Case Report

Progressive systemic sclerosis with intraoral manifestations: A case report and review

Rahul Srivastava, Bhuvan Jyoti, Manorama Bihari, Shobhit Pradhan

Abstract

The word scleroderma comes from two Greek words, “sclero” meaning hard and “derma” meaning skin. Scleroderma or progressive systemic sclerosis (PSS), a rare condition, was first characterized as a single condition in 1752 by Curzio of Naples. It generally affects woman between 30 and 50 years of age and has a low prevalence. Scleroderma is a disease of the immune system, blood vessels, and connective tissue. Dermal manifestations include stiff, tight, and shiny skin usually of the hands and feet due to swelling and thickening of the connective tissue as they become fibrotic or scarred. Other symptoms include difficulty in swallowing, bloating, abdominal pain, tiredness, lack of energy, weight loss, aching muscles, joints, and bones. The vital organs that may get involved are lungs, heart, and kidneys. We present a case report of PSS in a 45-year-old female patient with characteristic systemic and oral manifestations.

Key words: Immune system, progressive systemic sclerosis, scleroderma

INTRODUCTION

The word scleroderma comes from two Greek words, “sclero” meaning hard and “derma” meaning skin.[1] The term scleroderma is indelibly etched in the literature through common usage, the disease is currently called as “systemic sclerosis” (SSc). Since hidebound skin is the clinical hallmark of the disease, it is also called “hidebound disease.”[2] SSc is a clinically heterogeneous generalized disorder which affects the connective tissue of the skin and internal organs such as gastrointestinal tract, lungs, heart, and kidneys. It is characterized by alterations of the microvasculature, disturbances of the immune system and by massive deposition of collagen. The first detailed description of a scleroderma-like disease was published by Curzio in Naples in 1753.[3] The patient, a young woman, suffered from excessive tension and hardness of the skin. Nearly 100 years later, in 1847, Gintrac introduced the term scleroderma, as the skin was the most obvious organ involved.[4]

SSc is a multisystem, autoimmune disease affecting small arteries, microvessels and fibroblast resulting in vascular obliteration, collagen accumulation, and scarring of the skin and internal organs. This leads to hidebound skin and damage of gastrointestinal tract, lungs, heart, and kidneys. Autoantibodies and perivascular lymphocytic (mainly CD4 positive T lymphocytes) infiltrate indicate activation of immune system. The CD4 positive T cells can be activated by endothelial basement membrane components such as laminine and type IV collagen. Consequently, these cells secrete an endothelial cytotoxic factor named granzyme as well as tumor necrosis factor which activates endothelial cells and transforming growth factor - β (TGF - β) which activates fibroblasts...
to express TGF-β and platelet-derived growth factor (PDGF). PDGF activates fibroblasts to secrete increased amounts of collagen. The serological specificity of the disease is due to the presence of antinuclear antibodies (ANAs) which are directed mainly against cell nuclear enzymes, like DNA anti-topoisomerase-I (TOPO-I) and RNA polymerases, as well as centromeric proteins, anticientromere antibodies (ACA).[6]

SSc has a worldwide distribution and affects all races. Factors such as age, sex, genetic background, and environmental exposure may influence its susceptibility.[6] An early indicator of SSc is Raynaud’s phenomenon, characterized by a painful digital ischemia, which results in local resorption of terminal phalanges.[7] The disease has been classified into two major categories. One is the diffuse form in which there is generalized skin involvement and rapid progressive internal organ involvement. The other form is with limited cutaneous involvement confined to the distal aspect of fingers and the face.[2] The American College of Rheumatology (former American Rheumatism Association) has defined criteria, that are 97% sensitive and 98% specific for SSc as follows.[8]

**Major criterion**
- Proximal diffuse (truncal) sclerosis (skin tightness, thickening, nonpitting induration).

**Minor criteria**
- Sclerodactyly (only fingers and/or toes)
- Digital pitting scars or loss of substance of the digital finger pads (pulp loss)
- Bi-basilar pulmonary fibrosis.

The patient should fulfill the major criterion or two of the three minor criteria. Raynaud’s phenomenon is observed in 90–98% of SSc patients.[9] It may precede SSc for years, and its presence may have predictive value for the subsequent development of SSc, in particular in association with abnormal nail-fold capillaries and the occurrence of ANAs.[9,10]

Survival of scleroderma patients is determined by the severity of visceral involvement. Oral and facial tissues are often affected, presenting very characteristic features. Most clinical manifestations begin with tongue rigidity and facial skin hardening, which gives it a classic mask-like appearance.[7] The prevalence of scleroderma is estimated to be between 4 and 253 cases per million persons.[6] This is a case report of SSc with orofacial manifestations of the disease with a brief review of the literature focusing on the etiology, deontological alterations, and management of this rare entity.

