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ORIGINAL SCIENTIFIC ARTICLE

Localised scleroderma en coup de sabre affecting the skin, dentition and bone tissue within craniofacial neural crest fields. Clinical and radiographic study of six patients

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Abstract

Purpose When localised scleroderma occurs in the face, neck and scalp area, it is called scleroderma en coup de sabre (SCS) for its resemblance to the stroke of a sabre. Most observed characteristics: abnormal skin and dental development, facial atrophy and neurological complications. The aim was to evaluate the extent of SCS in the underlying subcutis, including teeth/bone tissues. The goal was to solve, how far the external visual skin abnormality extends in depth, and if the condition appears within and limited to craniofacial neural crest fields.

Methods Photographic and radiographic materials from six patients (one male, five females, aged 5–39 years) were included. The cases were divided in three groups, two in each, according to similarity in location of SCS in the skin. Dentition and gingiva were analysed clinically and from intra-oral photos, dental radiographs and orthopantomograms. Agenesis, dental maturity stage (root length), deviation in crown and root morphology (size and shape), and eruption disturbances were registered. Profile and frontal radiographs were analysed cephalometrically for jaw relationships and bone structures.

Results In SCS, skin affection corresponds to the neural crest regions/fields. A close spatial association between skin, teeth and bone affections within neural crest fields was found. No common traits in profile analyses were observed. Asymmetry from minor to severe appears in the frontal analyses. A malformation in planum sphenoidale was observed in two individuals with the same location of skin affections.

Conclusion SCS conditions seem to extend from the skin in the depth to the sella turcica area within neural crest fields.

Keywords Scleroderma · Skin · Dentition · Bone · Craniofacial radiographs

Introduction

Scleroderma is a relatively rare chronic disease. The condition is characterised by fibrotic changes of the skin with or without involvement of organs. Scleroderma is divided into systemic sclerosis, the most aggressive and progressive variant, and the milder variant, usually affecting only a solitary patch of skin, referred to as localised scleroderma (Marzano et al. 2003; Holland et al. 2006; Hørberg et al. 2015).

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The present paper deals with localised scleroderma. This condition primarily affects children, with 67% of patients diagnosed before 18 years of age (Holland et al. 2006). It is characterised by one or more linear streaks that can extend through the dermis, subcutaneous tissue and muscle to the underlying bone (Fischer and Patton 2000; Marzano et al. 2003; Jablonska and Blaszczyk 2005; Zulian 2008). These streaks are visible in the head and neck. Furthermore, the condition can affect the teeth and the oral mucosa (Hørberg et al. 2015), and be associated with facial atrophy and neurologic complications (Holland et al. 2006).

The pathogenesis of localised scleroderma is yet unknown, but it is believed that linear scleroderma may result from a genetic mosaicism where mutations in genes expressed in ectodermal cells play a central role in the origin of the disease (Weibel and Harper 2008).

When scleroderma occurs in the face, neck and scalp area, it is called scleroderma en coup de sabre (SCS) for

its resemblance to the stroke of a sabre. The condition was first described by Addison and co-workers in 1854 as cited by Fox (1892). Since then, several studies on prevalence and classifications have been published (Davis and Saunders 1946; David et al. 1991; Orozco-Covarrubias et al. 2002; Jablonska and Blaszczyk 2005; Zulian 2008; Christen-Zaech et al. 2008; Pascual-Castroviejo and Ruggieri 2008). The most characteristic conditions observed in SCS are abnormal skin development, abnormal dental development, facial atrophy, and neurological complications, which are referred to below. The SCS condition normally referred as a skin disease has also been described in the literature as a connective tissue disease (Marzano et al. 2003; Zulian 2008; Pascual-Castroviejo and Ruggieri 2008).

For the understanding of the possible interrelationship between these different symptoms, an overview is given of the skin, dentition, oral cavity, neurologic complications, face and cranial embryological development.

Skin

SCS lesions usually start with contraction and firmness of the skin in the affected areas (Orozco-Covarrubias et al. 2002; Zulian 2008). A linearly depressed groove can appear as a vertical, colourless line of the skin on the fronto-parietal region, which includes the underlying connective tissue (Holland et al. 2006). Loss of hair (alopecia) occurs on the scalp and eyelids (Pace et al. 2010). Muscle and bone have shown to become atrophic like the skin (Trainito et al. 2012). SCS is often restricted to one side of the face and has a slow but progressive course (Spackman 1999; David et al. 1991). Progressive facial hemiatrophy has been described (Orozco-Covarrubias et al. 2002; Jablonska and Blaszczyk 2005; Trainito et al. 2012). The complications of SCS depend on the anatomical area affected (Marzano et al. 2003).

Dematologists frequently manage and coordinate multidisciplinary care of patients with SCS.

In the initial phase (red or bluish "inflamed" skin), the lesion activity is registered by thermography for measuring the amount of infrared (heat) (Martini et al. 2002).

Current treatments including methotrexate medication are used in an effort to limit progression and long-term disability (Koch et al. 2013).

Dentition and oral cavity

The SCS extending downwards into the cheek, nose and upper lip may also involve the mouth and gingival tissues, recently described (Hørberg et al. 2015). The corresponding side of the tongue may be atrophic, although sometimes the lesion is located close to the midline of the tongue. Spacing of teeth and disturbance of the eruption process of the teeth have been reported (Looby and Burket 1942). Also, the gingiva is affected by the condition by scarring of the gingival tissue and depression of the alveolar process (Davis and Saunders 1946; Trainito et al. 2012). The periodontal ligament is widened, which is a result of deposits of collagen in the tissues or as a result of collagen deposition around nerves and vessels (Tolle 2008).

