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A Case Report on Scleroderma: A Diagnostic Dilema

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Scleroderma is a rare heterogenous group of autoimmune fibrosing disorder that mainly exists in two forms; localized scleroderma (LS) and systemic sclerosis (SSc). It involves thickening of the skin at fingers region extending from proximal to metacarpophalangeal joints. The diagnostic criteria of scleroderma include past history of patient, symptoms of patient, serology, and skin biopsy. The morbidity and mortality are much worse for SSc with the patients are at risk for life threatening lung, heart and other visceral organ fibrosis and vasculopathy. There is no drug that can cure or stop scleroderma over fibrosis, but certain drugs regulate the symptoms associated with it and boost the patient's quality of life, particularly steroidal creams that help alleviate swelling, joint pain, loosen tight skin; blood pressure drugs that dilate blood vessels; immunosuppressive agents. If the disease is severe amputation is necessary.

Keywords: Localized scleroderma; systemic sclerosis; vasculopathy; morbidity; mortality; over fibrosis; amputation.

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1. INTRODUCTION

Scleroderma is an autoimmune, rheumatic, chronic disease that affects tissues by changing the connective tissue. It is a long-term illness that affects the skin, connective tissue and vital organs, forcing the skin and other body tissues to harden [1]. There are several types of scleroderma that can vary in severity [1].localized scleroderma mainly affects skin. It happens in two forms morphea (oval shaped patches) and linear (lines or streaks)[2]; systemic scleroderma involves all body parts. It is of two forms firstly limited scleroderma effects mainly face, hand, feet. The five common signs are calcinosis (ca^{+} salts forms nodules under skin), Raynaud's phenomenon, esophageal dysfunction, sclerodactyly (skin becomes thin and shin), telangiectasia (small blood) vessels grows near to skin) finally diffuse scleroderma (occurs at middle parts of body i.e.; thighs, upper arms, hands, feet's and becomes thick [2].

The causes of scleroderma are due to family history, genes, triggers like medications, viruses, or chemicals[3]. Symptoms of scleroderma include ulcers or sores on fingertips, small red spots on face and chest, firm oval shaped patches on skin, painful or swollen joints, muscle weakness, dry eyes, SOB, heart burn, diarrhea, Raynaud's phenomenon and weight loss[4]. Complications of scleroderma includes digital infractions, pulmonary hypertension, myositis, renal failure, wound infections [5]. The might order tests including –imaging tests such as X-ray and CT-scans, blood tests, GIT tests, LFT's, heart tests such as ECG and echo [6]. There is no standard treatment for scleroderma only symptomatic treatment is available includes –NSAIDs (aspirin, Ibuprofen) and STEROIDS (hydrocortisones) for skin changes. BP medications that dilate blood vessels to prevent kidney and lung problems. Antibiotics creams to prevent infections of finger tips. Finally pain killers may or may not be used as they don't show much effect in relieving pain [7]. Non-pharmacological treatments include –exercise, physical therapy, stress management, organ transplantation, more fiber and fluids in diet, skin treatment includes laser and PUVA therapy. Finally, surgical options for scleroderma complications are Amputations and lung transplantation [8].

