IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

SYSTEMIC SCLEROSIS AFFECTS ONLY SKIN? OTHER SYSTEM INVOLVEMENT: AN ARTICLE

G. Jyoshna[1*], K.M.Jyoshna[1], K.Usha[1], Senthilvel Arunmozhishivam[1], Dr.K.Thirumala Naik[2]

1- Pharm D Intern, Pharmacy Practice, Krishna Teja Pharmacy College, Tirupathi

1-Mbbs House Surgeon, Sri Balaji Medical Collage , Hospital &Research Instutitue

2- Associate Professor & Clinical Preceptor, Krishna Teja Pharmacy Collage, Tirupathi

Abstract

Systemic sclerosis, also known as scleroderma, is a rare and complex autoimmune connective-tissue disease. Onceconsidered an untreatable and unpredictable condition, research advancements have improved our understanding of its disease pathogenesis and clinical phenotypes and expanded our treatment armamentarium.

Early and accurate diagnosis is essential, while ongoing efforts to risk stratify patients have a central role in predicting both organ involvement and disease progression. A holistic approach is required when choosing the optimal therapeutic strategy, balancing the side-effect profile with efficacy and tailoring the treatment according to the goals ofcare of the patient.

KEYWORDS

Raynaud phenomenon, Microstomia, telangiectasias

INTRODUCTION

DEFINITIONS

Systemic sclerosis is a multi system disease, characterised by autoimmunologic processes, vascular endothelial cell injury, inflammation, and an extensive activation of fibroblasts.
Skin, esophagus, lung, heart, and kidneys are the mostfrequently affected organs.[(1-17)]

EPIDEMIOLOGY

•The age of disease onset ranges between 30 and 50years.

•Autoimmune diseases often have a female predominance and this is the case in SSc, which has an overall female to male ratio of 3:1 or greater.

•The global SSc incidence and newly diagnosed population were estimated to be 8.64 per 100,000 person-years (1.78-23.57) and 0.67 million (0.14-1.84) people annually, respectively. Regarding prevalence, the global SSc prevalence and affected population were
18.87 per 100,000 persons (1.55-25.28) and 1.47 million(0.12-1.97) people, respectively.[(23-24)]

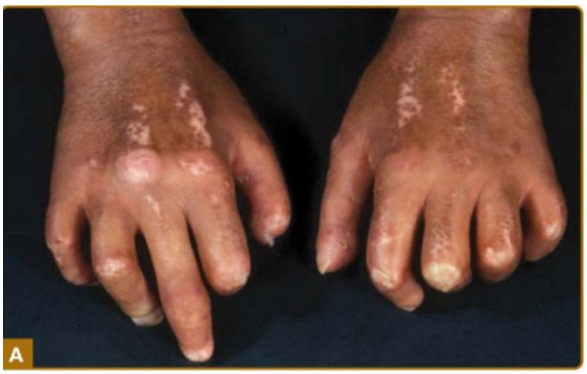
CLINICAL FEATURES OF SYSTEMIC SCLEROSIS

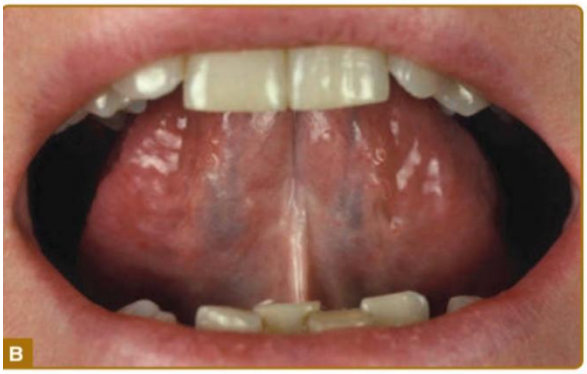
- SSc usually starts with a Raynaud phenomenon, whichcan precede the disease for many years.
- The clinical features of established SSc are diverse with severe fibrosis of the skin and all additional cutaneous

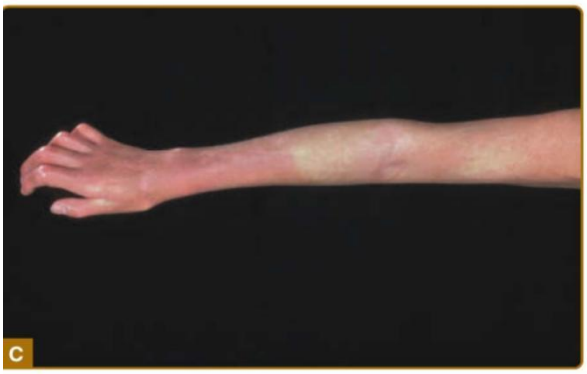
manifestations.