It has been demonstrated that the primary as well as the permanent dentition can be involved in SCS. Furthermore, it has been suggested that there is a link between the localised skin condition in SCS and the location of dental abnormalities (Hørberg et al. 2015).

It has been suggested that the dental defect could express not only the severity of the SCS condition, but also reveal when during childhood the SCS condition has started (Hørberg et al. 2015).

Facial atrophy

Progressive hemifacial atrophy has been associated with the SCS condition. It has been stated that overgrowth tendency of the anterior lower third of the face occurs in 82% of cases and skeletal asymmetry in 56% of cases with tempero-mandibular joint involvement in 19% (Trainito et al. 2012).

It is well known from conditions such as segmental maxillary dysplasia that the local malformation in the teeth and alveolar process can be associated with skin as well as jawbone affections (Becktor et al. 2002a, b; Kjær 2017).

Neurologic complications

Neurologic complications have been described in patients with SCS. Frequent neurologic abnormalities reported are seizure disorder, hemiparesis, trigeminal neuralgia, mental deterioration, migraine headache, and unilateral hippocampal atrophy (Marzano et al. 2003; Pascual-Castroviejo and Ruggieri 2008). Also white matter lesions of the brain have been described (Kister et al. 2008). Furthermore, opthalmological abnormalities have been observed (Gambichler et al. 2001).

As a conclusion, there seem to be an under-recognised relationship between neurologic complications and SCS, which, according to Holland et al. (2006) illustrates the importance of a thorough skin examination in patients with unexplained neurological diseases.

Face and cranial embryological development

Based on embryological and foetal pathological studies, developmental neural crest fields in the cranium have been described (Kjær 1995, 2010, 2012a, 2015, 2017). These fields extend all in a triangular, three-dimensional shape from the skin surface to the pituitary gland/sella turcica (Fig. 1). The fields are the fronto-nasal field, the maxillary

