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Cognizance, Pharmaceutical Care Manaeuvre and Clinical Pearls of Diffuse Systemic Sclerosis, A Strew of Multiple Systems Fraternization: A Rare Case Report

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ABSTRACT

Systemic sclerosis is an acquired sporadic disease affecting all races worldwide. In the United States, the incidence is estimated at 9 to 19 cases per million per year. Systemic sclerosis is an uncommon connective tissue disorder characterized by chronic progressive multisystem involvement. The most frequent extra cutaneous complications of systemic sclerosis are characterized by episodes of reversible vasoconstriction in the fingers and toes known as Raynaud's phenomenon and is classified as Primary Raynaud's phenomenon & Secondary Raynaud's phenomenon. Iodine deficiency remains a common cause of hypothyroidism worldwide. Neonatal hypothyroidism is due to thyroid gland dysgenesis in 80–85%, to inborn errors of thyroid hormone synthesis in 10–15%, and is TSH-R antibody-mediated in 5% of affected newborns. Primary Hypothyroidism is confirmed in clinical settings by finding elevated TSH and a low free T4 level. Secondary hypothyroidism, as a result of pituitary dysfunction, results in decreased of both T4 and TSH levels. Tertiary hypothyroidism results from decreased production of TRH by Hypothalamus. ILDs are nonmalignant disorders and are not caused by infectious agents. Clinical evidence of ILD is present in one-half of patients with Progressive systemic sclerosis and pathologic evidence in three-quarters of patients.

Keywords: Systemic sclerosis, Raynaud's phenomenon, Hashimoto's thyroiditis, Tyrosine kinase inhibitors, Nail-fold microscopy, Mycophenolate mofetil.

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SYSTEMIC SCLEROSIS

Definition

Systemic sclerosis is an uncommon connective tissue disorder characterized by chronic progressive multisystem involvement, presence of heterogeneous clinical manifestations, significant disability and mortality. Multiple genes contribute to disease susceptibility. Thickened skin is the distinguishing hallmark of systemic sclerosis. It is of two forms: Diffuse systemic sclerosis and Localized systemic sclerosis.

Epidemiology

Systemic sclerosis is an acquired sporadic disease with a affecting all races worldwide. In the United States, the incidence is estimated at 9-19 cases per million per year. The only community based survey of systemic sclerosis yielded a prevalence of 286 cases per million. Fewer than 1 million cases per year in India. It shows a strong female dominance (4.6:1 Ratio). It occurs mostly in 30 -50 years age group people. The incidence is higher in blacks than whites. [1]

Etiology

Auto-antibodies include Topoisomerase – 1, Centromere proteins, RNA polymerase –III
Family history

Risk factors

- **Environmental factors** include infectious agents , intestinal microbiota
- **Occupational factors** include silica dust in miners, poly vinyl chloride, epoxy resins and aromatic hydrocarbons
- **Dietary factors** include rapeseed oil
- **Drugs include** Bleomycin, Cocaine, Pentazocine and Appetite suppressants. [2]

S.NO	CHARACTERISTIC FEATURE	DIFFUSE SYSTEMIC SCLEROSIS
1.	***Skin involvement***	Rapid onset; diffuse to fingers, extremities, face, trunk and rapid progression
2.	***Raynaud's phenomenon***	Onset coincident with skin involvement; critical ischemia less common
3.	***Musculoskeletal***	Severe arthralgia, carpal tunnel syndrome, tendon friction rubs
4.	***Interstitial lung disease***	Frequent, early onset & progression, severe
5.	***Pulmonary arterial hypertension***	Often occur in association with interstitial lung disease
6.	***Scleroderma renal crisis***	Occur in 15 % ; generally early (< 4 yrs from disease onset)
7.	***Calcinosis cutis***	Less common, mild
8.	***Characteristic auto antibodies***	Anti-topoisomerase-1 (scl-70), anti-RNA polymerase – III

PATHOLOGY

Skin

Dermal expansion**,** Obliteration of hair follicles, Eccrine glands & other appendages**,** Collagen fiber accumulation in reticular dermis**,** intradermal adipose layer is diminished and may completely disappear.

