SYSTEMIC SCLEROSIS

DR.PRAVEEN NAGULA

It is much simpler to buy books than to read them and easier to read them than to absorb their contents.

SIR WILLIAM OSLER

Background

- Scleroderma is derived from the greek words *skleros* (hard or indurated) and ***derma*** (skin).
- HIPPOCRATES first described this condition as thickened skin.
- First detailed description by Carlo Curzio in 1752.
- Term scleroderma --- Giovambattista Fantonetti
- Systemic nature of the disease by Robert H.Goetz.

Introduction

DR.A.G.MAURICE RAYNAUD

- Chronic systemic disorder of unknown etiology.
- Characterised by thickening of the skin (scleroderma) and distincitive involvement of multiple internal organs most notably lungs , GIT , heart ,kidneys.
- Skin induration limited to fingers(sclerodactyly)
- No skin induration (SSc sine scleroderma)
- RAYNAUD'S phenomenon is predominant feature seen.

CASE

- A **40-year-old white woman** with a 2-year history of ***Raynaud's phenomenon*** presented because the skin on her hands was beginning to ***feel tight.***
- Five weeks earlier, her hands had been swollen, erythematous, and pruritic, but these symptoms resolved without treatment.
- The patient also described flulike symptoms during this same period of time.
- The review of systems was significant for slight dyspnea without chest pain, heartburn, difficulty swallowing pills, bloating, and abdominal distention.
- ***The patient's work-up included pulmonary function tests, which revealed a reduction in vital capacity and a decreased lung compliance.***

- ✓ The results of her blood work included an elevated sedimentation rate, positive antinuclear antibodies, and positive anticentromere antibodies…
- ***Scleroderma with calcinosis, Raynaud's phenomenon, esophageal dysfunction, sclerodactyly, and telangiectasia (the CREST variant of limited scleroderma).***

Definition

- SSc is a multisystemic ,autoimmune disease affecting small arteries,microvessels and fibroblasts resulting in vascular obliteration,collagen accumulation and scarring (fibrosis) of skin and internal organs.
- Leads to hidebound skin,damage of GIT,Lungs,Kidney,Heart.
- Serologic specificity of the disease is the presence of ANA ,directed against cellular nuclear enzymes, like DNA topoisomerase -1 (anti –Topo 1) and RNA polymerase,as well as centromeric proteins (anticentromere Ab)

Diagnostic criteria

- The AMERICAN COLLEGE OF RHEUMATOLOGY (ACR) criteria for the classification of systemic sclerosis.
- **One major criteria,two or more minor criteria for diagnosis.**
- **MAJOR criterion : PROXIMAL scleroderma** –characterized by SYMMETRICAL thickening,tightening and induration of the skin of the fingers and the skin proximal to the MCP /MTP joints. these changes may affect the entire extremity,face,neck,trunk.
- **MINOR**
- **1.SCLERODACTYLY** – thickening,induration,tightening of the skin limited only to fingers.
- **2.DIGITAL PITTING SCARS/LOSS OF SUBSTANCE FROM THE FINGER PAD** –due to ischemia.
- **3.BIBASILAR PULMONARY FIBROSIS-** b/l reticular pattern of linear or lineonodular densities in basilar portions of the lung on CXR.diffuse mottling/honey comb lung not attributable to primary pulmonary disease

Epidemiology

- ✓ Acquired sporadic disease
- ✓ Affects all races.
- ✓ Incidence is 9-19 cases/million/year.
- ✓ Female predominance.
- ✓ Child bearing ages.
- ✓ African americans >whites..earlier age
- ✓ Non mendelian pattern of inheritance.
- ✓ Concordance among twins is low.,but ANA is high..
- ✓ Juvenile onset systemic sclerosis is uncommon.
- ✓ ***No data on the prevalence of scleroderma in INDIA.***

Etiology

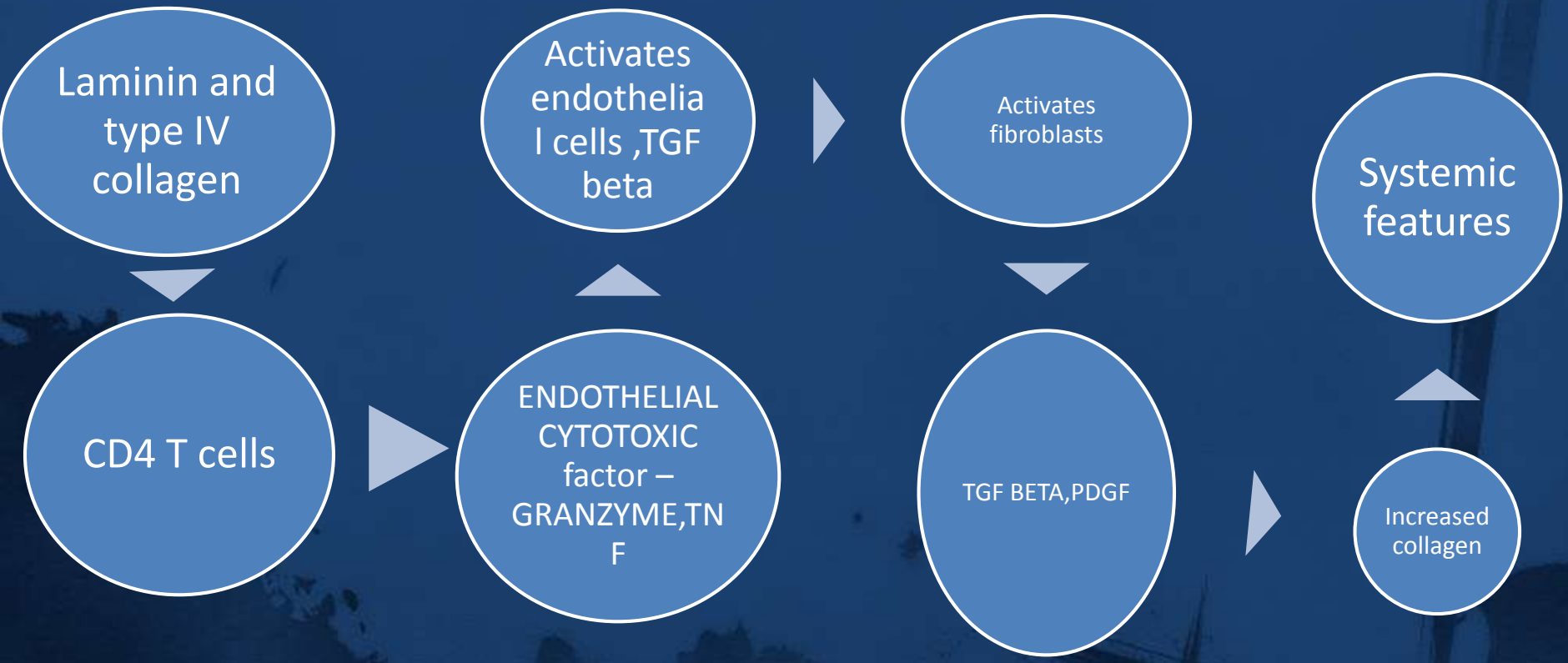
- Exact etiology is unclear.
- Environmental factors triggers or acclerators for the development of SSc - silica exposure,vinyl chloride,trichloroethylene,epoxy resins,benzene,CCl4
- Radiation exposure /radiotherapy
- CMV,HHV 5,PBV B19
- Drugs– bleomycin,pentazocine.l-tryptophan
- Common in coal and gold miners.
- ***Do not explain the spontaneously developed disease.***

Pathology

Following pathogenic mechanisms always present:

- Endothelial cell injury
- Fibroblast activation
- Cellular and humoral immunologic derangement.
- Activation of the immune system is an outstanding disease feature. –autoantibodies,perivascular lymphocytes (cd4 T)
- Chronic forms of GVHD shares features of SSc.

