CASE REPORT

A case report of open craniofacial sutures, a novel feature of systemic sclerosis?

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Scleroderma is an uncommon connective-tissue disease, its key feature being excessive collagen deposition resulting in fibrosis of the skin and internal organs. There are different types that can vary in severity from localized scleroderma to systemic sclerosis. Various clinical and radiographic findings can be attributed to the disease, which arise owing to the progressive nature of microvascular changes and collagen deposition. These include limited mouth opening, xerostomia, periodontal disease and cardiac and pulmonary disease. Whilst bone resorption has been reported, as far as we are aware, the literature has not described a case with failure of bony suture closure. Hence, we would like to describe what is probably a unique case of a patient with a 5-year history of systemic sclerosis, who was referred for management of increased mobility of her upper central incisors. Radiographic imaging (conventional and three-dimensional) confirmed increased bone resorption, partly owing to periodontal disease, but also owing to an open premaxillary suture. Similarly, other craniofacial sutures were diagnosed as being open, and, to our knowledge, this represents a yet undescribed finding in a patient suffering from scleroderma.

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Introduction

Scleroderma, which literally means “hard skin”, is an uncommon immune-mediated, connective-tissue disorder,^{1,2} leading to internal organ and skin fibrosis.¹ Its aetiology remains unknown, even though genetic and environmental factors, e.g. chemicals and chemotherapeutic agents, have been reported as potential triggers.^{2,3} The condition, which was first described by Goetz in 1945,³ shows a peak onset between the fourth and sixth decade and a female predisposition, with reported female:male ratios of as high as 6.²⁻⁴ The pathogenesis involves microvascular damage and changes, such as endothelial dysfunction or thickening of vessel walls, immune system dysregulation and fibrosis,⁵⁻⁷ which occurs as a result of substantial deposition of collagen Type I and III in skin and visceral organs.^{2,3,5,6}

There are two main types: a localized form primarily affecting the skin, and systemic sclerosis (SS) which affects the vascular system and internal organs including the skin. Several SS subtypes have been identified, i.e. limited or diffuse cutaneous SS, SS without skin involvement (sine scleroderma) and overlap syndrome.^{1-3,8}

Limited SS often starts as Raynaud’s phenomenon (RP) and along with other features is also known as CREST syndrome, consisting of calcinosis cutis (typically in the digits), RP, oesophageal dysmotility, sclerodactyly and teleangiectasis.^{2,3} It presents with skin involvement distal to elbows and knees, with or without affecting the skin of the face and neck.^{1,7} Serology tests often demonstrate evidence of anticentromere auto-antibodies.^{1,2,7}

In contrast, diffuse SS shows extensive skin involvement and is more frequently associated with considerable fibrosis of visceral organs, including lung and kidneys.^{1-3,7} Patients often complain of skin tightness

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or itching,¹ but weight loss, exertional breathlessness, musculoskeletal pain or even trigeminal^{1,9} and/or glossopharyngeal neuralgia¹ can also be accompanying symptoms. Serologically, presence of antiscl-70 (anti-topoisomerase) and anti RNA-polymerase III auto-antibodies has been associated with the diffuse cutaneous form.^{1,2,7}

A minority of SS patients (<5%) is diagnosed with SS sine (without) scleroderma. These present with clinical finding typical for SS, *i.e.* vascular symptoms, like RP, visceral organ involvement and serological evidence of auto-antibodies, however, without signs of skin involvement. Finally, overlap syndrome refers to patients, who are diagnosed with any of these SS subtypes, as well as with a further autoimmune rheumatic disease, *e.g.* rheumatoid arthritis.^{1,3}

Owing to the variety of, to some extent, unspecific symptoms and the scarce prevalence of approximately 10,000 reported cases worldwide,¹ achieving a definitive diagnosis of this orphan disease remains challenging. Cardinal signs are RP, which affects over 95% of patients^{1,2,4,5,10} and gastro-oesophageal reflux owing to oesophageal dysmotility.^{1,3} RP, alongside finger puffiness and/or sclerodactyly and antinuclear antibodies should be regarded as red flag signs to practitioners, which should trigger further investigations to facilitate early disease diagnosis.⁵ Radiographically, typical findings in scleroderma patients are bone resorption, typically of the phalanges and angles of the mandible, and widening of the periodontal ligament space.^{3,4,8} However, to the best of our knowledge, no cases of open craniofacial sutures have yet been reported in the literature. In this case report, we would, hence, like to present a patient with history of scleroderma and this so far undescribed and exceptional radiographic finding.