Lungs

Patchy infiltration of the alveolar walls**,** Vascular damage**,** pulmonary fibrosis**,** Non-specific interstitial pneumonia (Most common histologic pattern)**,** Progressive thickening of pulmonary arteries may result pulmonary hypertension, multiple pulmonary emboli and myocardial fibrosis.

Clinical features

- Soft tissue swelling
- Pruritus
- Diffuse skin hyperpigmentation
- Carpal tunnel syndrome
- Arthralgia
- Muscle weakness
- Fatigue
- Decreased joint mobility
- Skin induration with hair loss, reduced production of skin oils and decline in sweating capacity.
- The wrists, elbows, shoulders, hip girdles, knees & ankles become stiff.[3]

ORGAN INVOLVEMENT

Skin features

Edematous skin changes**,** Skin thickening starts in the fingers & then from distal to proximal extremities, Involved skin is firm, course & thickened, extremities and trunk may be darkly pigmented, Diffuse tanning, Salt, pepper appearance of skin on scalp, upper back, chest**,** Dermal sclerosis results in hair loss, decreased sweating, dry skin, Fixed flexion contractures of the fingers results in reduced hand motility, muscle atrophy, Reduced oral aperture and nose assumes a pinched, beak- like appearance

Pulmonary features

Intestinal lung disease

Clinically significant ILD develops in 16-43 %, Exertional dyspnea, Fatigue, Reduced exercise tolerance, chronic dry cough, Velcro crackles at the lung bases, Oxygen desaturation with exercise, pulmonary nodules

Musculosketal complications include

Carpal tunnel syndrome, General arthralgia, stiffness, Mobility of large joints are impaired, Contractures, Erosive polyarthritis (rare), Muscle weakness, Chronic non-inflammatory myopathy, Bone resorption.

Other disease manifestations include

Dry eyes, dry mouth, Hypothyroidism, Peripheral vascular disease, Coronary Artery Disease and Sensory trigeminal neuropathy

LABORATORY EVALUATION & BIOMARKERS

- **Anemia** (Normocytic, Macrocytic and Microcytic)
- **Drugs** (Methotrexate or Alkylating agents)
- **Thrombocytopenia & Leukocytopenia**
- **Auto- antibodies** (Topoisomerase--I, RNA polymerase--III)

Diagnosis

Based on symptoms**,** Based on physical examination**,** Serum autoantibodies**,** Complete blood picture**,** Peripheral smear test**,** Thyroid levels test **,** Skin biopsy**,** Barium filled X-ray**,** Nailfold microscopy**,** Fundoscopy**,** Ocular examination**,** Computed Tomography and Magnetic Resonance Imaging[4].

MANAGEMENT

Goals of treatment

- Establishing early and accurate diagnosis
- Evaluating internal organ involvement
- Defining clinical disease stage
- Tailoring individualized therapy to each patients unique needs
- Assessing treatment response
- Adjusting therapy as needed
- monitoring the disease progression regularly
- Continuing patient education

Pharmacological treatment

Disease modifying therapy includes

Immune suppressive agents with Glucocorticoids**,** Cyclophosphamide, Methotrexate, Mycophenolate mofetil, Rituximab and Stem cell transplantation for specific patients

Antifibrotic therapy includes D-pencillamine, Pirfenidone and Nintedanib

Vascular therapy includes Patient should dress warmly, Minimize cold exposure**,** Avoid drugs that

precipitate or exacerbate vasospastic episodes**,** Biofeedback therapy, Calcium channel blockers, Angiotensin- II receptor blocker, Alpha1 adrenergic receptor blockers, 5-phosphodiesterase inhibitors, Seratonin reuptake inhibitors, Topical nitroglycerine, Low dose aspirin, dipyridamole, Endothelin -1 receptor antagonist and Long term therapy with statins.