pathogenesis



Pathogenesis

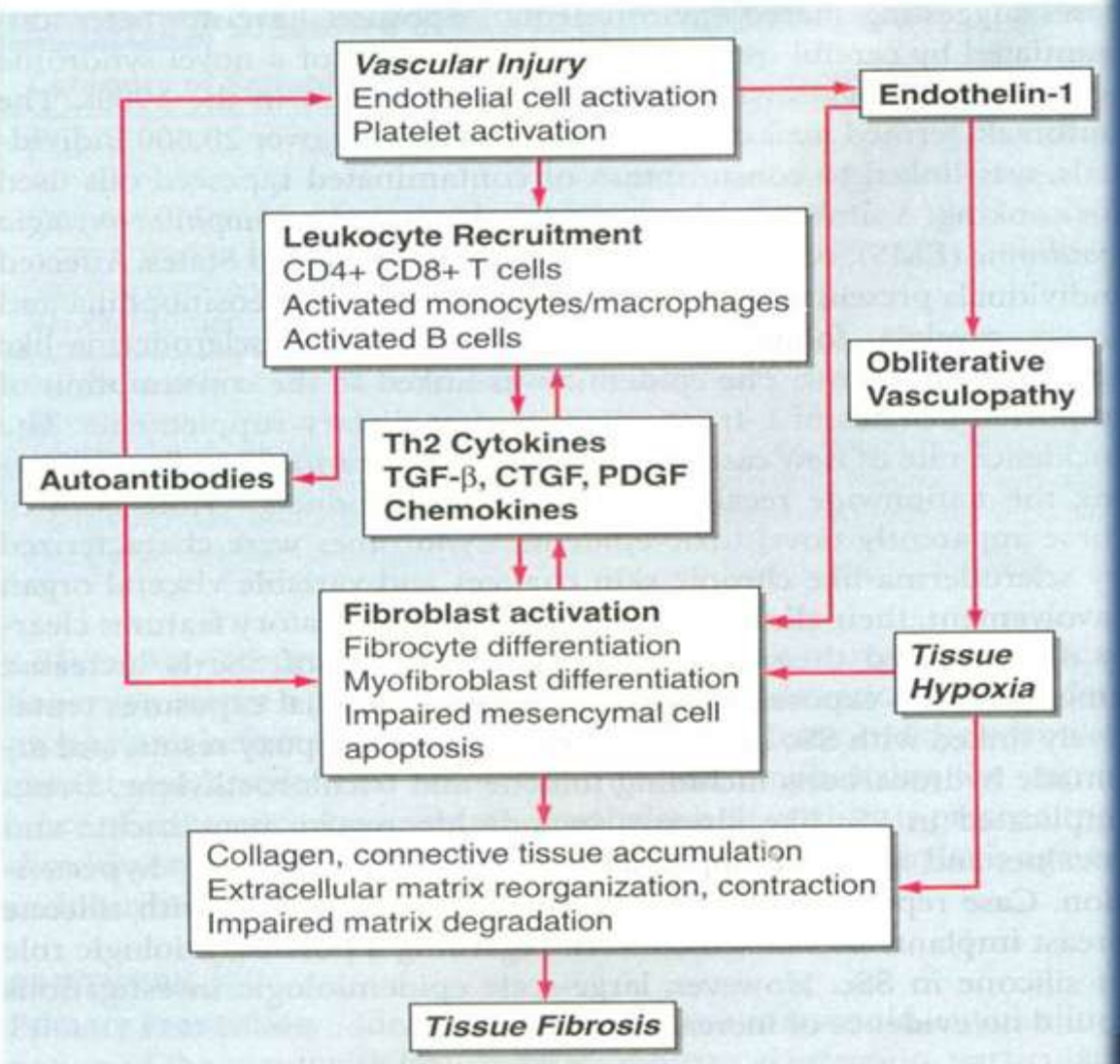


FIGURE 316-1 The pathogenesis of systemic sclerosis. Initial vascu
lar injury in genetically susceptible individuals leads to functional an
structural vascular alterations, inflammation, and autoimmunity. The
inflammatory and immune responses initiate and sustain fibroblast ac
tivation and differentiation, resulting in pathological fibrogenesis and
irreversible tissue damage.

Clinical description

- The condition may be divided into different subtypes
- **DIFFUSE CUTANEOUS SSc (DcSSc)**
- **LIMITED CUTANEOUS SSc (LcSSc)**
- **SYSTEMIC SCLEROSIS SINE SCLERODERMA**
- DcSSc – abrupt in onset,RP is common,thickening of trunk ,acral skin edema –earliest features,TFRs,Pfbirosis,renal crises.
- LcSSc – RP years before ,skin induration limited to hands,face,feet—CREST.
- SSSc ---visceral disease without skin involvement.

SUBSETS OF SYSTEMIC SCLEROSIS

TABLE 316-2 SUBSETS OF SYSTEMIC SCLEROSIS (SSC): LIMITED CUTANEOUS SSC VERSUS DIFFUSE CUTANEOUS SSC

Features	Limited Cutaneous SSc	Diffuse Cutaneous SSc
Skin involvement	Limited to fingers, distal to elbows, face; slow progression	Diffuse: fingers, extremities, face, trunk; rapid progression
Raynaud's phenomenon	Precedes skin involvement; associated with critical ischemia	Onset contemporaneous with skin involvement
Pulmonary fibrosis	May occur, moderate	Frequent, early and severe
Pulmonary arterial hypertension	Frequent, late, may be isolated	May occur, associated with pulmonary fibrosis
Scleroderma renal crisis	Very rare	Occurs in 15%; early
Calcinosis cutis	Frequent, prominent	May occur, mild
Characteristic autoantibodies	Anticentromere	Antitopoisomerase I (Scl-70)

Limited SSc/diffuseSSc

TABLE 316-3 INTERNAL ORGAN INVOLVEMENT: LIMITED CUTANEOUS AND DIFFUSE CUTANEOUS FORMS OF SYSTEMIC SCLEROSIS

Features	Limited Cutaneous SSc (%)	Diffuse Cutaneous SSc (%)
Skin involvement	90[a]	100
Raynaud's phenomenon	99	98
Esophageal involvement	90	80
Pulmonary fibrosis	35	65
Pulmonary arterial hypertension	25	15
Myopathy	11	23
Cardiac involvement	9	12
Scleroderma renal crisis	2	15

[a]10% of lcSSc patients have SSc sine scleroderma.

SYSTEMIC SCLEROSIS

clinical features-management

Dr.Praveen Nagula

Clinical features

- ***RAYNAUD'S PHENOMENON:***

✓ Episodic vasoconstriction in the fingers and toes.

✓ Tip of the nose , earlobes can also be affected.

✓ Triggers – exposure to cold,↓ temperature,stress,vibration.

✓ ↑ frequency ,severity in winter.

✓ Typical attack : PALLOR → CYANOSIS → ERYTHEMA.

Vasoconstriction → ischemia → reperfusion.