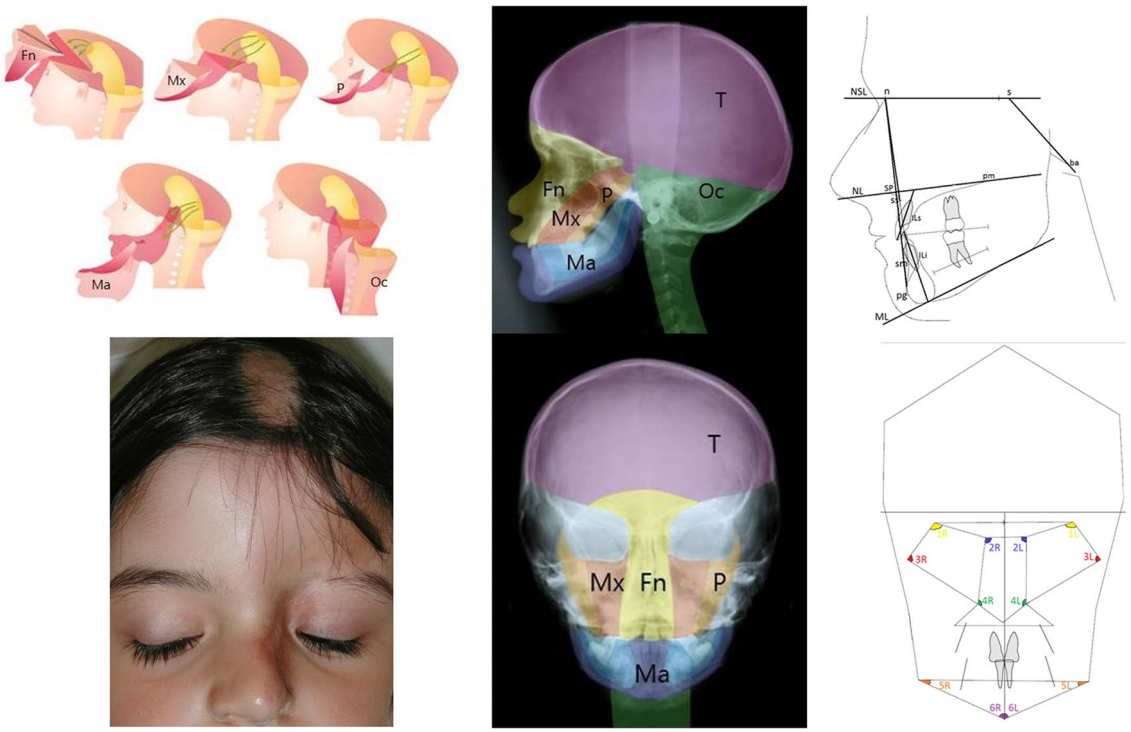


Fig. 1 Upper row: left: schematic illustrations of craniofacial fields. *Fn* bilateral fronto-nasal fields (right and left sides) including the maxillary incisors, *Mx* maxillary field (left side) including the maxillary canine and premolars, *P* palatal field (left side) including the maxillary molars, *Ma* the mandibular field (left side) including all mandibular teeth, *Oc* occipital and cervical spine field. Green arrows indicate migration paths of neural crest cells from different regions at the neural tube to the different developmental fields in the cranium. Centre: profile radiograph of a child, 9 years of age. The different neural crest fields are coloured and marked according to the left drawings. Purple indicates theca field (marked T). Right: cephalometric drawing of a profile radiograph with the following landmarks and registration lines inserted: *n* nasion, *s* sella, *ba* basion, *sp* anterior nasal spine, *pm* posterior nasal spine, *ss* subspinale, *sm* submentale, *pg* pogonion, *NSL* Nasion–Sella line, *NL* nasal line, *ML* mandibular line, *Ils* upper incisor line and *Ili* lower incisor line. Lower row: three images of frontal views. Left: photograph of a patient with SCS, 6 years of age. The skin is affected in the fronto-parietal region on the left side of the face including the lateral part of the nose. Loss of hair (alopecia) is observed. Centre: frontal radiograph of the same child as demonstrated in the centre image in the upper row. Neural crest field is marked accordingly. Right: cephalometric drawing of a frontal radiograph with inserted bilateral angles (*L* left angle, *R* right angle) for assessing symmetry/asymmetry in the upper facial region, the medial facial region, and the lower facial region. Angles were constructed, expressing the upper facial region (orbital region, angle 1 and zygomatic region, angle 3). The medial facial region (upper nasal area, angle 2 and lower nasal area, angle 4), and the lower facial region (mandibular angles 5 and 6). The bone structures analysed for construction of the bilateral angles in each contralateral region were: contour of the zygomatic arch, contours of the orbital margins, the contours of the nasal cavity, the nasal spine, the mandibular angulus, and the mental region. If the two bilateral angles in the contralateral regions had the same size, there was a 100% agreement, which expressed a total symmetry in the region. If two bilateral angles differed more than 5%, mild asymmetry in the region was described, and if the angles differed more than 10%, a more severe asymmetry was described. Severe deviation expressed in the profile and frontal analyses was used as an indicator for where and how far in the depth the craniofacial bone tissue was involved in the SCS Group

field, the palatine field, the mandibular field, the occipital field, and the thecal field. These fields extend from the skin surface in a triangular shape to the sella turcica, and are schematically demonstrated on profile and frontal radiographs (Fig. 1). Note that the maxillary incisors are included in the fronto-nasal field, the maxillary canine/premolars are included in the maxillary field and the maxillary molars are included in the palatal field.

These fields are defined according to the peripheral nerve paths in the jaws (Chavéz-Lomelí et al. 1996; Kjær 2012b). The early interrelationship between the peripheral nerves in the jaws and the formation of jaw bone has been investigated (Kjær 1990). Also the influence of the innervation on tooth development within the neural crest fields has been described (Christensen et al. 1993a, b).

Furthermore, the prenatal interrelationship between cranial development and development of the central nervous system has been highlighted (Kjær et al. 1991; Kjær 1995, 1998; Kjær and Hansen 1995a, b).

The normal prenatal developmental interrelationship between neural crest ectoderm (skin and mucosa), ectomesenchyme (subcutis, bone), and neuroectoderm (peripheral

and central nervous system) within the different neural crest regions has been illustrated postnatally in several pathological conditions (Nodal et al. 1994; Kjær et al. 1994, 1997, 2001, 2002; Becktor et al. 2002a, b; Bang et al. 1995; Tabatabaie et al. 2008; Kenrad et al. 2013; Kjær 2013; Riis et al. 2014). The postnatal interrelationships between pathologic cranial development and brain development have been described in several syndromes (Sejrsen and Jakobsen 1996; Kjær and Niebuhr 1999; Kjær et al. 2010; Mølsted et al. 2010; Kenrad and Kjær 2016).

Purpose

The overall goal is to evaluate the extent of the SCS disorder in the underlying subcutis, including teeth and bone tissues. The questions to solve are: how far does the external visual skin abnormality extend in the depth? And does this SCS condition appear within and limited to craniofacial neural crest fields?

Furthermore, it is the purpose to discuss how the neurological complications could be associated with the skin and hard tissue abnormalities.

Materials and methods

Material

SCS group

Photographic and radiographic materials from six patients (one male and five females, aged 5–39 years) were included in the study. The patients were referred from The Resource Centre for Rare Oral Diseases at Copenhagen University Hospital. The oral manifestations of SCS in one of these six patients have been described before by Hørberg et al. (2015). Concerning anamnestic information, one of the individuals had a reduced sight, one had a malformation of the ear morphology, and one had epilepsy. Two of the patients had also linear scleroderma on the body and reduced mobility of the appendicular skeleton.

Photographic material was extra-oral photos in the anterior view of the head and neck. Furthermore, a few intra-oral photos were available from single records.

Radiographic material was profile radiographs (including few dental films) from all six patients and frontal radiographs, available from five patients. Furthermore, orthopantomograms were available from all six patients.

Methods

Method for clinical extra-oral demonstration of SCS

The appearance of the extra-oral observation of the SCS condition in the skin of the head and neck was analysed from the extra-oral photos. An example is demonstrated in Fig. 1.

From each of the six patients, the extent of the SCS condition was drawn schematically in frontal view of the face (Fig. 2).

According to similarity in the location of SCS, the six cases were divided in three groups, two in each.

Group 1 SCS observed mainly in the scalp and forehead, not including the maxilla and nasal cavity. This abnormal skin condition occurred in the medial part of the frontal nasal field (Fig. 2).

Group 2 SCS observed with same appearance as Group 1, but also including the lateral aspects of the nasal cavity. This abnormal skin condition occurred in the lateral part of the frontal nasal field (Fig. 2).

Group 3 SCS observed in the maxilla and mandible with extensions to the neck. The abnormal skin condition registered in this group, corresponded to parts of the maxillary field, the palatal field, and the mandibular fields (Fig. 2).

Method for clinical and radiographic intra-oral demonstration of SCS

The affection of the dentition and gingiva was analysed clinically from intra-oral photos, dental radiographs, and orthopantomograms.