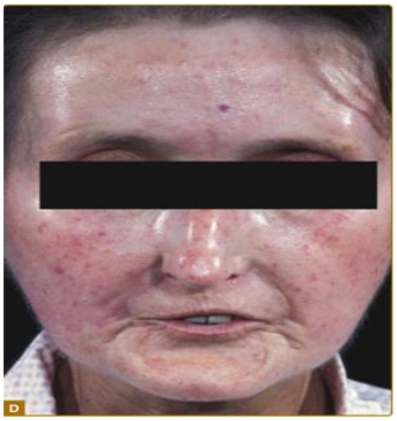
- These include hardening of the skin, development ofcontractures, digital ulcerations and calcifications.
- They also reflect the multiple patterns of internal organ involvement and the consequences of progression of the underlying pathologic processes of vasculopathy,inflamma-tion, and fibrosis.

Particular consideration must be given to the hallmark complications of hypertensive scleroderma renal crisis (SC),pulmonary arterial hypertension (PAH), pulmonary fibrosis (PF), and GI dysmotility.[17-20]









A. Sclerodacty dermatogenous contractures (restricted mobility of digital joints) and salt -and-pepper hyperpigmentations and hypopigmentation.

B. Microostomia (radical furrowing around the mouth) with frenulum sclerosis

C. Skin thickening proximal of the meacarpophalangeal joints.

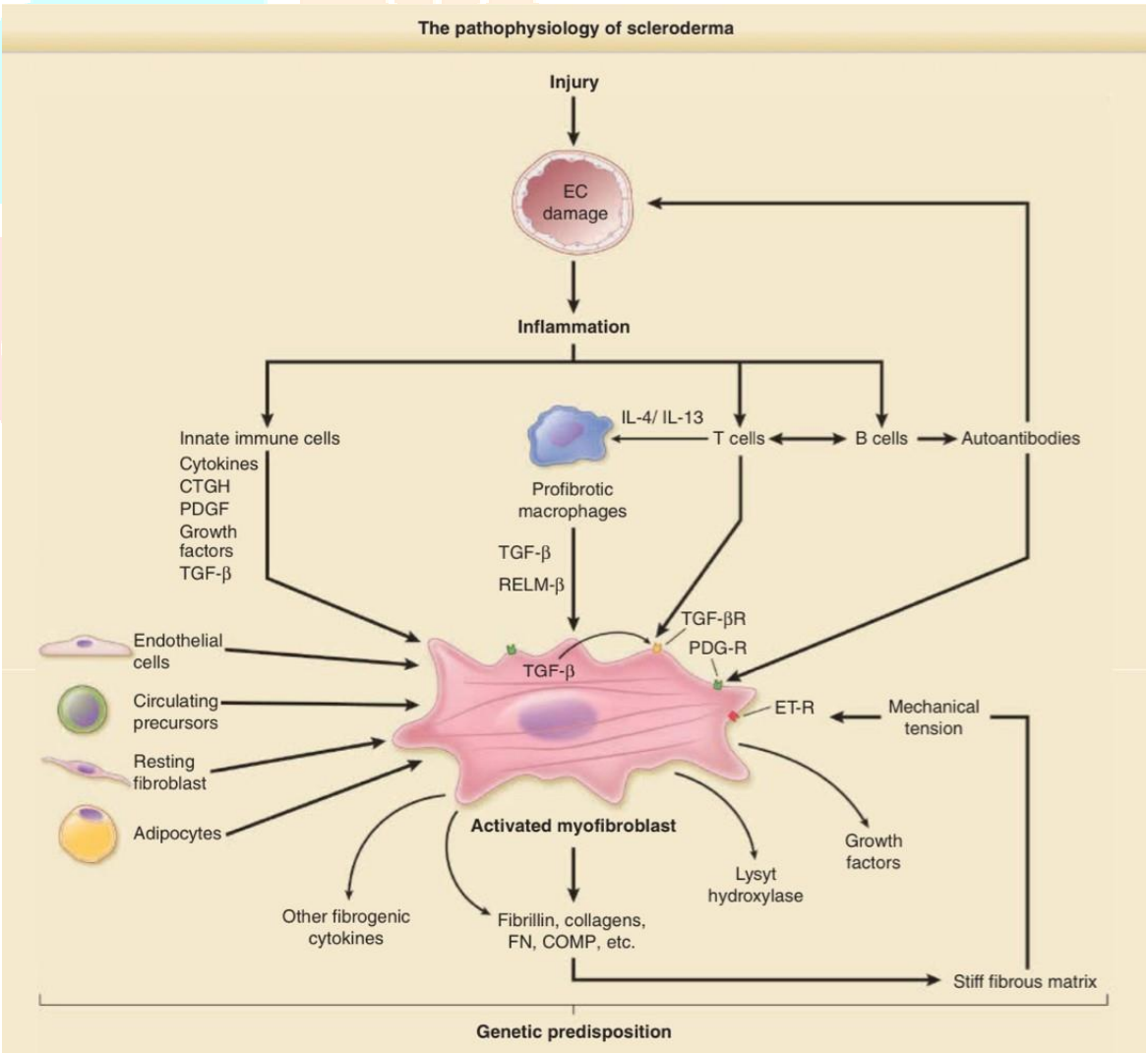
D. Typical scleroderma facial physiognomy with hyper-mimia, microstomia, telangiectasis and a beaked nose(17&19)