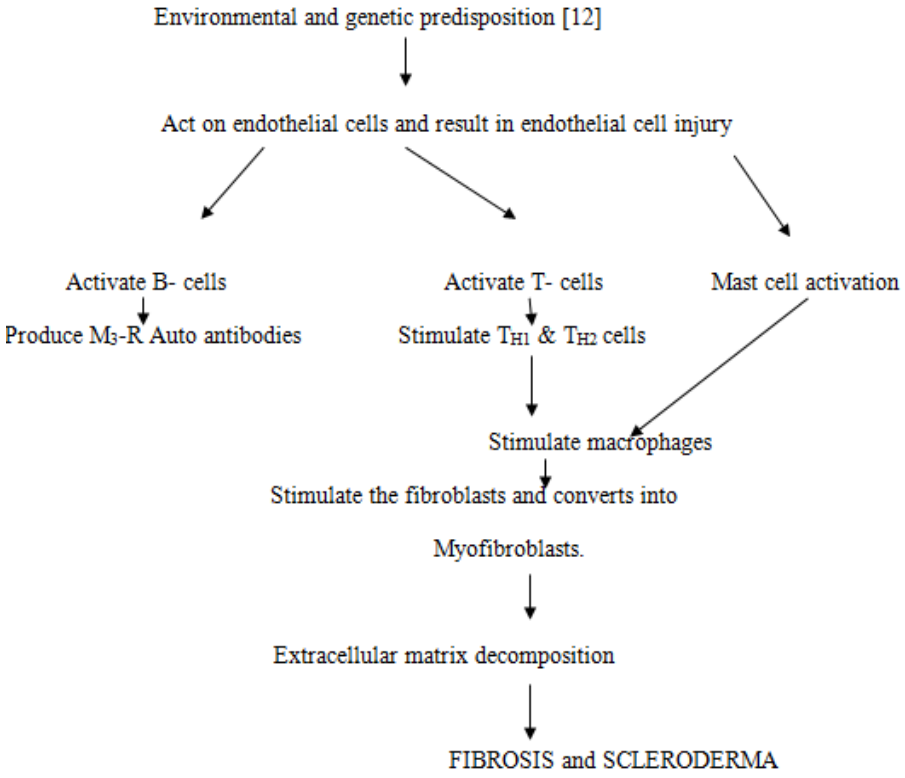

Fig. 1. Pathogenesis of scleroderma

2. CASE REPORT

A male patient of age 34 years and weight about 65kgs with chief complaints of arthralgia, digital pitting, sleep disturbances, paresthesia, Raynaud's, calcinosis, vitals pulse rate and temperature was found to be normal, BP-128/96 mm of hg,and systemic examination was fond to be normal based on signs and symptoms and lab data the patient is diagnosed as sarcoderma and recommended the following medications Tab. HCQ-OD Tab. Nifedipine- 5mg, Tab. Ultracet-SOS, Tab. Doxycyclin, Tab. Trental-400mg OD, Tab. Xyzal, Clonate ointment, Tab. Minoz , Inj.Amikacin-500mg, Tab. Metrogyl –TID , protein K powder. After 2 months the patient visited another hospital and suggested the following medications based on past history and lab data Tab. Mycophenolate mofetil-500mg BID, Tab.Losartan-25mg OD, Tab.Naproxen-500mg SOS, Tab.Amitel-10mg HS and advised to visit the hospital again. On next visit patient had same symptoms along with increase disturbance in the sleep, compliance on treatment, able to do daily activities, and advised to continue the same medication chart. On next visit the patient is associated with same symptoms which are present at the first and additionally reduced weight, vasculitis ulcer on right toe , the symptoms didn't control because patient had missed the administration of last dose of medication and advised to administer the following medications, Tab.Ecospirin-75mg OD, Tab. Naproxen -500mg SOS, Tab.Amitel-10mg HS, Tab. Mycophenolate mofetil-500mg BID, Tab. Nicardia-10mg BID, Inj. Endoxan -500mg NS 1hr.The patient again visited the another hospital the symptoms had worsen includes thickness of skin, digital pits, occasional episodes of digital gangrene, acid peptic disease, non-healing ulcer over left lateral malleolus since 10 months and severe increase in symptoms every winter season and on mycophenolate mofetil since January 2019. No history of diabetes, hypothyroidism, epilepsy and suggested with the following medications Tab.Nicardia-10mg TID, Tab. Sildenafil-25mg BID, Tab. Ecosprin-75mg OD, megaheal spray BID, Tab.Naproxen-500mg OD, Tab.Calten-D-500mg BID, in this medication chart the physician splitted the mycophenolate mofetil. On subsequent visit to hospital patient had mild pain in right ankle, rash which is healing slowly and weight gained and suggested with medication used before and added with few other include Tab.wysolone-7.5mg OD, Tab.Pan-40mg OD, Tab.pregabalin-M-75mg HS, Neosporn powder L/A.

3. DISCUSSION

The word scleroderma originated from Greek word 'scleros' which means hard and 'derma' which means skin [9]. Scleroderma is an autoimmune disease in which the autoantibodies produced will be targeting blood vessels and connective tissues[10].

3.1 Cancer and Scleroderma

Genetic alterations in the gene coding RNA polymerase III (POLR3A) have evidence of mutation specific T cell and produce immune responses with generation of POLR3A autoantibodies and elevate risk of cancer. Cancer therapies also trigger severe fibrosis which is hallmark in scleroderma, by this we can determine both the diseases are associated with each other. patients with scleroderma ,an syndrome of primary bilary cirrhosis(prone to liver metastasis) is observed, at the same time cyclophosphamide used to treat scleroderma ,high doses raises risk of bladdr and hematologic malignancies and cancer chemotherapy drugs also contribute to severe raynauds phenomena, ischemia and skin fibrosis[10]. The investigations includes physical examination include lymph node, skin, thyriod examination, colonoscopy, sigmoidoscopy, testicular examination, pap smear, anti-RNA antibodies test, family history of cancer or autoimmune disorders.

3.2 Pathogenesis of scleroderma

Scleroderma occurs in three distinct processes; Innate and adaptive immune system abnormalities leading to production of auto-antibodies and cell mediated autoimmunity, Microvascular endothelial cells and fibroproliferative vasculopathy of small vessels, Fibroblast dysfunction leading to excessive collagen and other matrix components in skin, blood vessels, and internal organs [10].

CAUSES: The etiology in this patient is idiopathic. Generally, the causes or etiology of scleroderma is exactly not known, but may be due to genetic predisposition and environmental triggers [11]. Commonly genetic predisposition of HLA genes [11]. Variations in JRF5 and STAT4 gene increases risk of scleroderma [12].