In the dentition, the following was analysed: deviation in tooth number, such as agenesis, dental maturity stage (expressed as root length), deviation in crown and root morphology (size and shape), deviation in location of tooth/teeth and eruption disturbances. The primary and permanent dentitions were analysed.

Severe deviation in the dentition within a craniofacial field indicated involvement of the dentition in the actual SCS Group.

Method for radiographic examination of craniofacial bone tissue in SCS

Profile radiographs were analysed cephalometrically according to methods described by Björk (1960). The landmarks and cephalometric lines used were: n = nasion, s = sella, ba = basion, sp = anterior nasal spine, pm = posterior nasal spine, ss = subspinale, sm = submentale, pg = pogonion, NSL = nasion–sella line, NL = nasal line, ML = mandibular line, Ils = upper incisor line and Ili = lower incisor line. From these landmarks and lines, shown in Fig. 1, jaw prognathia, cranial base angle, jaw inclination, and incisor inclinations

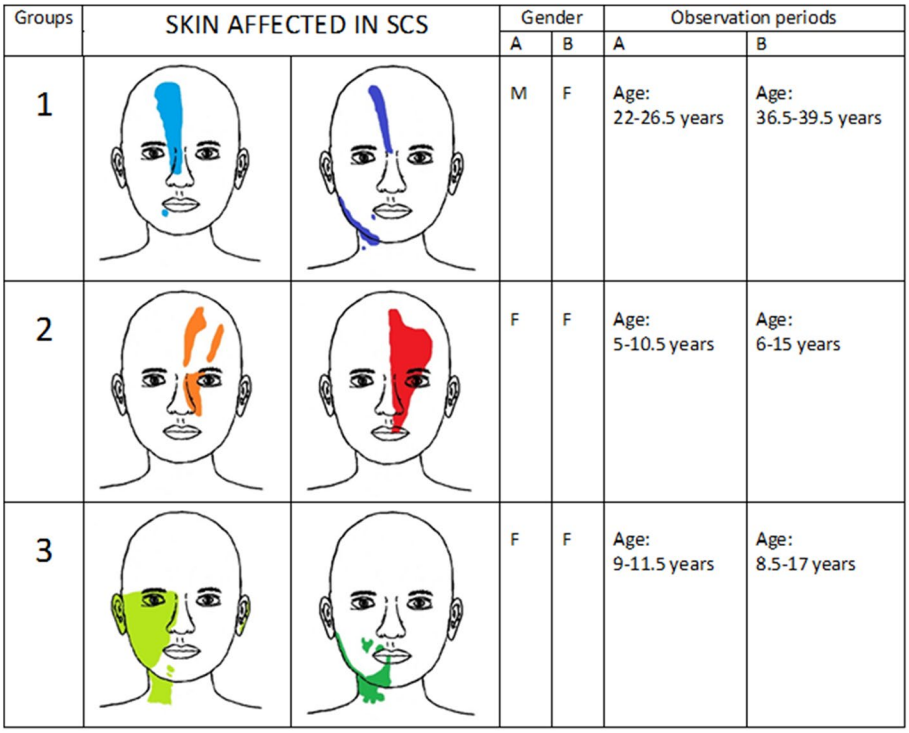


Fig. 2 Schematic drawings from extra-oral photos of the faces in six patients with SCS. The coloured areas mark the different locations of the skin affections. According to similarity in the location of SCS, the six cases were divided into three groups, two in each. Group (1) SCS observed mainly in the scalp and forehead, not including the maxilla and nasal cavity. This abnormal skin condition occurred in the medial part of the frontal nasal field. Group (2) SCS observed with same appearance as Group 1, but also including the lateral aspects of the nasal cavity. This abnormal skin condition occurred in the lateral part of the frontal nasal field. Group (3) SCS observed in the maxilla and mandible with extensions to the neck. The abnormal skin condition registered in this group, corresponded to parts of the maxillary field, the palatal field, and the mandibular fields. *F* female and *M* male. Ages indicating observation period appear to the right

were expressed. Furthermore, morphological inspections of the radiographic structures were performed.

Frontal radiographs Cephalometric analyses on the frontal radiographs were used as a modification of the methods by Svanholt and Solow (1977). For expression of frontal symmetry, the symmetry/asymmetry in the upper facial region, the medial facial region, and the lower facial regions, highlighted in Fig. 1, was used. Angles were constructed, expressing the upper facial region (orbital region, angle 1 and zygomatic region, angle 3), the medial facial region (upper nasal area, angle 2 and lower nasal area, angle 4), and the lower facial region (mandibular angles 5 and 6).

The bone structures analysed for construction of the bilateral angles in each contralateral region were: contour of the zygomatic arch, contours of the orbital margins, the contours of the nasal cavity, the nasal spine, the mandibular angulus, and the mental region.

If the two bilateral angles in the contralateral regions had the same size, there was a 100% agreement, which expressed a total symmetry in the region. If two bilateral angles differed more than 5%, a minor asymmetry in the region was described, and if the angles differed more than 10%, a more severe asymmetry was described.

Severe deviation expressed in the profile and frontal analyses was used as an indicator for where and how the craniofacial bone tissue was involved in the SCS group.

Results

Skin affections

According to extent of the SCS-affected regions in the head and neck of each of the six patients, they were divided into three groups and are schematically demonstrated in Fig. 2. There were two patients in each group. These were numbered A and B in each group. Information on gender and ages under observation appears also in Fig. 2.

The drawings of the six patients demonstrate differences in skin affections. Each drawing resampling an extension of a craniofacial field, as demonstrated in Fig. 1.