AETIOLOGY AND PATHOGENESIS

❖ The pathogenesis of this complex autoimmune disease involves multiple cell types (endothelial cells, epithelial cells, fibroblasts, and lymphocytic cells) interacting through a variety of mechanisms that are dependent on their microenvironment and several key mediators.

❖ Major facets of the disease include inflammation, vasculature, and the activation of connective tissue-producing cells .

❖ The clinical heterogeneity of Sc makes it likely that distinct pathogenetic mechanisms predominate in particular patientsor subsets of disease. Similarly, the key pathways are not necessarily the same at different stages of SSc. Although a genetic component to etiopathogenesis is likely and evidence supports genetic factors determining severity and sus-ceptibility, there are also strong arguments, supporting environmental and chemical factors as triggers for the disease.(30)



SKIN INVOLVEMENT

Skin involvement is a cardinal feature of Sc and usually appears first in the fingers and hands. Within time, patients develop nonpitting edema of the fingers (puffy fingers), hands, and extremities, followed by an increasing induration and skin thickening(sclero-dactyly)

The abnormal deposition of cutaneous and / or subcutaneouscalcium (calcinosis cutis), usually occurs over pressure points(acral, joints) in a period of time .

Digital ulcers are associated with strong, local pain and a major impact on quality of life regarding all-day functions (eg, dressing, eating). Other complications include critical digital i schemia, paronychia, infections, gangrene, osteomyelitis, and finger pulploss or amputation.

CARDIOPULMONARY MANIFESTATIONS

There are different ways that the cardiopulmonary system may beinvolved, most often appearing as fibrosis and PAH.
Dyspnea, arrhythmia[1-20]

GI INVOLVEMENT

GI involvement is the most common internal organ involvement in patients suffering from both limited and diffuse SSc (>60%).' Manyparts of the GI tract may be impaired, affecting motility, digestion, absorption, and excretion.

Esophageal involvement includes symptoms like dysphagia,heartburn resulting from reflux, nau-sea, and/or vomiting,esophagitis

Possible gastric manifestations include atrophy of mucous membrane-associated ulcerations and delayed gastric emptying.

KIDNEY INVOLVEMENT

SRC appears in 5% to 10% of SSc patients, and may cause an abrupt onset of significant systemic hypertension (>140/90 mm Hg,or a rise in systolic/ diastolic blood pressure 230/220 mm Hg), together with an increase in serum creatinine, proteinuria, hematuria, thrombocytopenia, or hemolysis followed by an acute renal failure.[1-20]

End-organ damage can result in encephalopathy with generalizedseizures or flash pulmonary edema.

MUSCULOSKELETAL SYSTEM

Musculoskeletal (MSK) involvement of the hands is a significantsource of morbidity, impacting on quality of life in patients with systemic sclerosis.

chronic joint pain, inflammation and swelling in muscles and joints Arthralgia Synovitis Muscle weakness are the ailments noted

VASCULAR SYSTEM

Raynaud phenomenon due to decreased blood flow to extremities

SSc causes noninflammatory macrovascular and microvascular changes with dramatic and possibly occlusive formation of a thickened neointima.