Table 1. Lab Investigations

Test	2016	2017	2018	2019	2020
Hb	13.4g/dl	13.4g/dl	13.4g/dl	13.4g/dl	13.4g/dl
TLC	5.5	5.5	4.6	4.8	5.0
PTC	-	257	230	-	-
ESR	-	45	45	-	35 increase
SGPT	35IU/L	38IU/L	26IU/L	26IU/L	26IU/L
SGOT	21IU/L	20IU/L	31IU/L	31IU/L	31IU/L
Sr. creatinine	0.6mg/dl	-	-	-	-
CRP	-	-	-	-	1.3

Modified rodnon skin score – 17/51; normal is 0/51; Serology –antinuclear antibodies was found, i.e. 0.80 presence of greater than 0.80 indicate SLE

Table 2. Serological similarities / differences of scleroderma patients in various regions across India[13]

	The western part of India	The northern part of India	The southern part of India
Disease onset			
dc*	40.9%	94%	
LcSSc*	29.1%	6%	-
Cutaneous			
Skin thickening	98.2%	-	-
Raynaud's phenomenon	68.2%	92.9%	17.3%
Gangrene	20.9%	-	-
Interstitial lung disease	88.2%	-	-
Pulmonary hypertension	61.2%	-	-
Renal	10.9%	3.4%	10.3%
Muskoskeletal	39.1%	36.7%	66.7%
Gastrointestinal	7.3%	-	-
Cardiovascular	13.6%	-	-
ANA*	85.5%	89.1%	-
Anti-Scl70	62.7%	55.5%	-
Anti-centromere	22.7%	-	-

**dc-diffuse cutaneous systemic scleroderma, LcSSc-limited cutaneous systemic scleroderma, ANA – antinuclear antibodies 1:80,thus >1:160 indicates the condition SLE. So here ANA presence doesn't indicate the presence of SLE. There are no published reports from eastern part of the country*

3.3 Treatment Options

The most important thing to remember is there is no curative therapy for scleroderma because as it is an auto immune disease, but the therapy to control the disease status is recommended. The treatment includes dihydropyridine type calcium channel blockers (CCB'S) as first line therapy, if there is no benefit use after CCB'S then a second vasodilators (topical nitroglycerin, Phosphodiesterase inhibitors) are given[14]. Patient with recurrent digital ulcers then endothelial receptor antagonist/inhibitor of 3-hydroxy – 3 – methyl glutaryl-coenzyme A reductase are started[14]. To treat skin effects associated with scleroderma there is no agent has proven effective but immunosuppressive agents (methotrexate, mycophenolate mofetil) were used, still there is a progression of the skin symptoms[14]. If there is a progressive skin disease and associated internal organ disease then immunoblotting therapy with haemopoietic stem cell transplant and solid organ transplantation(lung, kidney,cardiac etc..,) is recommended[14]. The scleroderma may affect muskoskeletal system, lungs, pulmonary vascular disease, scleroderma renal crisis, heart is also affected, based on the organ affected the treatment is given [15].

4. CONCLUSION

From this case study we conclude that In initial therapy immunosuppressants like Tab. prendnisolone and other drugs Tab. HCQ-OD Tab. Nifedipine- 5mg, Tab. Ultracet-SOS, Tab.Doxycyclin, Tab. Trental-400mg OD, Tab. Xyzal, Clonate ointment, Tab. Minoz, Inj.Amikacin-500mg, Tab. Metrogyl –TID, protein K powder are given without any appropriate diagnosis. But, in this condition due to corti-costeroids (prednisolone) caused RAYNAUD'S Syndrome caused serious symptoms during winter season that leads to punctures from tips of

fingers and toes**.** But after change in the regimen with Tab. Naproxen -500mg SOS, Tab.Amitel-10mg HS, Tab. Mycophenolate mofetil-500mg BID, Tab. Nicardia-10mg BID, Inj. Endoxan -500mg Symptoms are controlled. This shows that no selective targeted therapy for this threaten condition only symptomatic therapy and immunosuppressants such as MMF (mycophenolate mofetil) is available but this treatment also doesn't show any improvement in patient disease status instead it only controls the symptoms. So appropriate diagnosis established drug regimen has to be carried out to treat this scleroderma condition. Multidisciplinary approach is utmost important for right diagnosis. Research on Targeted drug delivery treatment in treating this scleroderma condition should be carried out. This case is a Diagnostic dilemma for the clinical practitioners for designing of proper drug regimen. Hopefully this case report may boost the researchers towards targeted drug development therapy for autoimmune disorders like scleroderma.

CONSENT AND ETHICAL APPROVAL

As per international standard or university standard guideline patients consent and ethical approval has been collected and preserved by the authors.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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