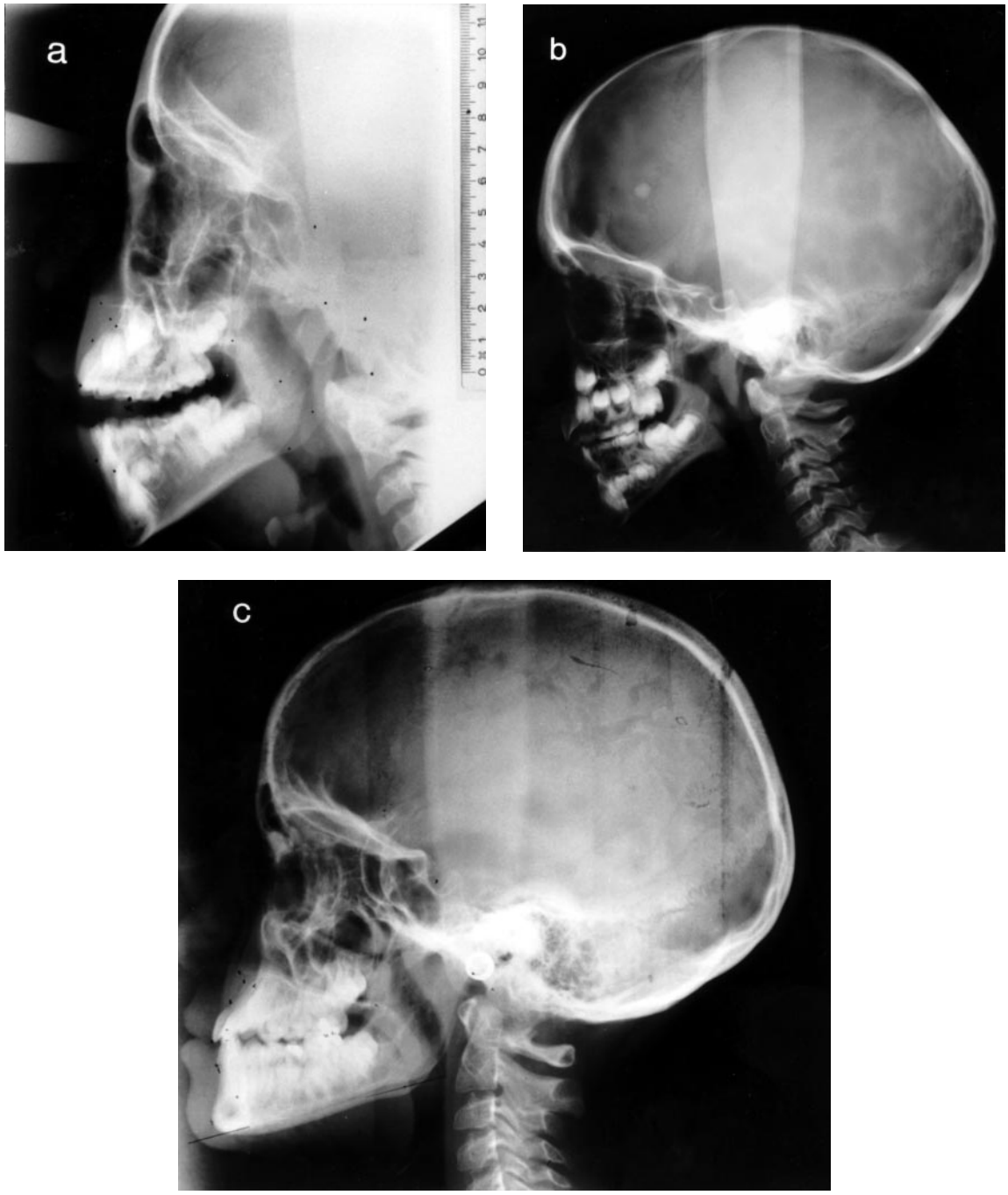

Figure 8 Profile radiographs of three children with a SMMCI. (a) Case 8. (b) Case 2. (c) Case 3. In all subjects the anterior cranial fossa and the maxilla are short. The results of the cephalometric analyses appear in Table 3. For detailed information about the sella turcica, see Figure 9.