- women > men

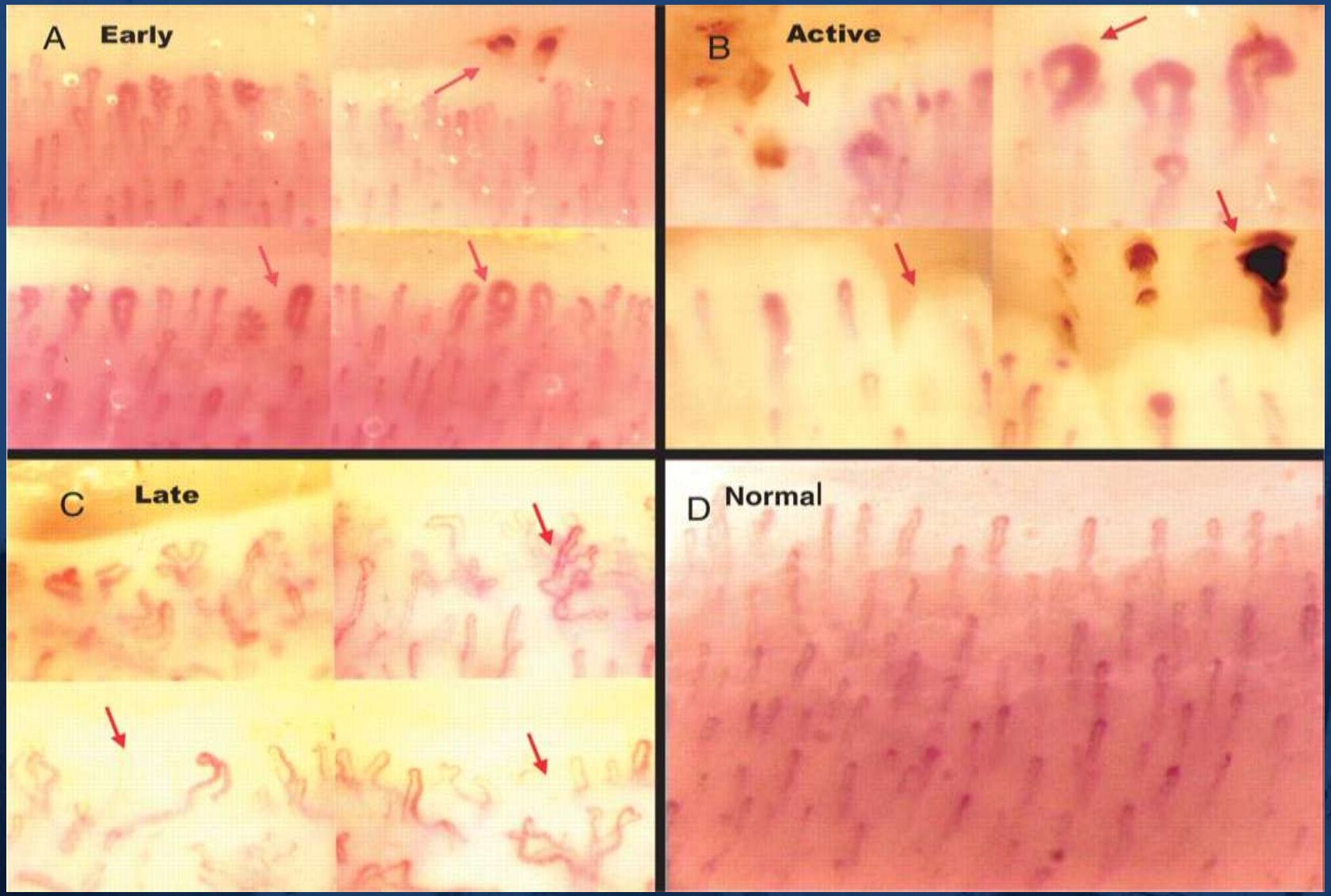
✓ PRIMARY –exaggerated physiological response to cold.

✓ SECONDARY --complication of SSc…

Raynaud's phenomenon

- Primary – no underlying causes
  - Positive family h/o
  - Absence of digital necrosis
  - No ulceration , gangrene
  - Negative ANA test
- Secondary ---- > 30 yrs
  - More severe
  - Assosciated with ischemia,infarction of digits.
- **NAIL FOLD MICROSCOPY** – normal with regularly spaced vascular loops – primary,distorted widened ,irregular loops,dilated lumen,vascular dropouts.
- ***Raynaud like abn. Activity ---pulmonary,renal ,GIT,coronary***

A, early SSc pattern; B, active SSc pattern; C, late SSc pattern and D, normal pattern (200x)



Cutolo M et al. Rheumatology 2006;45:iv43-iv46

RHEUMATOLOGY

SKIN features

- *Clinically evident skin thickening is the HALLMARK of SSc—distinguishes it from others..*
- Symmetrical ,B/L
- In diffuse type – edema replaced by skin thickening..distal to proximal – centripetal fashion.
- Skin is firm ,coarse and thickened.
- Darkly pigmented extremities and trunk.
- Diffuse tanning in the absence of exposure to sun –very early feature.
- Vitiligo like hypopigmentation –in dark skinned individuals.
- Pigment loss spares perifollicluar areas – *salt and pepper appearance* of skin –scalp ,upperback ,chest.
- Obliteration of appendages of hair.
- Loss of transverse creases on dorsum of fingers
- Fixed flexion deformity of fingers

- FACE – ***mauskopf appearance*** –
- Skin is firmly bound to subcutaneous fat – thinning and atrophy.

✓ MACULAR telangiectasia –localised scleroderma
  ✓ Resembles of HHT .face,lip,oral cavity.

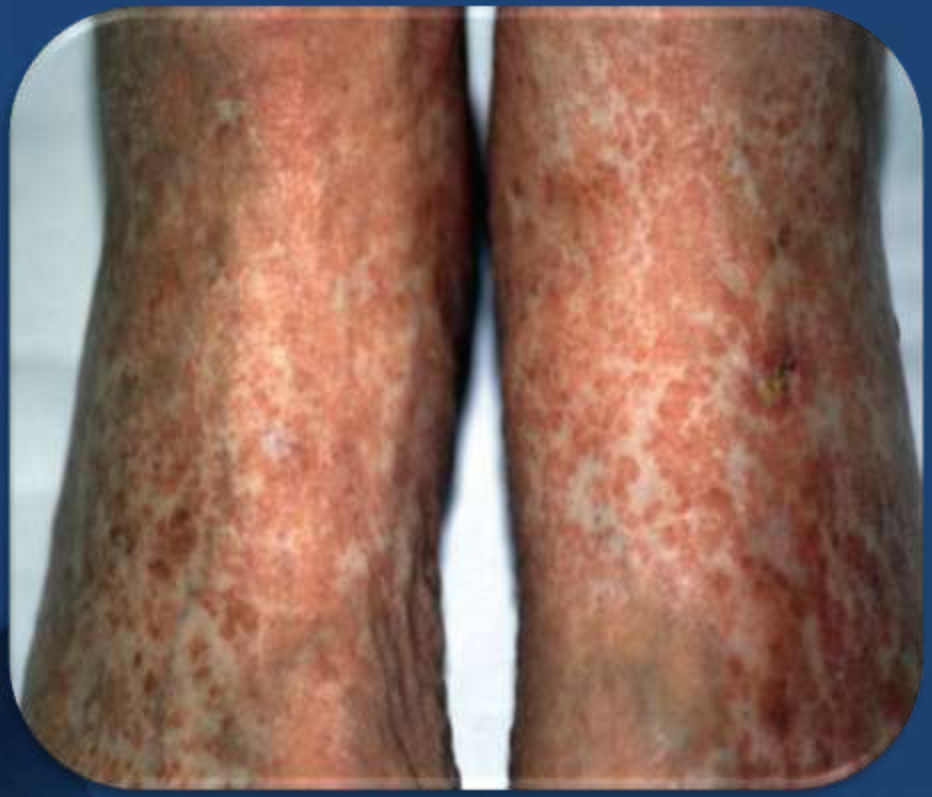
✓ ATROPHY of skin – slow healing ulceration on extensor surface of PIP joints.,volar pads.

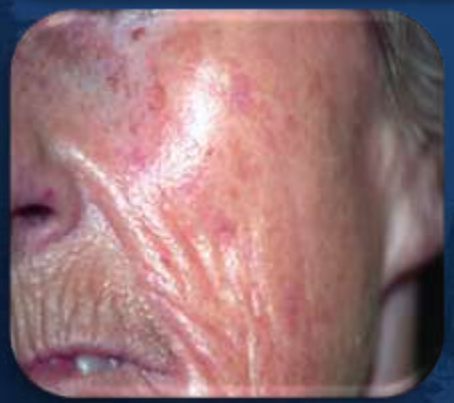
✓ DIGTIAL pits – healed ischemic ulcers.

✓ Resorption of terminal phalanges ***– acro osteolysis.***

✓ Calcium deposits in skin ,soft tissue..
CREST syndrome – calcium hydroxyapatite crystals.
  ✓ Finger pads,palms,extensor surfaces.
  ✓ Firm ,non tender subcutaneous lumps– ulcerate through skin –chalky white matter.