Case report

A 53-year-old female was referred for an assessment of the radiographic appearance of her upper central incisors in June 2017, which had developed a relatively sudden increase in mobility. The patient had noticed this approximately 1 year prior to the referral, which was made by a Specialist Periodontologist, who had provided the patient with non-surgical root surface debridement in early 2017. She denied any other associated symptoms, *e.g.* bleeding, swelling or pain. Despite an overall improvement in oral and periodontal health following her periodontal treatment, the increased mobility of her upper central incisors persisted.

Medically, the patient described a history of scleroderma (SCL-70 positive), diagnosed in 2012 and leading to development of pulmonary fibrosis in 2013. Her initial treatment regime was Cyclophosphamide and Methylprednisolone, but this was changed to Methotrexate and Folic Acid over time. Otherwise, she suffered from type-II diabetes, which was diet-controlled.

Figure 1 Full OPG, showing widened periodontal ligament space associated with teeth UR8, UR7, UR5, LR8, LR7 and LL7. OPG, orthopantomogram.

Clinically, she had scleroderma features, *i.e.* a pinched nose appearance and mild microstomia. Intraoral examination revealed good oral hygiene and a moderately restored dentition. The upper central incisors were Grade II mobile, the upper right lateral incisor was Grade I mobile. No abnormality was associated with the remaining dentition.

An orthopantomogram and a periapical radiograph of the upper central incisor teeth were performed as part of the initial radiographic examination. These demonstrated moderate bone loss owing to periodontal disease and extensive periapical bone loss in the upper central incisor region and a midline cleft (Figures 1 and 2). Furthermore, widening of the periodontal ligament space around several upper and lower molars was noted, representing a typical scleroderma feature. Owing to these findings, the decision was made to perform a cone beam CT scan for further investigation, as well as an ultrasound examination to exclude early changes of the salivary glands.

The cone beam CT scan confirmed the previously described dental findings, *i.e.* widening of the periodontal ligament space of the upper right wisdom tooth, upper right second molar, upper right second premolar, lower right wisdom tooth, lower right second molar and lower left second molar. The bone support in the upper central incisor area was reduced owing to periodontal bone loss, but demonstrated open or widened premaxillary and midline palatal sutures (Figure 3). Similarly, other sutures of the facial bones remained open, including the frontonasal suture and the sutures of the zygoma, sphenoid bone and the palatine process of the maxilla (Figure 4).

No resorption of the mandibular angles was noted. The articular surface of the right mandibular condyle was notched, however, no significant degenerative change was seen. No degenerative disease was associated with the left mandibular condyle.

Further skeletal changes were observed, *e.g.* degenerative changes affecting the first cervical vertebra which included sclerosis of the anterior arch, a lytic area within the anterior arch and a reduced joint space between the arch and odontoid peg. The odontoid peg showed similar degenerative change with anterior irregularity,

Figure 2 Periapical radiograph of the UR2, UR1 and UL1, demonstrating midline cleft.

a subarticular radiolucency and an area of erosion. Finally, loose bodies were found between the odontoid peg and the clivus tip.

The ultrasound examination excluded signs of Sjogren's syndrome or chronic inflammation with all four major salivary glands having a homogenous

Figure 3 Axial scan along the palate showing open midline and transverse palatine sutures.

Figure 4 Three-dimensionally rendered image, showing the right side with open sutures.

appearance, normal echotexture and brightness (Figure 5).

The patient now remains under care of the hospital to monitor her periodontal disease and manage the increased tooth mobility as required.