Skin care includes Antihistamines – prednisone <5 mg /day, D-pencillamine, Cyclophosphamide, Methotrexate, Hydrophilic ointments, Regular skin massage, Topical antibiotics and Surgical debridement

Treatment for Musculoskeletal Complications includes NSAID's, Methotrexate, Low dose corticosteroids and Physiotherapy. [5]

RAYNAUD'S PHENOMENON

Introduction

The most frequent extra cutaneous complications of systemic sclerosis are characterized by episodes of reversible vasoconstriction in the fingers and toes. It also affects tip of the nose and earlobes. 3-5% of general population has Raynaud's phenomenon. Raynaud's phenomenon is classified as Primary Raynaud's phenomenon & Secondary Raynaud's phenomenon.

Primary Raynaud's phenomenon

Absence of underlying cause (Idiopathic), Family history of Raynaud's phenomenon, Absence of digital tissue necrosis, ulceration or gangrene and Negative ANA test.

Secondary Raynaud's phenomenon

Presence of underlying cause (disease states, drugs, known causes of vasospasm), Develops at an older age (<30 years), More severe, more frequent, prolonged & painful. It is frequently associated with ischemic digital ulcers & loss of digits, Sequential development of digital blanching, Cyanosis, Rubor of the fingers or toes after cold exposure, Subsequent rewarming, Throbbing, painful sensation and Triphasic color response.

Clinical manifestations includes Sequential development of digital blanching, Cyanosis**,** Rubor of the fingers or toes after cold exposure**,** Subsequent rewarming, Throbbing, painful sensation, Triphasic color response**,** Ischemic fingertip ulcers, Gangrene and Auto-amputation. [6]

Diagnosis

Cold stimulation test, Nailfold capillaroscopy, Anti-nuclear antibody, ESR and C-reactive protein tests.

TREATMENT

For Mild and infrequent episodes

Requires reassurance, should be instructed to dress warmly and to avoid unnecessary cold exposure. In addition to gloves and mittens, patients should protect the trunk, head, and feet with warm clothing to prevent cold-induced reflex vasoconstriction.

For severe cases

Dihydropyridine calcium channel antagonists, Diltiazem, Postsynaptic Alpha 1-adrenergic antagonist, Phosphodiesterase type 5 inhibitors and Digital sympathectomy. [7]

HYPOTHYROIDISM

Introduction

Thyroid gland produces two hormones namely Thyroxine (T4) and Tri-iodothyronine (T3). Acting through thyroid hormone receptors α and β, these hormones plays a critical role in cell differentiation during development, to maintain thermogenic and metabolic homeostasis in adult human beings. Autoimmune disorders of the thyroid gland can stimulate overproduction of thyroid hormones (thyrotoxicosis) or cause glandular destruction and thyroid hormone deficiency (hypothyroidism). Iodine deficiency remains a common cause of hypothyroidism worldwide. In areas of iodine sufficiency, autoimmune disease (Hashimoto's thyroiditis) and iatrogenic causes are most common.

ETIOLOGY

Autoimmune Hypothyroidism

Hashimoto's thyroiditis, Atrophic thyroiditis.

Iatrogenic

131 I treatment, subtotal or total thyroidectomy, external irradiation of neck for lymphoma treatment.

Drugs

Iodine excess, Lithium, antithyroid drugs, P-Aminosalicylic acid, Interferon α, Cytokines, Aminoglutethimide and Tyrosine kinase inhibitors

Congenital hypothyroidism

Absent or Ectopic thyroid gland, and Dyshormonogenesis

TSH-R mutation Iodine deficiency Infiltrative disorders

Amyloidosis, Sarcoidosis, Hemochromatosis, Scleroderma, Cystinosis, Riedel's thyroiditis, Overexpression of type 3 Deiodinase in infantile Hemangioma.