Salt and pepper appearance of skin





SCLERODACTYLY

HIDE BOUND SKIN

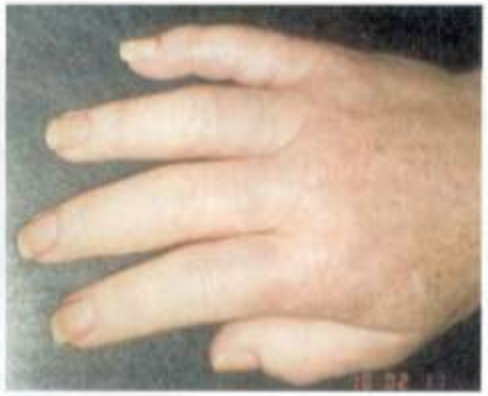
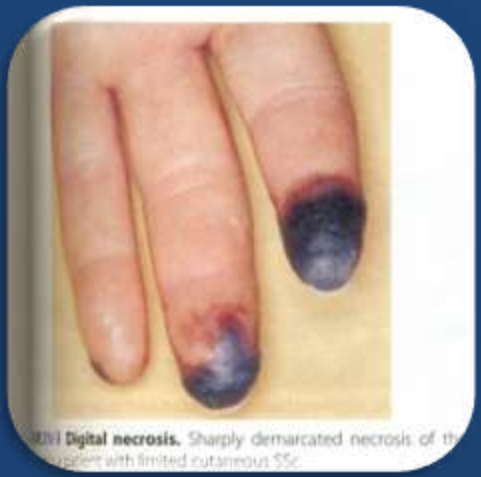
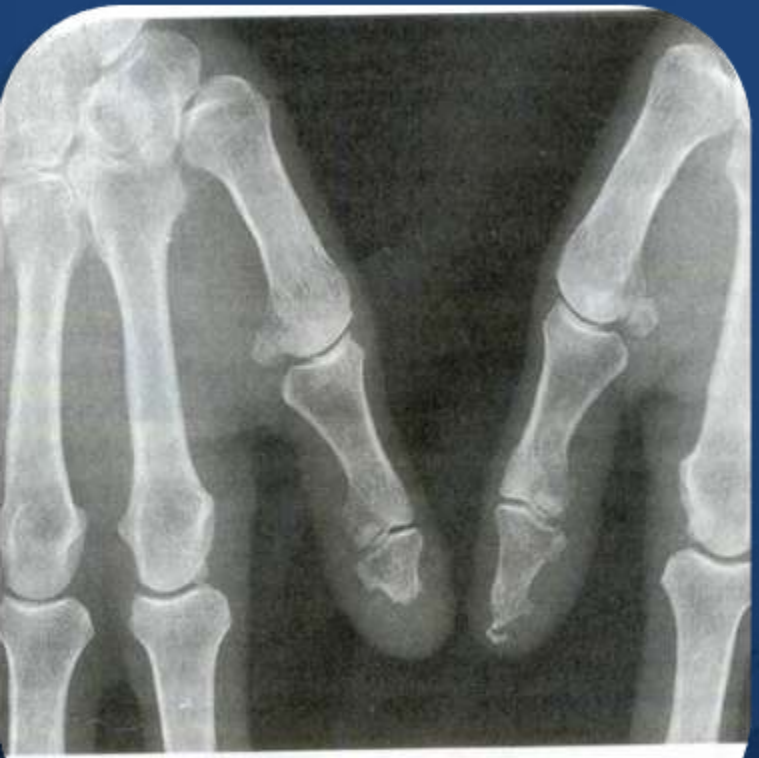


FIGURE 316-4 Sclerodactyly. Note skin induration and fixed flexion contractures at the proximal interphalangeal joints in a patient with limited cutaneous SSc.

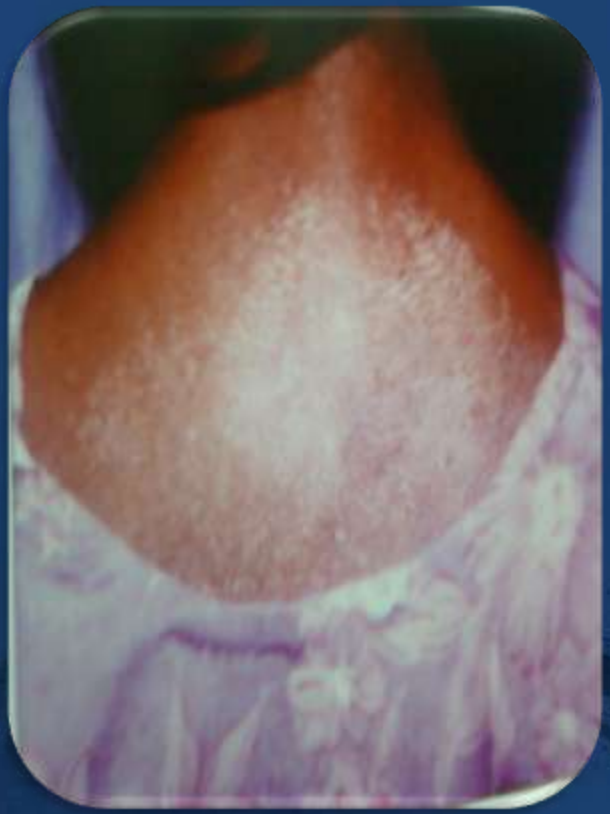


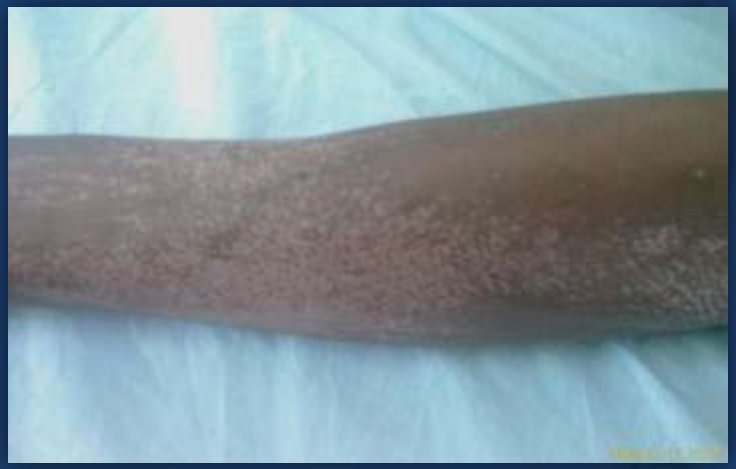
Digital necrosis. Sharply demarcated necrosis of th
patient with limited cutaneous SSc

FIGURE 316-6 Calcinosis cutis. Note large calcific deposit breal
rough the skin in a patient with limited cutaneous SSc.



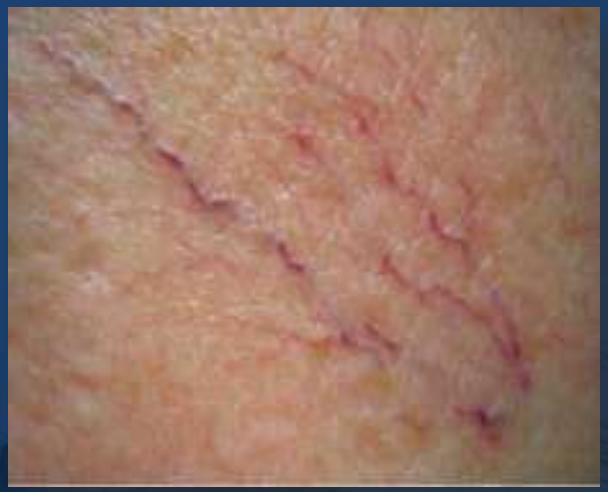
URE 316-5 Acro-osteolysis. Note dissolution of terminal phal
a patient with long-standing limited cutaneous SSc.