It involves vascular disease involves vasculopathy with luminalocclusion, thrombosis, and vasospasm[1-20]

RECOMMENDED DIAGNOSTIC PROCEDURES[29]

Vascular system	Raynaud phenomenon	▪ Coldness provocation ▪ Nailfold capillaroscopy ▪ Antinuclear antibody levels
Skin	Scleroderma Calcinosis cutis	▪ Clinical assessment regarding puffy fingers, telangiectasias, mechanic hands, hypopigmentations/hyperpigmentations, digital ulcerations, dermatogenous contractures ▪ Modified Rodnan skin score ▪ 20-MHz ultrasonography ▪ Radiography (X-ray, MRI, CT)
Musculoskeletal system	Arthralgia Synovitis Muscle weakness	▪ Clinical assessment regarding fist closure deficiency, joint contractures, tendon friction rub, muscle weakness ▪ Laboratory parameters: erythrocyte sedimentation rate, rheumatoid factor, antinuclear autoantibodies ▪ Creatine kinase (greater than threefold?) ▪ MRI, electromyography ▪ Muscle biopsy
GI tract	Reflux Dysphagia Gastric antral vascular ectasia Diarrhea, obstipation	▪ Gastro-/esophageal endoscopy ▪ Esophageal scintigraphy, esophagus manometry ▪ Gastro-/esophageal endoscopy with laser coagulation, if necessary ▪ Colonoscopy
Respiratory system	Dyspnea	▪ Lung function test (carbon monoxide transfer factor corrected for hemoglobin [TLCOc] single breath (SB), total lung capacity [TLC], forced vital capacity [FVC]) ▪ Radiography (X-ray or high resolution CT) ▪ Bronchioalveolar lavage (BAL) (optional)
Cardiac system	Dyspnea, arrhythmia	▪ Electrocardiography (conduction blocks?) ▪ Echocardiography (mean pulmonary artery pressure, diastolic dysfunction?, ventricular ejection fraction) ▪ (Spiro-)Ergometry ▪ 24-Hour blood pressure controls ▪ Right-heart catheterization ▪ Cardio MRI
Kidney	Renal function failure	▪ Regular blood pressure controls (>140/90 mm Hg) ▪ Ultrasonography ▪ Serum levels of creatinine, urine analyses (protein, albuminuria, microelectrophoresis)

TREATMENT IN SYSTEMIC SCLEROSIS

VASULOPATHY

◆ Raynaud phenomenon

◆ Consistent warm keeping, paraffin-bath, patient education

◆ Calcium channel blockers (eg, nifedipine) by mouthAngiotensin receptor antagonists

◆ Alternatives: selective serotonin reuptake inhibitors (SSRIs), a-blockers, sympathectomy with or without botulinum toxin injection

◆ Digital ulcers

◆ Prostacyclin (eg, iloprost) IV

◆ Endothelin receptor blockade (eg, bosentan by mouth)Phosphodiesterase Type 5 inhibitors (off-label)

◆ Wound dressing (hydrocolloid membrane, Mepilex)

MUSCULOSKELETAL SYSTEM

◆ Synovitis/myositis

◆ Methotrexate (by mouth, IM)

◆ rituximab (off-label)[28]

GI SYSTEM

◆ Reflux Proton pump inhibitors, prokineticsDysphagia H.-receptor antagonists

◆ Diarrhea, obstipation. Change habit of eating, parenteralnutrition

◆ Antibiotics (eg, ciprofloxacin) Symptomatic managementwith antidiarrheal agents or laxatives

RESPIRATORY SYSTEM

◆ Dyspnea
◆ Oxygen
◆ Alveolitis / lung fibrosisCyclophosphamide IV
◆ Mycophenolate mofetil by mouth (used as an alternative orafter cyclophosphamide)
◆ Glucocorticoids (short dated, if necessary)

CARDIAC SYSTEM

Pulmonary arterial hypertension

◆ Endothelin receptor blockade (eg, bosentan by mouth,macitentan)
◆ Inhaled iloprost
◆ Phosphodiesterase Type 5 inhibitors (eg, sildenafil bymouth, tadalafil)
◆ Epoprostenol by mouth Combination of different agents

Systolic heart failures

◆ Immunosuppression with or without pacemakerCardioverter defibrillator
◆ Angiotensin-converting enzyme inhibitors and carvedilol (selective -blockers may be considered, but consider worsening of Raynaudphenomenon)

Diastolic heart failure

◆ Diuretics
◆ Calcium channel inhibitors

RENAL SYSTEM

◆ Scleroderma renal crisis
◆ Calcium channel inhibitors
◆ Angiotensin-converting enzyme-Hemmer (high-dosed)[28]

MAIN REFERENCES

1.Hunzelmann N, Genth E, Krieg T, et al. The registry of the German Network for Systemic Scleroderma: frequency of disease subsets and patterns of organ involvement. Rheumatology (Oxford). 2008;47(8):1185-1192.