### CASE REPORT

A 45-year-old female patient reported to the department of oral medicine and radiology with the chief complaint of mobility of left lower back teeth and metallic taste since 2 years. Her past dental history revealed extraction of teeth (26, 27, and 36) 3 years back due to mobility. The patient gave a history of loss of appetite and blue coloration of fingertips as a response to cold. The patient was poorly built and nourished. Her vital signs were within the normal limits. Morning stiffness affecting both small and large joints was present. General physical examination revealed tightening of the skin of extremities, claw-like the appearance of hands [Figure 1] with hypopigmented areas on hands, knee, ankle, pre- and post-auricular region [Figure 2]. Fingertips were pale, swollen, stiff and deformed. Extraoral examination revealed smooth, taut mask-like appearance of the facial skin and atrophied nasal alae giving rise to mouse facies appearance [Figure 3]. Intraoral examination revealed reduced mouth opening [Figure 4], missing 13, 26, 27, 31, 36, 43, 41 mobile 12, 33, 35, 42 and root stumps of 18, 16, 24, 28, 34, 45, 46. Blanching was present on the buccal mucosa, soft palate, hypopigmented areas on mandibular labial mucosa along with depapillation and restricted movement of the tongue. There was generalized edema of gingiva with bleeding on probing and deposits of stains and calculus. Intraoral periapical radiographs [Figure 5] and orthopantomogram revealed widening of periodontal ligament (PDL) space in the molars. Routine blood investigation was performed, all the values were within the normal limits except erythrocyte sedimentation rate which was found to be raised 36 mm and ANAs test was positive. Anteroposterior view of hands [Figure 6] and feet [Figure 7] revealed shortening and resorption of phalanges along with soft tissue calcific deposits. Esophageal constriction could be appreciated in barium swallow radiograph [Figure 8].

Skin biopsy was performed, and section shows epidermis and dermis. Epidermis was normal to thin and flattened at places. Dermis was largely replaced by compact collagen. Only occasional thick walled dermal blood vessels were present. Areas of hyalination and sparse infiltration of lymphocytes were also present. Histopathological findings were suggestive of scleroderma [Figure 9].

Based on history, clinical examination and investigations final diagnosis of progressive systemic sclerosis (PSS) was made. The patient was advised to take tablet D-penicillamine 250 mg two times daily, tablet Nifedipine 5 mg once daily at night and tablet Ranitidine and Domperidone.
150 mg two times daily. The patient was recalled after a week and was relieved of her symptoms. Extraction of the mobile teeth and root stumps was performed. The patient was advised to continue the medications for 1 month and was kept on regular follow-up.
DISCUSSION

SSc is a multisystem disorder of connective tissue characterized by extensive cutaneous and visceral fibrosis and small vessel vasculopathy. While the etiopathogenesis of SSc is unknown, pathological findings indicate that fibroblasts are activated to produce excessive amounts of collagen and other extracellular matrix components. Moreover, endothelial cell damage causing capillary loss and neo-intimal proliferation in small vessels plays a prominent role in tissue damage. Autoimmune mechanisms also are believed to be operative, because patients with SSc spontaneously elaborate a variety of highly disease-specific circulating autoantibodies to nuclear and nucleolar antigens. The most common of these autoantibodies are directed against DNA TOPO-I; centromeric proteins, especially centromeric protein B; and RNA polymerases I, II, and/or III. Less frequent autoantibody specificities include anti-U3-ribonucleoprotein (RNP) (fibrillarin), polymyositis/scleroderma autoantigen, T helper cells (Th)/To, and U1-RNP. Each SSc patient typically produces only one of these autoantibodies, which, in turn, correlates with certain disease manifestations and prognosis. It is unknown, however, whether autoantibodies directly participate in any of the pathological manifestations. SSc-specific antibodies also are associated with specific class II alleles of the major histocompatibility complex. Considerable evidence suggests that such autoantibodies result from autoantigen-driven Th cell-mediated immune responses.[11] Factors such as age, sex, genetic background, and environmental exposure may influence susceptibility.[6] Haustein et al. in 1991 stated that spectrum of sclerodermatous diseases comprises a wide variety of clinical entities such as morphea (patchy, linear, generalized), pseudo-scleroderma and the overlap-syndromes with similar cutaneous and histopathologic manifestations [Figure 10].[12] The subtypes of scleroderma include localized scleroderma and PSS. Three major types of localized scleroderma exist: Morphea, generalized morphea, and linear scleroderma.[13] SSc differs from localized scleroderma because it is accompanied by Raynaud’s phenomenon, acrosclerosis, and internal organ involvement. It generally affects woman between 30 and 50 years of age and has a low prevalence. PSS often affects oral and perioral tissues.[17] Oral manifestations of PSS may include limited ability to open the mouth, xerostomia, periodontal disease, increased PDL width and osseous resorption of the mandible.[14] The skin develops a diffuse, hard texture which is difficult to pinch (hide bound skin) and