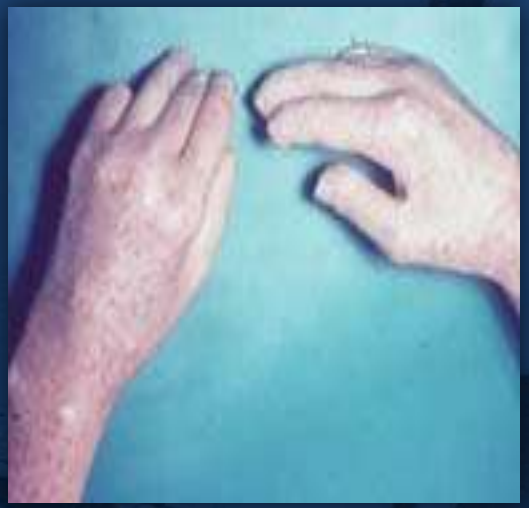


Skin features

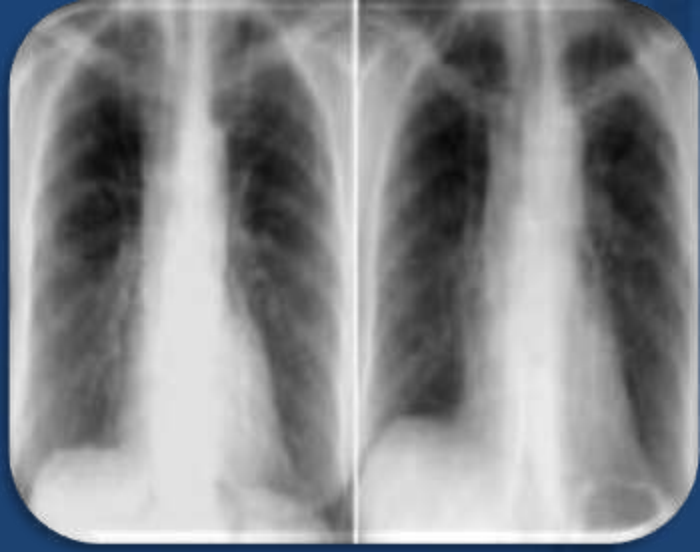
Calcinosis



telangiectsias

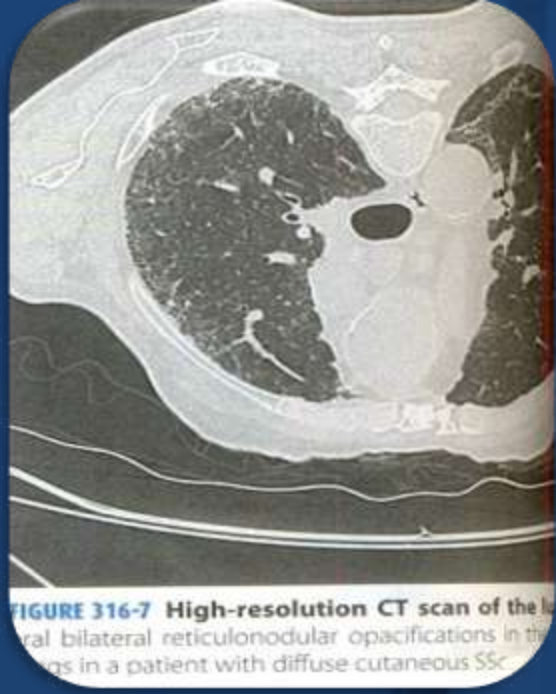


Pulmonary features



- Leading cause of death.
- ILD,PAH
- Less frequently –aspiration pneumonitis , pulmonary hemorrhage , obliterative bronchiolitis , pleural involvement , restrictive ventilatory defect due to chest wall fibrosis , spontaneous pneumothorax.
- ***↑broncho alveolar carcinoma***
- Asymptomatic until advanced.
- Most frequent symptoms of pulmonary inv. Are subtle .
- Velcro crackles at lung base.
- PFT for detection -- ↓FVC, ↓ DLCO ,,,DLCO ↓↓↓ FVC

INTERSTITIAL LUNG DISEASE



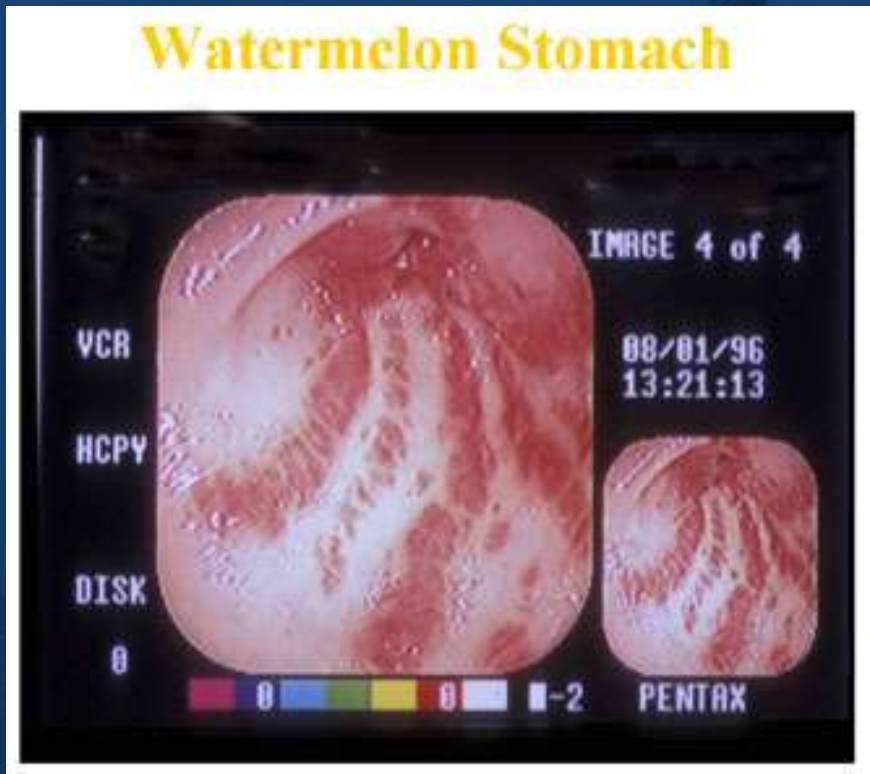
- 90% cases at autopsy.HRCT –85%cases.
- 16-43% are affected.
- NORMAL FLOW RATES.
- At risk are MALE,AFRICAN,diffuse skin inv.,severe GERD,topoisomerase I autoAb.
- Rapid progression in first 3 yrs of onset –32% ↓ /year.
- CXR,HRCT,BAL,LUNG BIOPSY.
- HRCT more sensitive,reticular linear opacities in lower lobes,mediastinal lymphadenopathy,ground glass appearance.
- Non specific interstitial pneumonitis –better prognosis.
- ***KL– 6 ,A GLYCOPROTEIN,type II pneumocytes,alveloar macrophages –earlier detection of ILD***

Pulmonary Arterial Hypertension

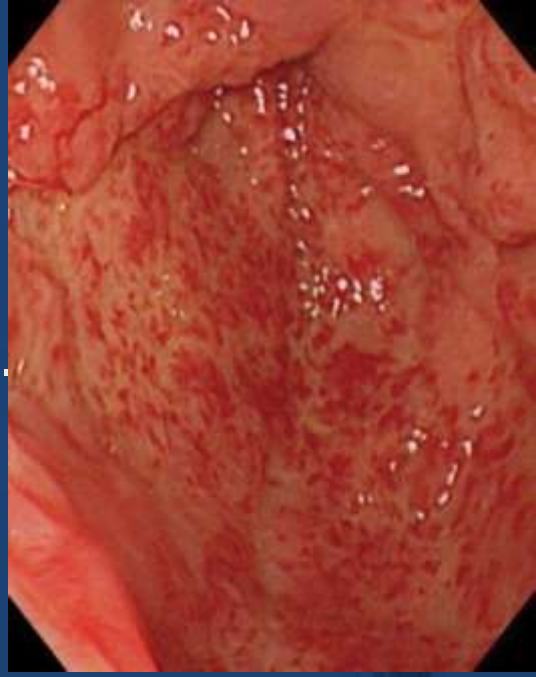
- Mean Pulmonary arterial pressure > 25 mm Hg at rest.
- 12-25% have PAH
- In assosciation with ILD/solitary.
- Usually downhill course –RHF –death.
- ***At risk are – Ls SSc with anticentromere antibodies,late age of onset,severe raynauds,U1 –RNP,U3 RNP fibrillarin,B23 Ab.***
- Asymptomatic,exertional dyspnea.
- PASP >40 mm Hg at rest in 2d echo.
- Decreased DLCO
- Right heart catheterisation accurate.
- Increased BNP,Nt BNP levels
- Prognosis $\propto$ degree of pulmonary artery pressure elevation.