Transient causes include Silent thyroiditis, Withdrawal of supra-physiologic thyroxine treatment in individuals with intact thyroid after 131 I treatment or subtotal thyroidectomy for Graves' disease.

Secondary causes include Hypopituitarism that occur due to Tumors, Pituitary surgery, Infiltrative disorders, Sheehan's syndrome, Trauma, Genetic forms of combined Pituitary hormone deficiencies and Isolated TSH deficiency. [8]

DIFFERENT TYPES OF HYPOTHYROIDISM

Congenital Hypothyroidism

Hypothyroidism occurs in about 1 in 4000 newborns. It may be transient, especially if mother has TSH-R blocking antibodies. Neonatal hypothyroidism is due to thyroid gland dysgenesis in 80–85%, to inborn errors of thyroid hormone synthesis in 10–15%, and is TSH-R antibody-mediated in 5% of affected newborns. The developmental abnormalities are twice as common in girls. Mutations that cause congenital hypothyroidism are being identified, but most remain idiopathic.

Autoimmune Hypothyroidism

Autoimmune hypothyroidism may be associated with a goiter, Hashimoto's thyroiditis, Goitrous thyroiditis or Atrophic thyroiditis. Because the autoimmune process gradually reduces thyroid function, there is a phase of compensation when normal thyroid hormone levels are maintained by a rise in TSH. Some patients have minor symptoms and is known as subclinical hypothyroidism. Later, unbound T4 levels fall and TSH levels rise further; symptoms become more readily apparent at this stage (usually TSH >10 mIU/L), which is referred to as Clinical Hypothyroidism or Overt Hypothyroidism.

Iatrogenic Hypothyroidism

It is a common cause of Hypothyroidism and can be detected by screening before symptoms develop. In the first 3–4 months after radio-iodine treatment, transient hypothyroidism may occur due to reversible radiation damage. Low-dose thyroxine treatment can be withdrawn if recovery occurs. Because TSH levels are suppressed by hyperthyroidism, unbound T4 levels are better measures of thyroid function than TSH in the months following radio-iodine treatment. Mild hypothyroidism after subtotal thyroidectomy also gets resolved after several months.

Secondary Hypothyroidism

It is usually diagnosed in the context of Anterior pituitary hormone deficiencies and Isolated TSH deficiency is very rare. TSH levels may be low, normal, or slightly increased in secondary hypothyroidism which is due to secretion of immunoactive but bioinactive forms of TSH. The diagnosis is confirmed by detecting a low unbound T4 level. The goal of treatment is to maintain T4 levels in the upper half of the reference range, because TSH levels cannot be used to monitor therapy.

Clinical features

Tiredness, Weakness, Dry skin, Feeling cold, Hair loss, Difficulty concentrating, Poor memory, Constipation, Weight gain with poor appetite, Dyspnea, Hoarseness of voice, Menorrhagia, Paresthesia, Impaired hearing. Dry coarse skin, Cool peripheral extremities, Puffy face, Myxedema, Diffuse alopecia, Bradycardia, Peripheral edema, Delayed tendon reflex relaxation, Carpal tunnel syndrome and Serous cavity effusion. [9]

Diagnostic criteria

Primary Hypothyroidism is confirmed in clinical settings by finding elevated TSH and a low free T4 level. Secondary hypothyroidism, as a result of pituitary dysfunction, results in decreased of both T4 and TSH levels. Tertiary hypothyroidism results from decreased production of TRH by Hypothalamus. Secondary hypothyroidism can be distinguished from tertiary hypothyroidism by imaging of the pituitary and hypothalamus. There is a TRH stimulation test in which exogenous TRH is administered and serum TSH response is measured, but these tests have a limited value. Secondary hypothyroidism and Tertiary hypothyroidism are not very common.