Conclusion Group 1 expresses mainly the uppermost part of the fronto-nasal field. Group 2 expresses as well the extension in Group 1 as the lower part of the fronto-nasal field, bordering the nasal cavity and the upper lip. Group 3 expresses different areas in the maxillary and mandibular fields.

Dentition/oral cavity affections

Orthopantomograms and dental films from patients in Groups 1, 2, and 3 are demonstrated in Figs. 3, 4, 5. From the radiographs, it can be concluded that different teeth are affected in the different groups.

Group 1 (Fig. 3)

In this group, the central maxillary incisor is affected on the same side (right), where the SCS condition appears. Patient A has a minor apical malformation, while patient B has a nearly complete root loss (repaired by dental implant), also on the right side.

Group 2 (Fig. 4)

In this group, the central maxillary incisor as well as the lateral maxillary incisor are severely malformed. There is a deviation of these incisors in the crown and root morphology, and also a change in location/eruption. The disturbances are all seen on the same side, where SCS skin affections are observed.

Group 3 (Fig. 5)

In this group, the molars are affected in both individuals. The second mandibular molar is affected (short roots) in case A and the second maxillary molar is affected (severe resorption) in case B, where also the first permanent molar on the same side has been extracted. Furthermore, a labially malpositioned mandibular central incisor with retraction of the facial gingiva appeared in case B.

A bandlike scleroderma lesion is observed at the oral aspect of the lip. This central mandibular incisor has been extracted before orthodontic treatment.

The dental deviations in group 3 appear in the same side where the SCS skin affection occurs.

Conclusion dental deviations in tooth morphology and tooth location appear in the same regions/neural crest fields, where skin affection occurs in SCS.

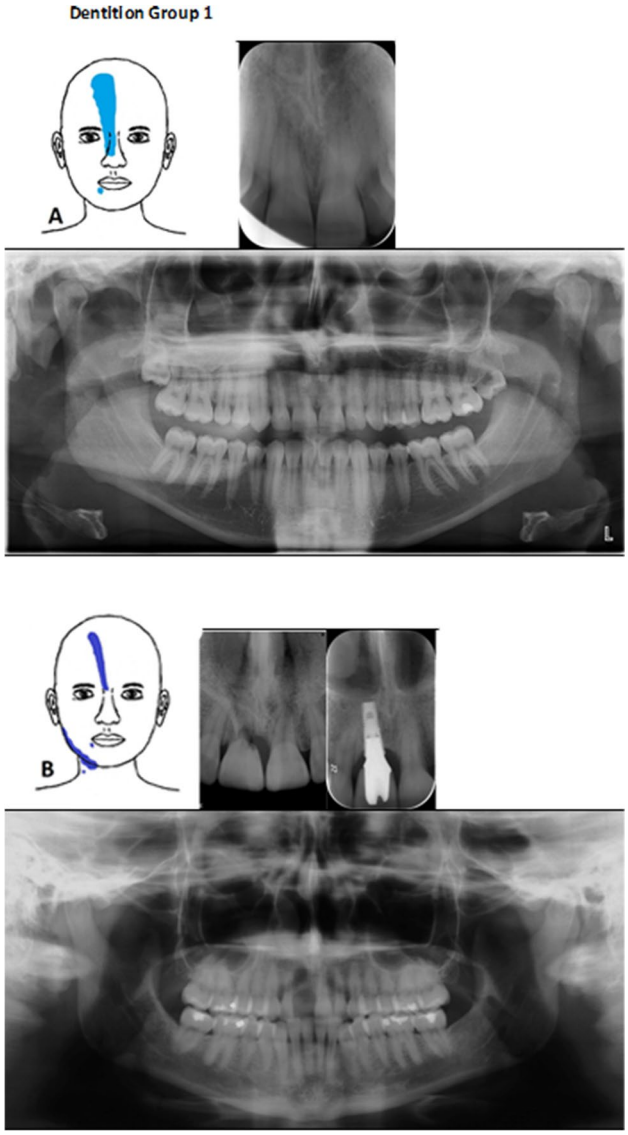


Fig. 3 The dentition in Group 1. Upper patient A, lower patient B. Upper: A: overview of the dentition in patient A, Group 1, age 25.6 years. The right central maxillary incisor might be slightly resorbed apically. Otherwise, the dentition appears normal except for agenesis of the third mandibular molars. Lower: B: overview of the dentition in patient B, Group 1, age: 26 years and 36.5 years. The right central maxillary incisor was completely resorbed or the root not developed. This incisor was later replaced by a dental implant. Otherwise, the dentition appears normal except for marginal bone loss in the medial part of the right fronto-nasal field, comparable to the region for skin affections in Group 1. See inserted drawings of faces A and B

Craniofacial bone tissue affections

The results of the cephalometric analyses of the three groups are summarised in Table 1.