GASTROINTESTINAL

- 90% Pts.
- Asymptomatic /weight loss
- Abn motility of intestines.
- Prominent atrophy ,fibrosis of smooth muscle,intact mucosa,obliterative small vessel vasculopathy – all over GIT .
- Oropharyngeal – common
  - Xerostomia
  - ↓Oral aperture
  - Periodontal disease
- GERD – early
  - ↓LES pressure
  - ↓ clearance
  - Increased emptying time.
- Gastroparesis – early satiety
  - Distention,abd pain
  - Increased reflux
  - Radionuclide studies



GIT



- GASTRIC VASCULAR ECTASIAs – seen in the antrum.
  - Subepithelial lesions
  - Diffuse small vessel vsculopathy
  - ***Watermelon appearance***
  - Recurrent GI bleed occult
- Fat ,protein malabsorption,vitamin b12
- Wide mouth sacculations in the colon occur –perforation.
- ***Pneumatosis cystoides intestinalis***
- Primary biliary cirrhosis may coexist.
- May present with acute abdominal pain recurrent –differentiate from pseudoobstruction.

RENAL

- HTN,chronic non progressive proteinuria.
- ***SCLERODERMA renal CRISIS*** –dreadful complication of SSc.
  - 20-25% pts
  - < 4 yrs of onset of diseases
  - Survival <10 % until ACEI
  - It is due to OBLITERATIVE VASCULOPATHY of renal cortical arteries.
- **↓RBF → JGA hyperplasia → renin secretion → RAAS → renal vasoconstriction →malignant HTN.**
- ↓RBF ← vasospasm,dehyration,hypotension.
- **At risk -- african american,male,diffuse skin involvement,ab to RNA polymerase III**
- Impending renal crises – palpable tendon friction rubs,pericardial effusion,new unexplained anemia,thrombocytopenia.
- Localised scleroderma –infrequent development.
- Prednisolone to be avoided.

RENAL

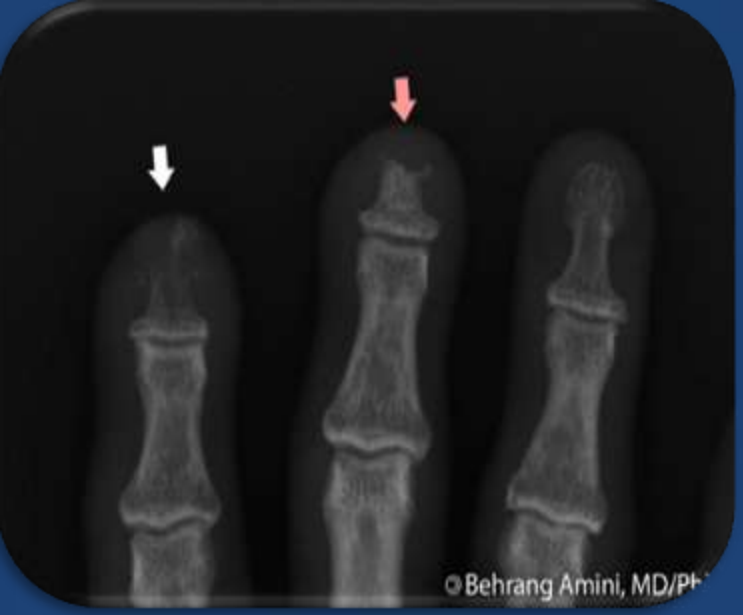
- Presentation –abrupt onset of malignant HTN, severe headache,blurred vision,chest pain.
- 10% normal BP – normotensive renal crises.
- Urinalysis -- proteinuria,microscopic hematuria,fragmented RBCs
- Rapidly progressive oliguric renal failure follows
- D.D – TTP commonly misdiagnosed.
- Creatnine > 3 mg/dl at presentation –poor prognosis.—permanent hemodialysis –high mortality,
- Prompt use of ACEI to make BP under control before renal failure occurs –imporved prognosis.

Cardiac

- Myocardial ,pericardial ,conduction abnormalities.
- Can occur secondary to renal ,pulmonary involvement.
- LVDD is frequent.
- LVDD –due to HTN ,myocardial fibrosis.
- Asymptomatic until HF ,arryhthmias occurs.
- Myocarditis in assosciation with inflammatroy polymyositis.
- Conduction defects due to fibrosis of conduction system.
- Pericardial effusion –symptoms– rarely tamponade.

Musculoskeletal

- CARPAL TUNNEL SYNDROME –may be a presenting feature.
- Early disease –generalised arthralgia,stiffness.
- Joint mobility affected in diffuse disease.
- HANDS –PIP joints,wrists.
- Tendon friction rubs are present.—extensive fibrosis,adhesion of tendon sheaths.
- True joint inflammation is reduced.
- Muscle weakness due to disuse,malnutrition.
- Chronic noninflammatroy myopathy is usually seen.
- Bone resorption –a freq late complication –terminal phalanges –loss of distal tufts –ACRO OSTEOLYSIS.
  - Mandible affected—biting difficulty
  - Ribs,distal clavicle



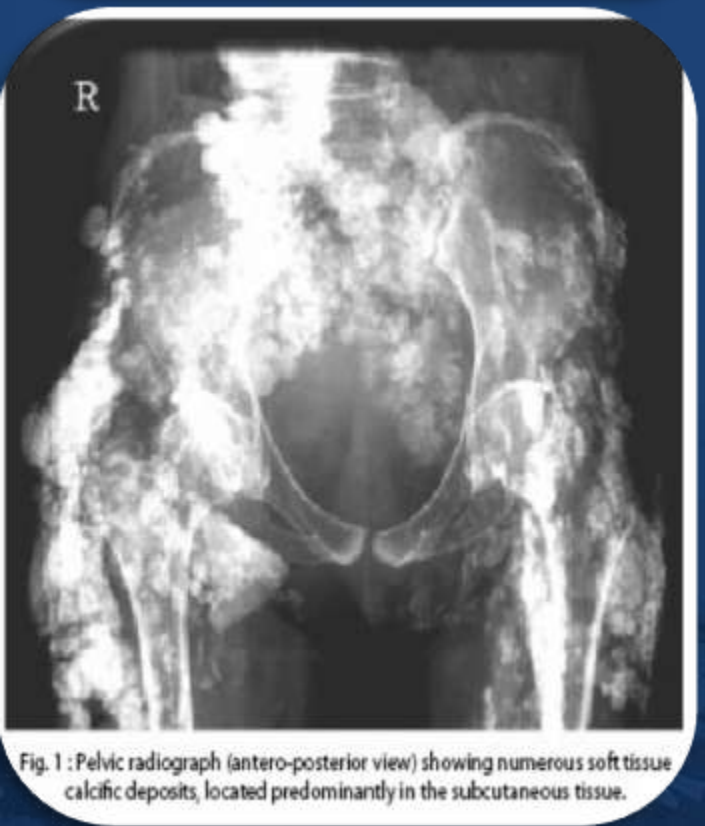
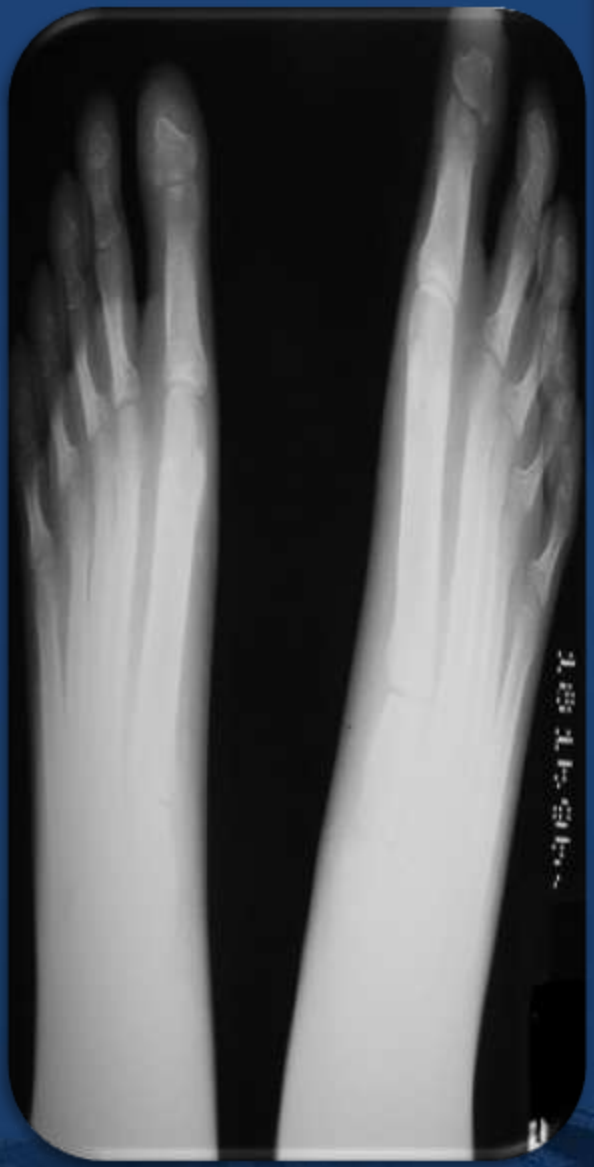
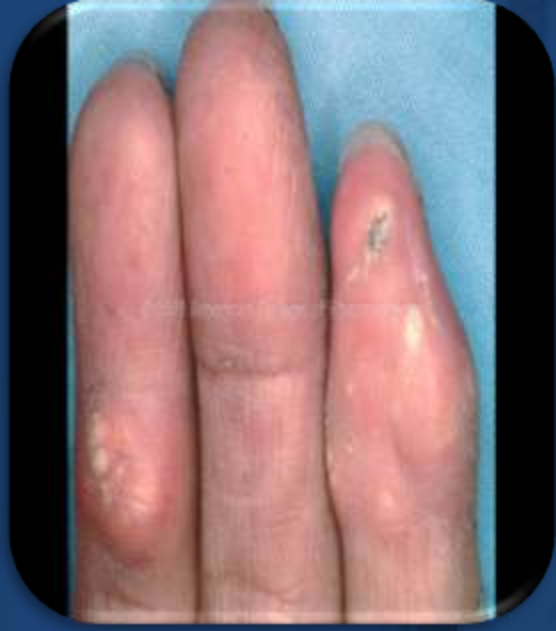
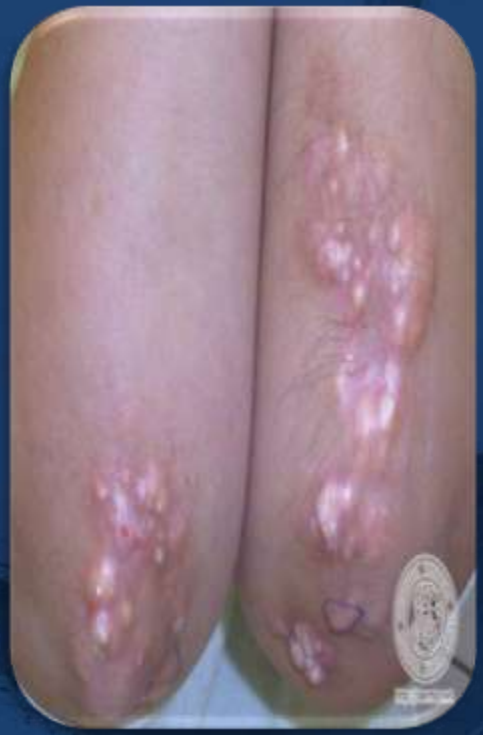