Treatment

If there is no residual thyroid function, Daily replacement dose of Levothyroxine is usually 1.6 μg/kg body weight (typically 100–150 μg), ideally taken 30 minutes before breakfast.

Levothyroxine

12.5 to 100 mcg/dl. ***Liothyroxine***: 25mcg/dl and ***Liotrix***-50mcg/dl. In many patients, lower doses suffice until residual thyroid tissue is destroyed. In patients who develop hypothyroidism after the treatment of Graves' disease, there is underlying autonomous function and necessitating lower replacement doses (i.e., 75–125 μgm/dl). Adult patients under 60 years old without evidence of heart disease may be started on 50–100 μgm of levothyroxine (T4) daily. The dose is adjusted on the basis of TSH levels, with the goal of treatment being a normal TSH, ideally in the lower half of the reference range. TSH responses are gradual and should be measured for 2 months after instituting treatment or subsequent change in levothyroxine dosage. The clinical effects of levothyroxine replacement are slow to appear. Patients may not experience full relief from symptoms until 3 to 6 months after normal TSH levels are restored. Adjustment of levothyroxine dosage is made in 12.5 or 25 μgm increments if TSH is high. Decrements of the same magnitude should be made if TSH is suppressed. Patients with a suppressed TSH of any cause, including T4 overtreatment, have an increased risk of atrial fibrillation and reduced bone density. [10]

Interstitial lung diseases

ILDs represent a large number of conditions that involve the parenchyma of the lungs alveoli, alveolar epithelium, capillary endothelium, and spaces between perivascular and lymphatic tissues. The disorders in heterogeneous group are classified based on similar clinical, roent-genographic, physiologic or pathologic manifestations. These disorders are associated with considerable rates of morbidity, mortality and little consensus exists regarding the best therapeutic management

Classification

ILDs have been difficult to classify because >200 known individual diseases are characterized by diffuse parenchymal lung involvement, either as primary condition or as a significant part of a multi organ process that occur in connective tissue diseases (CTDs). One useful approach for classification is to separate the ILDs into two groups based on histopathology: (1) Associated with predominant inflammation and fibrosis and (2) Associated with a predominantly granulomatous reaction in interstitial tissues or vascular tissues. [11]

Fibrosis

Known Causes include Asbestos, Fumes, Drugs (Antibiotics, Amiodarone) chemotherapy drugs Radiation, Aspiration pneumonia, Residual of acute respiratory distress syndrome, Smoking related desquamative interstitial pneumonia, Respiratory bronchiolitis associated interstitial lung disease, and Pulmonary Langerhans cell granulomatosis.

Unknown Causes include Idiopathic interstitial pneumonias, Idiopathic pulmonary fibrosis, Acute interstitial pneumonia, Cryptogenic organizing pneumonia, Nonspecific interstitial pneumonia, Idiopathic lymphocytic interstitial pneumonia, Pulmonary alveolar proteinosis, Lymphocytic infiltrative disorders, Eosinophilic pneumonias, Lymphangioleiomyomatosis and Inherited diseases.

Rare and ill-defined entities include Idiopathic pleuroparenchymal fibroelastosis Acute fibrinous, organizing pneumonia Bronchiolocentric patterns of interstitial pneumonia, Connective tissue diseases such as Systemic lupus erythematosus, Rheumatoid arthritis, Ankylosing spondylitis, Systemic sclerosis, Sjogren syndrome, polymyositis and

dermatomyositis, Pulmonary hemorrhage syndromes such as Good pasture syndrome, idiopathic pulmonary hemosiderosis and isolated pulmonary capillaritis, Amyloidosis, Gastrointestinal or liver diseases such as Crohn's disease, Primary biliary cirrhosis, Chronic active hepatitis and ulcerative colitis

Granulomatous

Known Causes include Hypersensitivity pneumonitis, organic dusts, Inorganic dusts such as Beryllium and Silica

Unknown Causes include Sarcoidosis, Bronchocentric granulomatosis, Granulomatous vasculitides, Lymphomatoid granulomatosis, Granulomatosis with polyangiitis and Eosinophilic granulomatosis with polyangiitis. [12]

Pathogenesis

ILDs are nonmalignant disorders and are not caused by infectious agents. The precise pathways leading from injury to fibrosis is unknown. Although there are multiple initiating agents of injury, Immunopathogenic responses of lung tissues are limited and the mechanisms of repair have common features.