Figure 7: Anteroposterior view of feet showing shortening of phalanges and soft tissue calcific deposits

Figure 9: Histopathological picture of scleroderma

Figure 8: Barium swallow radiograph reveals esophageal constriction

Figure 10: Clinical entities of scleroderma
Table 1: Common oral findings associated with scleroderma

| Oral findings associated with scleroderma |
|------------------------------------------|
| Facial and mucosal telangiectasia         |
| Dysphagia                                |
| Limited mouth opening                    |
| Xerostomia                               |
| Lip retraction                           |
| Fibrosis at the soft and hard palate     |
| Increased risk of periodontal disease and caries |
| Widening of periodontal ligament space   |
| Atrophy and blanching of oral mucosa     |
| Tongue fibrosis                          |
| Mandibular bone resorption               |
| Trigeminal neuralgia                     |

The exact etiology of the osteolysis in unknown, but there are three proposed theories:
- Tightening of facial skin may exert excessive pressure on the mandible and induce bone loss
- The vasculopathy associated with this disease may diminish the blood supply to the mandible resulting in bone ischemia and necrosis
- Atrophy of the muscles of mastication may lead to bone necrosis.

In our case, there was PDL widening as the earliest manifestation of the disease before mandibular bone resorption. ANAs have been detected in up to 90% of cases of SSc ACAs are more likely to be associated with limited SSc, whereas autoantibodies to TOPO-I (anti-Scl-70) are more likely to be associated with diffuse SSc. D-penicillamine is an effective drug in the treatment of SSc patients with early, rapidly progressive diffuse cutaneous involvement. D-penicillamine (D-3-mercaptopovaline) has several effects on collagen metabolism. Its primary action is blocking of aldehyde groups involved in the inter- and intra-molecular cross-linkage of mature (insoluble) collagen. It also accelerate the turnover of insoluble collagen by cleaving intermolecular bonds that stabilize the fibrous structure. In addition, D-penicillamine inhibits collagen biosynthesis and have immunosuppressive activity. As scleroderma can give rise to a variety of oral problems, maintenance of existing dentition is important. A small mouth in scleroderma makes lip, mouth movements, and oral hygiene difficult. Mouth stretching exercises and facial grimacing are probably the best treatment. These exercises can be done, by covering the teeth with the lips then opening the mouth as wide as possible without showing the teeth, then again close lips and press hard (as if blotting lipstick), open the mouth so that the lips are as wide apart as possible, open the mouth so that the teeth are as far apart as possible, push the jaw forward to create an underbite (bottom teeth in front of the upper teeth), make a grin as wide as possible without showing the teeth. Dental caries is due to the destruction of the tooth substance by acids produced by dental plaque and can be minimized by: effective tooth-cleaning, control of dietary sugars and use of fluorides. Teeth should be brushed at least twice daily and an ideal toothbrush should have nylon bristles of an even length, and of medium hardness. The toothbrush should be small enough to be easily placed in the mouth. Fluoride has no notable oral or other side-effects, patients with scleroderma are advised to use a fluoride containing toothpaste. Fluoride mouthwashes are recommended for patients who have a dry mouth (xerostomia) as they may be particularly at risk of dental caries. Dental plaque formation is greatly enhanced by sugar (sucrose), therefore frequent intake of sticky sugary foods

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between meals may lead to increased dental decay. Try to limit the consumption of sugary foods to meal times. Some patients with scleroderma can develop dry mouth as a consequence of the destruction of the salivary glands (secondary Sjogren’s syndrome). The lining of the mouth (oral mucosa) can become sore. A lack of saliva can give rise to an unpleasant taste, and foods may become bland in taste. The management of long-standing dry mouth in scleroderma comprises salivary substitutes, moisturizing gels, nonspecific stimulation of salivary secretion stimulation of saliva production. Salivary substitutes comprise two main approaches – water and drinks that the patient sips on a regular basis, and artificial salivary substitutes. Certainly drinking or sipping sucrose-containing drinks must be avoided. Nonspecific stimulation of saliva production is best achieved with chewing gums. At least two chewing gums are suggested these are Biotène® dry mouth gum and BioXtra® chewing gum. A nonsucrose based pastille (Salivex®) is also available. Pilocarpine (Salagen®) stimulates saliva production. The efficacy of Salagen® depends on the existence of residual gland function.[1]

CONCLUSION

Scleroderma presents great challenges to both medical and dental professionals and has a profound impact on oral health. Since the mouth is a mirror of the systemic health of the body, dental practitioners may be the first to note some of the signs of PSS. Instructions in and reinforcement of oral hygiene along with frequent dental assessment and management are essential measures to preserve the oral health.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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