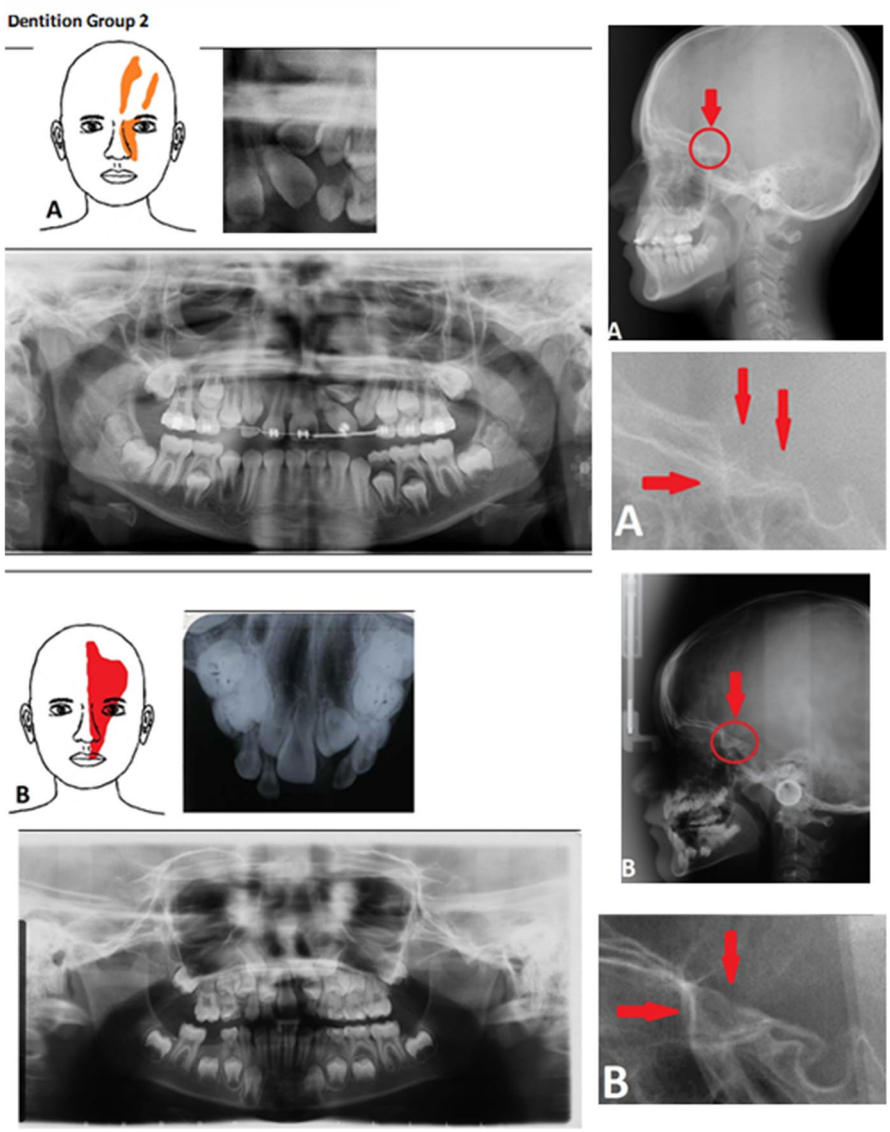


Fig. 4 The dentition and bone morphology in Group 2. Upper patient A, lower patient B. Upper left: A: overview of the dentition in patient A, Group 2, age 8.5 years. The left maxillary central incisor and the left maxillary lateral incisor appear malformed (crown and root) and malpositioned. Orthodontic fixed appliance has been inserted (orthopantomograms). Treatment not finished. Otherwise, the dentition appears normal. Lower left: B: overview of the dentition in patient B, Group 2, age 7 years. The left maxillary central incisor appears malpositioned and possibly malformed, but this cannot be proven from the radiographs. Otherwise, the dentition from this young child appears normal. The figure demonstrates that the dental deviations observed in Group 2 appear within the lateral part of the fronto-nasal field, comparable to the region for skin affections in Group 2. See inserted drawings of faces A and B. Upper and lower right: overview of profile radiographs with corresponding cephalometric drawings from patients in Group 2 (two patients, A upper and B lower). Note the malformed areas on the planum spheoidale in both patients in Group 2. The malformed areas are marked by red circles and red arrows. Cephalometric results for the four patients are listed in Table 1

Profile The cephalometric analyses of the profile radiographs demonstrated individual differences. There were no common traits in the profile analyses. In four of the six patients, bimaxillary prognathia was registered. Concerning incisor occlusion, one patient had a vertical overjet (patient B in Group 1) and one patient had a vertical open bite (patient B in Group 3).

Of specific importance was the registration in the bone morphology of a deep cavity, in the planum sphenoidale anterior to the sella turcica in two patients (patients A and B in Group 2), demonstrated in Fig. 4. These two patients had more or less the same skin extend of the SCS condition.

Frontal Analyses of the frontal radiographs demonstrated nearly complete symmetry in the less affected SCS patient