Granulomatous lung disease

This process is characterized by accumulation of T lymphocytes, macrophages and epithelioid cells organized into discrete structures called granulomas in lung parenchyma. The granulomatous lesions further progresses to fibrosis.

Inflammation and Fibrosis

Initial insult is an injury to the epithelial surface that causes inflammation in air spaces and alveolar walls. If the disease becomes chronic, inflammation spreads to adjacent portions of the interstitium and vasculature, eventually causes interstitial fibrosis.

ASSOCIATED WITH CONNECTIVE TISSUE DISORDERS

Clinical findings suggestive of a CTD (musculoskeletal pain, weakness, fatigue, fever, joint pain or swelling, photosensitivity, Raynaud's phenomenon, pleuritis, dry eyes, dry mouth) should be treated in any patient with ILD. The CTDs are difficult to rule, since pulmonary manifestations occasionally precede more typical systemic manifestations for months or years. The most common form of pulmonary involvement is presence of nonspecific interstitial pneumonia histopathologic pattern. However, determining the precise nature of lung involvement in most of the CTDs is difficult due to the high incidence of lung involvement caused by disease-associated complications of esophageal dysfunction, respiratory muscle weakness, complications of therapy and associated malignancies. For the majority of CTDs, with the exception of progressive system sclerosis, recommended initial treatment for ILD includes oral glucocorticoids in association with an immunosuppressive agent (usually oral or intravenous cyclophosphamide or oral azathioprine) or mycophenolate mofetil. [13]

Progressive systemic sclerosis

Clinical evidence of ILD is present in one-half of patients with Progressive systemic sclerosis and pathologic evidence in three-quarters of patients. Dyspnea is the most common symptom. Pulmonary function tests shows a restrictive pattern and impaired diffusing capacity, before clinical or radiographic evidence of lung disease appears. The HRCT features of lung disease in Progressive systemic sclerosis range from predominant ground-glass attenuation to a predominant reticular pattern and are mostly similar to idiopathic NSIP. Histologic findings NSIP is the histo-pathologic pattern in most patients (75%) and the UIP pattern is rare (<10%).

Treatment

The most widely used initial treatment regimen is low-dose glucocorticoid therapy and immunosuppressive agents or pulse cyclophosphamide. Prednisone 0.5 to 1 mg/kg once daily oral dose. This dose is continued for 4–12 weeks, at which time the patient is reevaluated. If the patient is stable or improved, the dose is tapered to 0.25–0.5 mg/kg and is maintained at this level for additional 4–12 weeks, depending on the course. Rapid tapering or a shortened course of glucocorticoid treatment can result in recurrence. If the patient's condition continues to decline on glucocorticoids, a second agent is added and prednisone dose is lowered or maintained at 0.25

mg/kg per day. Cyclophosphamide, azathioprine 1–2 mg/kg lean body weight per day is also advisable.

A CASE REPORT ON DIFFUSE SYSTEMIC SCLEROSIS

Subjective evaluation

A 35 years old female patient was admitted in general medicine female ward with the chief complaints of weakness, unable to sit, walk, decreased mobility of joints, vomitings (20 episodes) and breathlessness since four days. She was suffered with fever & headache since one week for which she took OTC medication (Paracetamol). Patient was suffering with body pains for the past one month. Patient had past medical history of systemic sclerosis since 4 months, Hypothyroidism and was on irregular medication. Her personal history shows that she had normal appetite, good bowel & bladder, adequate sleep, not a known smoker & non-alcoholic & her occupation is paint mixing. Patient had no relevant family history.