Fig. 1 : Pelvic radiograph (antero-posterior view) showing numerous soft tissue calcific deposits, located predominantly in the subcutaneous tissue.







Other disease manifestations

- Dry eyes,dry mouth –SICCA complex.
- Biopsy of the minor salivaryglands –fibrosis rather than lymphocytic infitration.(sjogren's syndrome)
- Hypothyroidism –fibrosis of gland.
- ***CNS is generally spared . Sensory trigeminal neuropathy due to fibrosis /vasculopathy can occur.***
- Pregnancy -adverse outcomes
- Cardiopulmonary complications,new onset renal crises can occur.
- Erectile dysfunction in the male.

Laboratory features

- Anemia – frequent
  - Most common is mild normocytic /microcytic anemia –chronic inflammation
  - Serum iron is low or normal,ferritin is elevated.
  - Iron deficiency anemia –occult GI bleed (WATERMELON STOMACH),chronic esophagitis.
  - Macrocytic anemia – vitmainb12,folate,bacterial overgrowth,drugs
  - Acute microangiopathic anemia –mechanical trauma—renal crises
- Thrombocytopenia ,leukopenia –DRUG toxicity.
- ESR is normal
- Increased ESR –MYOSITIS ./MALIGNANCY

ANTINUCLEAR ANTIBODIES

- ✓ All patients of SSc
- ✓ Highly specific are anti topoisomerase –I (Scl 70) and anti centromere Ab
- ✓ Specific ab profile remains stable over time.
- ✓ Topoisomerase I ab 31% of dcSSc ,13% of lcSSc
- ✓ Anticentromere ab in 38% of lcSSc,2% of dcSSc.
- ✓ U3RNP fibrillarin –characteristic nucleolar fluoroscence pattern,Th/To,PM/Scl .
- ✓ No direct pathogenic role has been established for SSc associated autoantibodies..
- ✓ Antibody titers correlate with disease severity .

Auto antibodies in SSc

TABLE 316-4 AUTOANTIBODIES IN SYSTEMIC SCLEROSIS (SSC)

Target Antigen	SSc Subset	Characteristic Clinical Association
Topoisomerase-I	dcSSc	ILD, cardiac involvement, scleroderma renal crisis
Centromere proteins	lcSSc	Digital ischemia, calcinosis, isolated PAH
U3-RNP	dcSSc	PAH, ILD, scleroderma renal crisis, myositis
Th/T0	lcSSc	ILD, PAH
PM/Scl	lcSSc	Calcinosis, myositis
U1-RNP	MCTD	PAH
RNA polymerase III	dcSSc	Extensive skin, scleroderma renal crisis

Note: dcSSc, diffuse cutaneous SSc; lcSSc, limited cutaneous SSc; ILD, interstitial lung disease; PAH, pulmonary arterial hypertension.

S.NO	ANTI TOPOISOMERASE AB	ANTI CENTROMERE AB
1.	Dc SSc patients,early ILD	lcSSc with PAH
2.	Cardiac and renal involvement is common	Rare. ILD is also not seen.
3.	Reduced survival	Improved survival
4.	31% of dcSSc	38% of lc SSc
5.	13% of LcSSc	2% of Dc SSc

Diagnosis

- ✓ Diagnosis on clinical grounds.
- ✓ Presence of skin induration with a characteristic symmetrical distibution pattern,typical visceral organ manifestation-establishes the diagnosis with high certainity.
- ✓ Full thickness biopsy – required for diagnosis of scleredema,scleromyoxedema,nephrogenic systemic fibrosis.
- ✓ lcSSC– CREST for diagnosis
- ✓ Nail fold microscopy for differentiation from primary raynaud's
- ✓ Diffuse edema of fingers..
- ✓ SSc sine scleroderma– anticentromere ab

Differential diagnosis

Localized scleroderma
- Guttate morphea, diffuse morphea
- Linear scleroderma, coup de sabre, hemifacial atrophy

Overlap syndromes
- Mixed connective tissue disease
- SSc/polymyositis

Undifferentiated connective tissue disease

Scleredema and diabetic scleredema

Scleromyxedema (papular mucinosis)

Nephrogenic fibrosing syndrome (nephrogenic fibrosing dermatopathy)

Chronic graft-versus-host disease

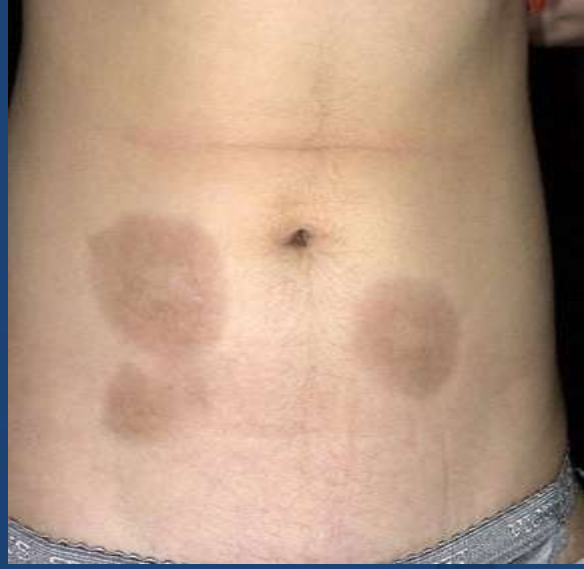
Diffuse fasciitis with eosinophilia (Shulman disease, eosinophilic fasciitis)