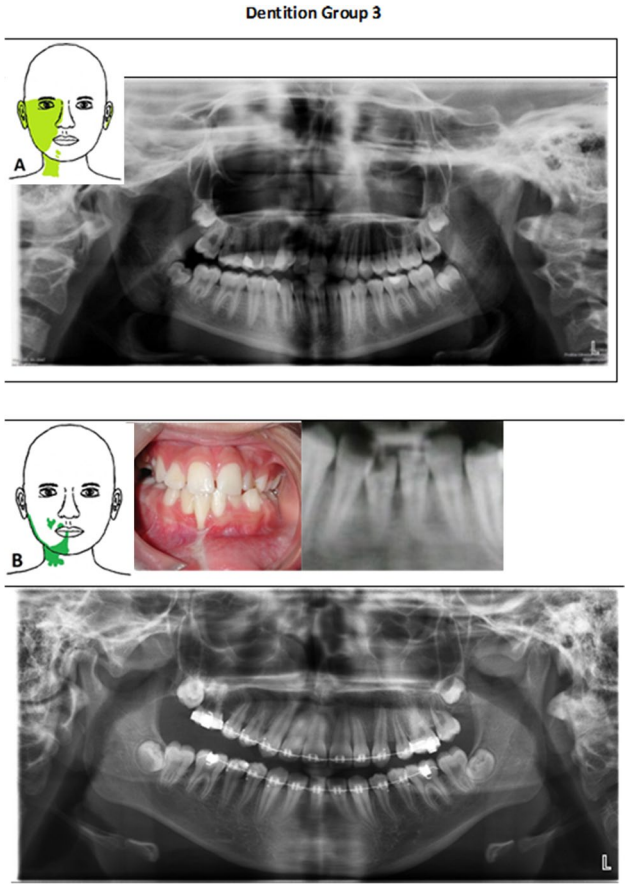


Fig. 5 The dentition in Group 3. Upper patient A, lower patient B. Upper: A: overview of the dentition in patient A, Group 3. Age 11.5 years. The second mandibular molar is affected (short roots) in case A. Otherwise, the dentition appears normal. Lower: B: overview of the dentition in patient B, Group 3. Ages 13.5 years. The second maxillary molar is affected (severe resorption) in case B, where also the first permanent molar on the same side has been extracted. The intra-oral photo (age 10 years and 6 months) demonstrates a central mandibular incisor with retraction of the facial gingiva. A bandlike scleroderma lesion is observed in the oral aspect of the lip. This central incisor has been extracted before orthodontic treatment. The dental deviations in group 3 appear on the same side where the SCS skin affection occurs

(1A). The four patients in Groups 2 and 3 demonstrated more or less asymmetry, associated with the region of SCS skin abnormality. The asymmetry in the patient A in Group 2 demonstrated severe asymmetry in the upper face region, and patient A in Group 3 demonstrated severe asymmetry, as well in the upper face region as in the lower face region.

Conclusion Concerning the bone involvement in the craniofacial area in SCS, the overall conclusion is that there is an association between the location and extent of the SCS skin defect and the underlying bone. Most interesting was the finding of the same severe malformation in the planum sphenoidale observed on profile radiographs in both individuals (A and B) in Group 2. Concerning the frontal radiographs, severe asymmetry occurred in Group 2 (patient A) and in Group 3 (patient A).

Summary of all findings

In SCS, the skin affection appears corresponding to the neural crest regions/fields.

There is a close association between skin, teeth and bone affections in neural crest fields, affected in SCS. The malformation in the SCS condition in the craniofacial region seems to extend from the skin in the depth to the sella turcica area, within the respective neural crest fields.

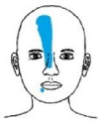
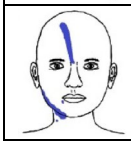
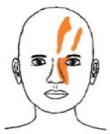
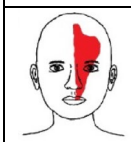
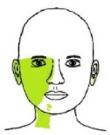
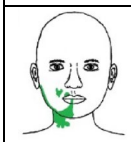
Discussion

Analyses demonstrated in this study focus on the underlying bone tissue in patients with SCS. A new finding in this study was the interrelationship between the same skin deviation in two patients and the same bone malformation anterior to the sella turcica (Group 2). The findings suggest an association between the regional skin defects and the affection on the underlying bone tissue, similar to regional maxillary dysostosis observed before (Becktor et al. 2002a, b). The finding in this study needs to be proved in an even larger material (extended study). Also a control material of frontal radiographs from healthy individuals is needed for future comparisons to frontal radiographs from SCS individuals.

Characteristic for the extension of the skin defects in the six patients analysed is that there exists a sharp borderline between the affected and the non-affected skin. Also the observation that the skin defects did not cross the mid-axial line supports the theory of an inborn defect in the embryological development. Possibly, a single cell line of the neural crest cells within a developmental field could be the aetiologic explanation for the skin and bone affections (Weibel and Harper 2008).

It is supposed that the neural crest fields represent different dermatomes (Schoenwolf et al. 2009). The dermatomes develop close to the body axis very early in the embryogenesis. From there, they migrate anteriorly and form all tissue types, developed from ectomesenchyme; among these tissue types are bone, cartilage, subcutis, and dentin. The dermatomes are innervated, each by specific peripheral nerves (Schoenwolf et al. 2009). Regarding the SCS condition, the dermatomes form the abnormal subcutis, which is essential for teeth and jaw development. Furthermore, the subcutis interacts with the overlying cutis (ectoderm) molecularly. Therefore, dermatomes, expressed in fields, could explain the interrelationship between the abnormal skin in SCS, dentition, and bone. In the dentition, the crown formation

Table 1 Schematic overview of the results from the craniofacial analyses of six profile radiographs (left) and five frontal radiographs (right) from patients with SCS

Groups	Profile radiographs	Frontal radiographs		
		Upper face	Medial face	Lower face
1 	**A:** Sag. : Harmonious profile. Mandibular prognathia Vert.: Normal relationship Morf.: Normal bone morphology	99.5% (An.1) 97.7% (An. 3)	**92.3%** (An. 2) **91.9%** (An. 4)	98% (An. 5) 97% (An. 6)
	**B:** Sag.: Bimaxillary prognathia, dento-alv. compensated Vert.: Anterior inclination of the mandible Morf.: Normal bone morphology			
2 	**A:** Sag.: Bimaxillary prognathia, specifically mandible Vert.: Normal vertical jaw relation. Ant. max. inclin. Morf.: **Abnormal bone morphology in the planum sphenoidale**	**89.9%** (An. 1) **82.2%** (An. 3)	**92.6%** (An. 4)	**92.1%** (An. 5)
	**B:** Sag: Bimaxillary prognathia, Enlarged sag. jaw relation Vert.: Normal vertical jaw relation. Ant. mand.inclin. Morf.: **Abnormal bone morphology in the planum sphenoidale**	**95%** (An. 1) 95.5% (An. 3)	**93.4%** (An. 2)	100% (An. 5) 99.2 (An. 6)
3 	**A:** Sag.: Maxillary retrognathia, Enlarged mand. Prognathia Vert.: Diminished vertical jaw relation. Ant. mand. Inclin. Post max. inclin. Morf.: Normal bone morphology	**88.5%** (An. 1) **88.3%** (An. 3)	**92.2%** (An. 2) **97.2%** (An. 4)	**84.2%** (An. 5)
	**B:** Sag.: Bimax retrognathia. The right maxillary first molar extracted. Vert.: Enlarged vertical jaw relationship post mand. Inclin. Enlarged lower face hight. Morf.: Normal	**93.8%** (An. 1) **92.9%** (An. 3)	**97.9%** (An. 2) **94.7%** (An. 4)	**94.7%** (An. 5)