OBJECTIVE EVALUATION

On General examination

Patient was Conscious & Coherent

On Physical examination

Patient was Afebrile,

Pulse Rate: 92 beats / minute

Blood Pressure: 100/80 mm of Hg

Respiratory rate: 20 cycles / minute

On Systemic examination

Cardio Vascular System: Normal Heart sounds are heard using Stethoscope

Central Nervous System: shows No abnormalities

Respiratory System: shows Bilateral Vesicular breath sounds, CREPTS found to be HIGHLY POSITIVE.

On Local examination

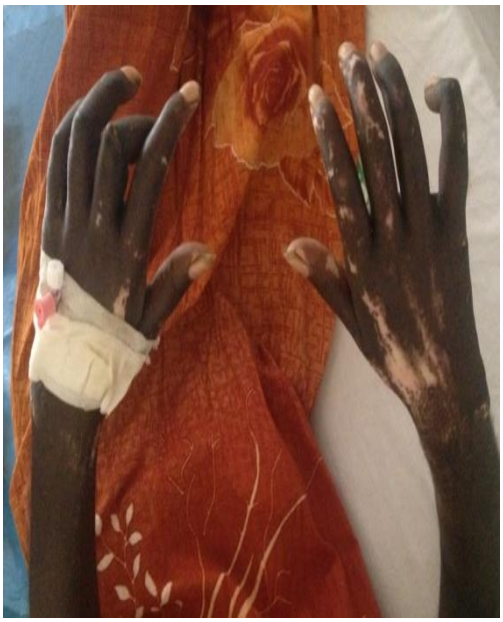
Patient was found to be suffering with following metabolic disturbances. It includes:

1. Presence of patchy hair loss
2. Presence of scaly skin over scalp
3. Loss of eye brow (LEFT EYE BROW)
4. Presence of epicanthic hypo-pigmentation of both the eyes
5. Presence of peri-angular hypo-pigmentation of mouth
6. Presence of salt & peppery skin all over the body especially trunk.

Skin biopsy

Revealed the presence of Dermis expansion, Loss of skin appendages, Inflammation of Reticular dermis and Evidence of Systemic Sclerosis (SSC).

SCARING TYPE OF ALOPECIA



DIFFUSE SYSTEMIC SCLEROSIS

RAYNAUD'S PHENOMENON

Laboratory investigations

- Haemoglobin was found to be 12.2 gms/dl
- White Blood Cells found to be 14,800 cells /cu.mm
- Thyroid Stimulating Hormone was found to be 16.36 m IU/ml (**INCREASED**)

Ultrasound scan of Abdomen

Showed Hepatomegaly (16.4 cms) & cystitis

Computed Tomography scan

Showed the presence of Interstitial Lung Disease (ILD)

Assessment

Based on the subjective & objective evaluation, the patient was diagnosed with

"Diffuse Systemic Sclerosis"

Planning

Initially the treatment was started with Inj. Pantoprazole, which is a Proton pump Inhibitor, given at a dose of 40mg, intravenously, once daily. Inj. Ondansetron, which is an Anti Emetic, given at a dose of 4mg, intravenously, once daily. Nebulisation with Asthalin, which is a Bronchodilator, given at a dose of 4 puffs for every 6 hours. Injection Optineuron, which is a Multivitamin supplement, given at a dose of 1gm intravenously, given twice daily. 1 litre (2 Tints, consisting 500ml each) Normal Saline was infused on Day 1 and Day 2. On Day 3, she was confirmed with Diffuse Systemic Sclerosis. Diseased specific symptomatic treatment was started from day 3 to day 31 with the following medication.