Table 4 Comparison of the facial morphology of the nine females in the study group with the reference groups.

	Study group			Reference group[1,2]			Difference between groups
Variable	*n*	Mean	SD	*n*	Mean	SD	Mean
s–n–ss (°)	9	75.5	4.5	27[1]	81.4	3.6	–5.9**
s–n–pg (°)	8	73.3	6.1	27[1]	78.4	3.4	–5.1*
ss–n–pg (°)	8	2.4	4.4	50[2]	1.3	2.7	1.1
NSL/NL (°)	9	5.2	3.1	27[1]	8.3	2.4	–3.1**
NSL/ML (°)	8	43.1	8.4	27[1]	34.1	5.3	9.0**
NL/ML (°)	8	37.8	7.0	27[1]	25.8	5.1	12.0**
n–s–ba (°)	9	134.4	4.0	27[1]	130.4	5.2	4.0*
N–S (mm)	9	65.7	4.0	27[1]	74.9	3.0	–9.2**
S–Ba (mm)	9	43.8	4.5	27[1]	44.3	3.7	–0.5
Sp–Pm (mm)	9	45.1	4.3	27[1]	49.6	2.9	–4.5*

[1]Riolo *et al*. (1974).
[2]Sarnäs and Solow (1980).
*$P \leq 0.05$; **$P \leq 0.01$.

The prenatal facial and palatal midline malformations in holoprosencephaly are therefore associated not only with cerebral midline deviations, but also with sella turcica malformations and craniofacial morphology. These prenatal findings seemingly are of importance for differential diagnosis in subjects with a SMMCI. A child with a SMMCI, a palatal ridge, sella turcica malformations, and abnormal craniofacial morphology might thus constitute a previously undiagnosed subgroup of holoprosencephaly. Similarly, it is possible that a child with a SMMCI and very short stature (Lo *et al*., 1998) also has holoprosencephaly and that the deviation in linear growth is associated with abnormal pituitary gland development.

Of the children in this study, the mental status was only evaluated by a child neurologist in two subjects. These were patients 8 and 10, who were mentally retarded. In these individuals there were deviations in the palate and in the craniofacial morphology, as well as malformations of the sella turcica and, in addition, short stature. These findings are in agreement with the above-mentioned association between palatal, facial, cerebral, and craniofacial development.

A SMMCI may occur in individuals with CNPAS (Arlis and Ward, 1992; Lo *et al*., 1998). In this connection it is worth mentioning that a SMMCI in an individual with VATERL association (vertebral anomalies, anal atresia, tracheo-eosophageal fistula, renal defects, and limb dysplasia) has been reported (Wesley *et al*., 1978).

In the current investigation the following main traits were found in individuals with a SMMCI: indistinct philtrum, arch-shaped upper lip, absence of the fraenulum of the upper lip, midpalatal ridge, and nasal obstruction or deviation. The craniofacial morphology in these patients showed a short anterior cranial base, short retrognathic and posteriorly inclined maxilla, retrognathic and posteriorly inclined mandible, and various forms of deviation in the morphology of the sella turcica. These are all skeletal symptoms of more profound deviations in the craniofacial profile, indicating that a SMMCI is a symptom of a more extensive malformation. These study results suggest that facial characteristics, traits in the lip and palate, and in the craniofacial profile should be incorporated in the criteria applied in diagnosing a SMMCI patient. From the results of this study it is also recommended that these criteria are associated with neuropaediatric diagnosis in future studies.