Eosinophilia-myalgia syndrome

Chemically induced scleroderma-like conditions
- Vinyl chloride–induced disease
- Pentazocine-induced skin fibrosis

Paraneoplastic syndrome

Differential diagnosis



- **Based on vascular changes:**
- ✓ 1.PRIMARY raynaud's phenomenon
- ✓ 2.physical trauma –jack hammer
- ✓ 3.chemical exposure
- ✓ 4.drugs toxins – toxic oil syndrome,ergotamine,Bblockers ,carbidopa,5HT .
- ✓ 5.SLE,DM/PM,RA.,cryoglobulinemia.
- **Based on skin changes**
- ✓ 1.localized scleroderma
- ✓ 2.scleroderma like skin changes
- ✓ 3.metabolic –genetic disorders –scleredema/scleromyxedema
- **Based on visceral involvement**
- ✓ 1.idiopathic pulmonary HTN
- ✓ 2.idiopathic pulmonary fibrosis
- ✓ 3.sarcoidosis
- ✓ 4.amyloidosis

Treatment

- ✓ No therapy has been shown significantly to alter the natural h/o SSc till date.
- ✓ Multiple interventions are avialable in alleviating the symptoms –slowing progression of organ damage.
- ✓ Treatment approaches to be individually tailored.
- ✓ Optimal management – prompt,accurate diagnosis,classification,risk stratify,early recogntion of organ based complicatyions,regular monitoring of progression,disease activity,response to treatment,[patient education.
- ✓ Holistic approach is needed.
- ✓ Combination of drugs are used.
- ✓ Physician –patient relationship to be mainatined.

Disease modifying treatments

- Immunosuppressive agents –modest or no benefit in Rx of SSc.
- **Glucocorticoids -** ↓ stiffness and aching in pts with early stage disease.
  - Do not influence the progression of skin/internal organ involvement.
  - ↑risk of scleroderma renal crises at high doses.
  - Avoid if possible.
  - Low dose ,brief periods.
- **Cyclophosphamide** –daily oral/IV in SSc related ILD.
  - Reduces the progression of ILD ,stabilises,improvement in skin induration.
  - Early stage SSc/extensive pulmonary involvement –candidate
  - Rx for 6- 12 months ,optimal duration not known.
  - Benefits <> toxicities
  - Bonemarrow suppression,opp infections,hemorhhagic cystitis,bladder Ca.

Disease modifying treatments

- **Methotrexate** – modest therapeutic benefit
  - Potential profibrotic effects --? Use in fibrotic phase
- **Mycophenolate mofetil** – improvement in skin induration
  - Well tolerated
- **Immunomodulation** – cyclosporine,azathioprine,extraxorporeal photopheresis,thalidomide,rapamycin.
- **Immune ablation** with high dose chemotherapy followed by autologous peripheral stem cell reconstitution
- **Stem cell transplantation** –experimental.

Drugs that interfere with fibrotic process

- **D penicillamine** – antifibrotic agent
  - Immunosuppressive activity
  - Prevents cross linkage of collagen fibres.
  - Stabilises,improves skin induration
  - Prevents new organ involvement
  - Improved survival
  - No effect in early active SSc
  - 750 mg/d
- **Minocycline**
- **Recombinant relaxin**
- **IFN γ**

Vascular therapy

- Dress warmly
- Minimize cold exposure.,Avoid drugs
- Biofeedback therapy.
- CCBs –diltiazem,nifedipine –ADVERSE effects
- **ACEI –not effective**
- ARBs –losartan well tolerated.
- α1 blocker –prazosin
- Sildenafil ,Fluoxetine ,Topical NTG, IV PROSTAGLANDINS.
- Empiric treatment with statins,antioxidants
- Low dose asprin,dipyridamole –useful
- Digital sympathetectomy in severe cases
- Bosentan prevents new ulcers

Rx of GI complications

- Elevate head end of the bed.
- Eat frequent small meals
- PPIs ,H2B at higher doses are effective.
- ***Laser photocoagulation –recurrent bleeding from watermelon stomach***
- Metronidazole,erythromycin,tetracycline –bacterial overgrowth.
- Parenteral nutrition in case of severe disease.
- Hypomotility of the gut –octreotide.

Rx of PAH

- **SCREEN ON REGULAR BASIS.**
- Symptomatic –oral endothelin receptor antagonist
- Diuretics
- Oral anticoagulants
- Digoxin
- Bosentan –increases exercise tolerance,decreases PAH progression.
- 0 2 –nasal cannula
- Sildenafil –short term benefit
- Parenteral prostaglandin analogues –epoprostenol,teprostinil IV/sc infusion.
- Iloprost –inhalation
- Lung transplantation

Rx of Renal Crises

- Medical emergency
- Outcome determined by amount of renal damage
- **Avoid NSAIDs,glucocorticoids**
- Rx –ACEI ,short term dialysis.
- Kidney transplantation.

Skin care

- 5 mg prednisone
- D penicillamine
- Cyclophosphamide
- Regular skin massage
- Telangiectasia –laser pulse dyed laser
- Finger tip ulcerations –occlusive dressings
- Infected ulcers –topical Abs
- Surgical debridement
- No therapy effectvie in preventing the formation of calcific deposits.

Course,Prognosis

- ***DcSSc has more progressive disease than lcSSc.***
- Early inflamatory changes subside in 2-4 yrs..organ involvement occurs here.
- New organ involvement is rare after skin involvement reaches peak.
- Skin regression occurs in the order of occurrence
- Sclerodactyly ;contractures persist.
- lcSSc better prognosis.
- dcSSc –5 ,10 YR SURVIVAL RATES –70%,55%
- lcSSc – 90% ,75%

Poor prognosis

- Male gender
- young age of onset
- African american race
- Extensive skin thickening
- Truncal involvement
- Visceral organ involvement
- Topoisomerase I ab
- Increased ESR ,anemia ,proteinuria on initial presentation –high mortality…

future

- IMATINIB mesylate

- **Scope for research**

✓ Unresolved questions

✓ Etiology

✓ Pathogenesis

✓ Therapuetic potential of various regimens

Trials

141 TRIALS

- Sleep Disturbances and Pulmonary Artery/Aorta Diameter in Scleroderma Patient
- High Dose Cyclophosphamide for Treatment of Scleroderma
- Digital Ischemic Lesions in Scleroderma Treated With Oral Treprostinil Diethanolamine (DISTOL-1)
- Pulmonary Involvement in Scleroderma: A Clinical Study of the Safety and Efficacy of Mycophenolate Mofetil in Scleroderma Patients With Lung Involvement
- Sildenafil Effect on Digital Ulcer Healing in sClerodErma SEDUCE STUDY
- Effect of Bosentan in Scleroderma Renal Crisis (ScS-REINBO)
- Efficacy and Safety of Imatinib in Scleroderma (SCLEROGLIVEC)
- Comparison of Therapeutic Regimens for Scleroderma Interstitial Lung Disease (The Scleroderma Lung Study II) (SLSII)

Take home message

- ✓ SSc is a chronic systemic disorder.
- ✓ RULE out other causes.
- ✓ Anti topoisomerase –dcSSc,anti centromere ab -LcSSc
- ✓ After diagnosis risk stratify the patient.
- ✓ Regular follow up and monitoring.
- ✓ Patient education is needed.
- ✓ Treatment is individualised.
- ✓ Renal crises is an emergency.
- ✓ ACEI are to be started in a pt with HTN.
- ✓ No treatment for calcinosis cutis
- ✓ Imatinib in near future….
- ✓ Scope for research ..

References

- HARRISON'S principles of internal medicine ,17 th Ed
- www.medscape.com
- www.clinicaltrials.gov
- www.scleroderma.org
- www.dermatologylib.com
- www.ncbl.nbi.com
- www.google.com
- www.dailyquotes.com
- www.orpha.net

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