Discussion

This case report presents a patient with typical scleroderma features, but also, a yet undescribed and exceptional finding of open craniofacial sutures. To the best of our knowledge, no similar radiographic findings have yet been described in scleroderma patients, which appears to make this case unique. Open (or delayed closure of) cranial sutures or fontanelles have, however, been reported in association with other disorders, such as cleidocranial dysplasia.^{11,12} The clinical relevance of these findings in scleroderma patients remains,

Figure 5 Transverse ultrasound image of right parotid gland, demonstrating a normal appearance.

nonetheless, unclear. It has to be acknowledged, as we did not have access to any previously performed radiographs, that we assumed that the sutures in this patient failed to close rather than reopened at some point during child-/adulthood. Also, as this presents a single patient case, open craniofacial sutures might not actually be associated with SS, but this could represent an incidental presentation of unknown origin. Furthermore, it is questionable whether this feature would generally affect patient management.

Our radiographic examination also revealed degenerative changes of the first vertebra and odontoid peg. This corresponds to previous reports describing polyarthralgia in scleroderma patients. Bassett et al described calcifications in patients' fingers, as well as erosions and severe destructions in joints of hands and feet, which represent a non-rheumatoid erosive arthropathy in affected individuals.¹³ Other anatomical locations, such as the temporomandibular joint can also be affected.^{2,14}

With regards to radiographic findings, a main feature in the head and neck region is a widened periodontal ligament space, diagnosed in approximately a third of patients.^{4,8,14} Baron et al furthermore suggested a correlation between a widened periodontal ligament space and disease severity.¹⁴ Bone resorptions are also commonly seen, which can potentially lead to pathological fractures. In the head and neck region, mandibular osteolysis is reported in up to 33% of cases, which mainly affects the mandibular angles, but can also be seen in the mandibular condyle, coronoid process and zygomatic arches.^{3,4,8,10,15} In their study, Baron et al described an association between mandibular erosions and a decreased interincisal distance (mouth opening), however no correlation with disease severity was observed.¹⁴

An ultrasound examination was performed as part of our investigation in order to assess evidence of potential salivary gland fibrosis. This feature subsequently leads to dry mouth symptoms in affected patients, and xerostomia in turn promotes dental caries and erosions.^{2,3,10} These can additionally be aggravated by the presence of gastro-oesophageal reflux disease. Similarly, fibrosis of lacrimal glands can be seen, provoking xerophthalmia and keratoconjunctivitis.³

Clinically, several findings of the head and neck region represent typical scleroderma features, which

practitioners should be aware of. As the disease progresses, patients often present with an expressionless, mask-like face,^{2,4} associated with a pinched nose appearance.^{2,3} A frequent accompanying symptom is microstomia, which can be present in over 80%.^{2,3,6,9,10} Tongue rigidity can lead to dysphagia and dysphonia.^{2,4,10} Dentally, degenerative changes can also be seen in scleroderma, namely root resorption, which has been reported in up to a third of patients⁴ and calcification of the pulp and/or periodontal ligament.⁶ Recently, Arroyo-Bote et al documented a yet undescribed clinical finding, *i.e.* external cervical resorption.⁶

Our patient's current treatment regime is Methotrexate, which is one of the primary therapeutic agents prescribed in SS patients and recommended medication for skin involvement.^{5,7} Previously, she had been prescribed Cyclophosphamide, which is also effective in managing the disease; however, studies revealed that the medication loses its efficacy after 24 months of use, which might have also been a reason for the change to Methotrexate in our case.⁷ Novel treatment options include biologic disease-modifying antirheumatic drugs, which have in part demonstrated promising efficacy and tolerability results. Nonetheless, further larger randomized controlled trials with longer follow-up periods are needed to draw conclusions regarding long-term efficacy and safety.^{5,7}

Despite recent advances in patient management, the prognosis of SS patients remains poor. This is highlighted by the fact that mortality rates have stayed relatively unchanged for the last 40 years, which can mainly be attributed to major organ involvement, in particular, cardiopulmonary disease.^{5,7} This underlines the importance of early diagnosis and development of more effective therapies.

Consent

Written informed consent for this case to be published was obtained from the patient. The patient provided written consent to potential use of her records in presentations and publications prior to having imaging performed.

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