Location of SCS skin affections divided into three groups is seen in the far left column. Cephalometric analyses of the profile radiographs demonstrated no common traits. Malformation in planum sphenoidale was observed in both patients in Group 2 (marked red). Cephalometric analyses of six bilateral angles (see Fig. 1) in each frontal radiograph were compared for demonstration of symmetry/asymmetry, and expressed in percentages. In few cases, the angles could not be measured. 100% expressed complete symmetry. Differences in angles (marked An) expressed asymmetry. Above 95% minor asymmetry (marked red) and below 95% severe asymmetry (marked purple)

Minor asymmetry appeared in the medial face of all patients, and severe asymmetry in the upper face in two patients (patient A in Group 2 and patient A in Group 3). Severe asymmetry occurred in the lower face in patient A, Group 3. This patient had the most extended skin abnormality, covering also the neck

depends on its initial phase mainly on the ectoderm and the root formation, mainly on the ectomesenchyme (Andersen et al. 2004; Kjær and Nolting 2009). Concerning jaw development, there is a close interrelationship between peripheral nerves and early bone formation (Kjær 1990). Interrelationship between cranial development and the central nervous system has been described in normal and pathological conditions (Kjær et al. 1991, 2010; Kjær 1998).

A former study demonstrated that dental deviations occurred, within the field demarcated by the skin deviations in SCS (Hørberg et al. 2015). This finding supports the theory of developmental field affection in SCS. Concerning segmental odontomaxillary dysplasia, observations on regional affections in the skin, teeth and jaw bone have formally been described (Becktor et al. 2002a, b). Furthermore, in conditions such as Hyper-IgE, skin defects have been observed in patients with premolar canine eruption deviations (Becktor

et al. 2001). Also regional skin deviations in conditions such as incontinentia pigmenti and regional occurrence of tooth agenesis have been described (Kjær et al. 1994).

It is important to distinguish between regional abnormalities, restricted to fields with a common innervation (Kjær 2012b) and conditions, not restricted to fields. Field defects can generally be caused by deviations in innervation and/or ectomesenchyme, while defects not restricted to fields can be caused by ectoderm (Kjær 2012b).

This study is based on few patients, due to the low incidence of the SCS condition. The incidence has been calculated in Olmsted County, Minnesota, to be 0.13 cases per 100,000 individuals (Peterson et al. 1997). SCS is more frequent in females than in males (Fischer and Patton 2000).

It is important to evaluate the present results in an extended study. Also 3D analyses would be valuable to incorporate in future studies, such as performed by Trainito et al. (2012). The evaluation of the observed bone malformation in two patients in Group 2 with skin affections in the lateral part of the fronto-nasal field is in agreement with the extent of this field, from the skin surface extending in the depths to the sella turcica (Kjær 2012a). Bone malformations might in the future be visible on 3D scanning in patients from Groups 1 and 3. Superimposing of bony structures in profile radiographs prohibits observation of bony defects, not visible mid-axially.

Future studies should incorporate neurology perspectives, focusing on brain pathology related to skin and bone pathology. Former studies have documented interrelationships between postnatal cranial abnormalities, dental abnormalities, brain defects and neuropsychiatric deviations (Kjær et al. 2010; Kenrad and Kjær 2016). This is highly important to be aware of, when SCS is first diagnosed.

As a conclusion, attention should be given to the interrelationship between deviation in skin and the underlying hard tissue, bone, teeth, and the central/peripheral nervous system. Distinction should be made between deviations, restricted to fields and deviations, seemingly not restricted to fields. In SCS where the deviations are restricted to fields, it is important to involve different medical disciplines in early diagnostics, already when the first sign of skin affections has been observed (Martini et al. 2002). This is important, not only for dentists, who might be the first to observe this condition, but also for medical specialists, as neurological complications, including epilepsy, can develop in SCS during puberty.

The neurological aspect described in SCS, might be valuable to consider, also in the evaluation of the dentition in non-SCS patient treated in general orthodontic practice (Kenrad and Kjær 2016).

This study focuses on the interrelationship between regional deviation and skin, teeth and the underlying bone in SCS. For the dentist, it is important to refer the patients to an interdisciplinary collaboration between specialists in dental sciences, dermatology, neurology, rheumatology and ophthalmology.

In severely affected patients with facial asymmetry, early orthodontic treatment plans are important.

The described and explained interrelationships between development of teeth, jaws and nervous tissue should call attention to specialists in orthodontics, treating patients (not only SCS patients) with severe malocclusion including dental deviations. These symptoms could possibly be interrelated with an undiagnosed neurologic/neuropsychiatric condition.

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Compliance with ethical standards

Conflict of interest The authors declare that there is no conflict of interest regarding the publication of this article.

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