2.Mayes MD, Lacey JV Jr, Beebe-Dimmer J, et al. Prevalence, incidence, survival, and disease characteristicsof systemic sclerosis in a large US population. Arthritis Rheum. 2003;48(8):2246-2255.

3.Silman AJ. Epidemiology of scleroderma. Curr Opin Rheumatol. 1991;3(6):967-972.

4.Tamaki T, Mori S, Takehara K. Epidemiological study of patients with systemic sclerosis in Tokyo. Arch Der-matolRes. 1991;283(6):366-371.

5.Medsger TA Jr, Masi AT. Epidemiology of systemic sclerosis (scleroderma). Ann Intern Med. 1971;74(5): 714-721.1

6.Preliminary criteria for the classification of systemic sclerosis (scleroderma). Subcommittee for scleroderma criteria of the American Rheumatism Association Diagnostic and Therapeutic Criteria Committee.

7.Arthritis Rheum. 1980;23(5):581-590.

8.van den Hoogen F, Khanna D, Fransen J, et al. 2013 Classification criteria for systemic sclerosis: an American College of Rheumatology/European League Against Rheumatism collaborative initiative.

9.Arthritis Rheum. 2013;65(11):2737-2747.

Reference

1.LeRoy EC, Medsger TA Jr. Criteria for the classification of early systemic sclerosis. J Rheumatol 2001;28(7):1573-1576.

2.Nadashkevich O, Davis P, Fritzler MJ. Revising the classification criteria for systemic sclerosis. Arthritis Rheum.2006;55(6):992-993.

3.Walker JG, Pope J, Baron M, et al. The development of systemic sclerosis classification criteria. Clin Rheuma-tol. 2007;26(9):1401-1409.

4.Maricq HR, Valter I. A working classification of scleroderma spectrum disorders: a proposal and the resultsof testing on a sample of patients. Clin Exp Rheuma-tol. 2004;22(3)(suppl 33):S5-S13.

5.LeRoy EC, Maricq HR, Kahaleh MB. Undifferentiated connective tissue syndromes. Arthritis Rheum. 1980;23(3):341-343.

6.Alarcon GS. Unclassified or undifferentiated connective tissue disease. Baillieres Best Pract Res Clin Rheumatol. 2000;14(1):125-137.

7.Poormoghim H, Lucas M, Fertig N, et al. Systemicsclerosis sine scleroderma: demographic, clinical, and serologic features and survival in forty-eight patients. Arthritis Rheum. 2000;43(2):444-451.

8.Bennett RM. Scleroderma overlap syndromes. RheumDis Clin North Am. 1990;16(1):185-198.

9.Ciang NC, Pereira N, Isenberg DA. Mixed connective tissue disease-enigma variations? Rheumatology (Oxford).2017;56(3):326-333.

10. Gunnarsson R, Hetlevik SO, Lilleby V, et al. Mixed connective tissue disease. Best Pract Res Clin Rheumatol.2016;30(1):95-111.

11. laccarino L, Gatto M, Bettio S, et al. Overlap connective tissue disease syndromes. Autoimmun Rev. 2013;12(3):363-373.

12. Krieg T, Takehara K. Skin disease: a cardinal feature ofsystemic sclerosis. Rheumatology (Oxford).

13. 2009;48(suppl 3):ili 14-iii 18.

14. Chaisson NF, Hassoun PM. Systemic sclerosis- associated pulmonary arterial hypertension. Chest. 2013;144(4):1346-1356.

15. Thakkar V, Nikpour M, Stevens WM, et al. Prospects for improving outcomes in systemic sclerosis-related pulmonaryhypertension. Intern Med J. 2015;45(3):

16. J Scleroderma Relat Disord. 2016 May-Aug; 1(2): 177–240

17. Published online 2016 Jul 23. doi: 10.5301/jsrd.5000209

18. Global, regional, and national incidence and prevalenceof systemic sclerosis

19. Jingru Tian 1 , Shuntong Kang 2 , Dingyao Zhang

20. 3 , Yaqing Huang 4 , Ming Zhao 5 , Xianhua Gui 6 , XuYao 7 , Qianjin Lu 8

21. Affiliations expand

22. PMID: 36804224 DOI: 10.1016/j.clim.2023.109267

23. Ciang NC, Pereira N, Isenberg DA. Mixed connective tissue disease-enigma variations? Rheumatology (Oxford).2017;56(3):326-333.

24. Gunnarsson R, Hetlevik SO, Lilleby V, et al. Mixed connective tissue disease. Best Pract Res Clin Rheumatol