Treatment chart

S.NO	DRUG	CATEGORY	DOSE	ROA	FREQUENCY
1	Prednisolone	Corticosteroid	5mg	Oral	Once daily
2	Hydroxy chloroquine	Anti Inflammatory	100mg	Oral	Twice daily
3	Cetrizine	Antihistaminic	10mg	Oral	Once daily
4	Levo thyroxin	Anti Hypothyroid drug	125mg	Oral	Once daily
5	Ranitidine	H2 receptor antagonist	150mg	Oral	Once daily
6	Capsule A & D	Vitamin supplement	5400IU	Oral	Twice daily
7	Folic acid	Folic acid supplement	1mg	Oral	Once daily
8	Domperidone	Anti Emetic	30 mg	Oral	Once daily
9	Syp.Zinc Acetate	Appetite Enhancer	5ml	Oral	Once daily
10	Irimist Eye drops	Ophthalmic Lubricant	2 drops	Instilled into Eye	5 times daily
11	Ointment Clobetasol propanoate	Topical corticosteroid	0.05% w/w	Apply over neck.	Twice daily

The patient was advised to take salt rich & protein rich diet. On day 32, Patient developed Constipation for which she was treated with syrup Lactulose, at dose of 15ml, given orally in 3 divided doses.

On day 35, Patient was relieved with constipation & vomiting, and she was discharged with the following medication.

Discharge medication

S.NO	DRUG	CATEGORY	DOSE	ROA	FREQUENCY
1	Prednisolone	Corticosteroid	5mg	Oral	Once daily
2	Hydroxy chloroquine	Anti Inflammatory	100mg	Oral	Twice daily
3	Cetrizine	Antihistaminic	10mg	Oral	Once daily
4	Levo thyroxin	Anti Hypothyroid drug	125mg	Oral	Once daily
5	Pantoprazole	Proton pump inhibitor	40mg	Oral	Once daily
6	Capsule A & D	Vitamin supplement	5400IU	Oral	Twice daily
7	Folic acid	Folic acid supplement	1mg	Oral	Once daily
8	Syp.Zinc Acetate	Appetite Enhancer	5ml	Oral	Once daily
9	Irimist Eye drops	Ophthalmic Lubricant	2 drops	Instilled into Eye	5 times daily
10	Ointment Clobetasol propanoate	Topical corticosteroid	0.05% w/w	Apply over neck.	Twice daily

The patient was counseled regarding Life style modification and was asked for review after one month.

For Raynaud's phenomenon

- Wear warm Dresses
- Wear gloves
- Avoid exposure to cold
- Avoid smoke

For Skin involvement

- Don't take hot baths or showers as it may leads to drying of skin
- Use skin lotion after bathing
- Apply sunscreen before you go outside
- Keep home moist
- Exercise regularly to improve blood circulation & flexibility

Hypothyroidism

- Don't eat cabbage and cauliflower
- Maintain healthy weight
- Avoid stress by doing yoga or meditation
- Sleep atleast 7 to 9 hours per day

Musculoskeletal system involvement

- Regular strengthening exercises and stretching helps bones, joints and muscles strong.
- It is also important to complete everyday activities in safe ways.
- Maintain a tall posture to prevent back pain
- Be careful when picking up heavy objects and try to keep repetitive motions to a minimum.

DISCUSSION

The present set of recommendations addresses only a limited number of the most relevant pharmacological treatments for systemic sclerosis. As systemic sclerosis has heterogeneous clinical course and is an uncommon disease, many treatment options have not yet been able to be appropriately tested. It should be recognized that "absence of evidence for efficacy" does not imply that "efficacy is absent". Indeed, some treatment options were not translated into recommendations. This set of recommendations should be helpful to make clinical decisions but should always be used in the context of the patient, clinical judgment and balance of efficacy and toxicity. There are also other treatment options for the management of systemic sclerosis patients, such as physiotherapy, education and new experimental therapies which were beyond the scope of this case report or could not be included due to lack of expert consensus. In view of the heterogeneity of systemic sclerosis, complexity of diagnostic evaluation and the wide array of available treatment options to

specialized center should also be strongly considered. [15]

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