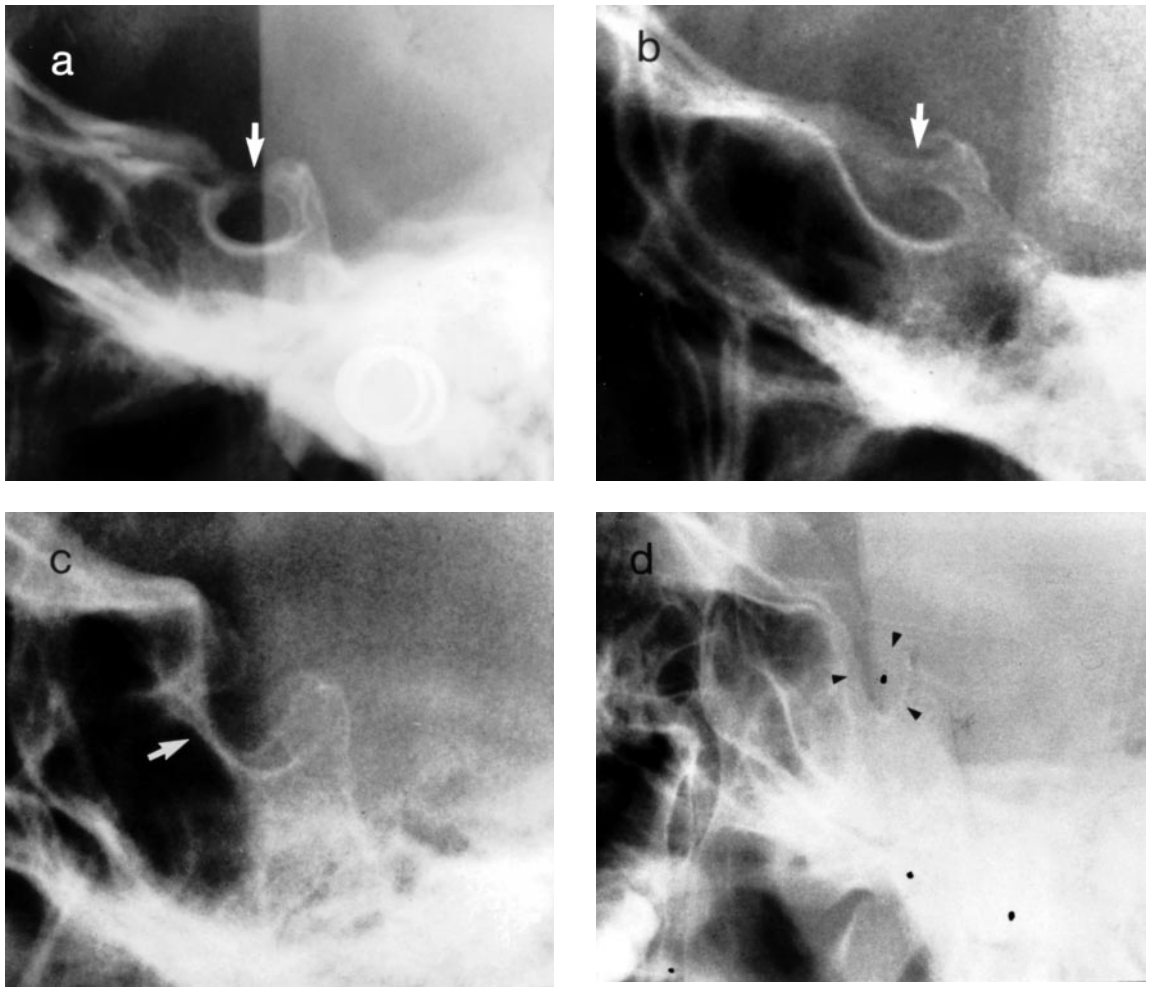

Figure 9 Four different sella turcicas enlarged from profile radiographs. (a) Case 2. (b) Case 4 (from Figure 8b). (c) Case 3 (from Figure 8c). (d) Case 8 (from Figure 8a). The radiographs show the presence of a sella turcica bridge in Figure 9a,b, an oblique anterior wall in Figure 9b,c, and a diminished sella turcica volume in Figure 9a (moderate) and d (severe).

Address for correspondence

Inger Kjær
Department of Orthodontics
Faculty of Health Sciences
University of Copenhagen
Nørre Allé 20
DK-2000 Copenhagen
Denmark

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