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## Systemic sclerosis: Clinical manifestations, anesthetic and orthopedic considerations in a patient

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## ABSTRACT

**INTRODUCTION:** Systemic sclerosis is a rare and progressive multisystem autoimmune disorder that is characterized pathologically by vascular abnormalities, connective tissue sclerosis and atrophy of skin and various internal organs (e.g., alimentary tract, lungs, heart, kidney, CNS), and autoantibodies. With an unknown etiology, Scleroderma is a complex polygenetic disease. A recent Genome Wide Association Study (GWAS) confirmed a strong association with the Major Histocompatibility Complex (MHC) and autoimmunity. We provide a case scenario along with a review of the systems involved and challenges physicians can face in dealing with this rare disease.

**CASE PRESENTATION:** Our patient, a known case of systemic sclerosis, was admitted with a history of right femur fracture following a fall. We highlight the medical, anesthetic and surgical challenges faced by our team in the management of this patient. We will explain the stages patient faced in treatment process till her death. We combined the case report with detailed literature review of this rare disease.

**DISCUSSION:** Systemic sclerosis is a complex disease process with many different levels of system involvement. Patient needs to be reviewed thoroughly in preoperative period by multidisciplinary team and counseled in detail about the difficulties in procedure, risks and complications.

**CONCLUSION:** Patient with scleroderma presents a challenge to the surgical team and anesthetist and a multidisciplinary approach should be followed with all of these patients to avoid catastrophic results.

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## 1. Introduction

Systemic sclerosis is a rare and progressive multisystem autoimmune disorder that is characterized pathologically by vascular abnormalities, connective tissue sclerosis and atrophy of skin and various internal organs (e.g., alimentary tract, lungs, heart, kidney, CNS), and autoantibodies [1].

Systemic sclerosis has an incidence between 2.3 and 10 per million population [2,3]. There is considerable regional variation, most likely due to environmental changes [4]. The ratio of female to male is between 3 and 6:1 depending on the source [4]. The peak onset is in the fourth decade for females and usually later for males; the overall age of presentation is between 20–60 yrs [3]. It is seen in all races, but is less common in Asians [5]. Although most patients

have long survival, some of them progress rapidly to death. Sixty percent of deaths are secondary to heart or lung involvement and (or) to pulmonary hypertension [6].

With an unknown etiology, Scleroderma is a complex polygenetic disease. A recent Genome Wide Association Study (GWAS) confirmed a strong association with the Major Histocompatibility Complex (MHC) and autoimmunity [7]. SSc can be clinically sub-classified based on patterns of skin fibrosis into limited and diffuse forms, the distinctions principally being made by the extent of cutaneous involvement, but also included are certain other clinical and immunological features (Table 1) [8]. In addition, the majority of SSc patients (90%) have circulating anti-nuclear autoantibodies (ANA) [9]. The three most common autoantibodies (auto-Abs) are anti-DNA topoisomerase I (topo I), anti-RNA polymerase III, and anti-centromere antibodies, in which the first two auto-Abs tend to be associated with diffuse SSc, the last one being strongly correlated with limited SSc, although these associations are not complete [9].

To our knowledge, only few case reports have been published about this rare disease from medical and anesthesia point of view

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and even fewer about surgical implications and considerations required.

We present a case review of a patient with systemic sclerosis who was admitted to our university hospital tertiary care center, with history of fracture of femur following a fall. We intend to highlight the anesthetic and surgical challenges faced by our team in the management of this case.

The work has been reported in line with the SCARE criteria [10].

## 2. Case review

A 64 year old female patient, limited community ambulant without walking support, known case of scleroderma, ischemic heart disease, hypertension and hypothyroidism was admitted to our hospital with a history of ground level fall complaining of pain in right thigh and inability to bear weight on right leg. General examination revealed tightness of lips and skin around the neck and multiple telangiectasias. Local examination revealed tenderness without open wound at right thigh. Right and left feet had non healing superficial wounds with serous discharge. Distal pulses were not palpable bilaterally. Both hands showed sclerodactyly and digital pitting scars on multiple digits.

Her x-rays showed comminuted fracture at the diaphysis-metaphysis junction of right femur (Fig. 1).

On preoperative assessment she had multiple problems including Raynaud's phenomenon and pulmonary hypertension. Her ECHO showed EF of 55%. Her MPS scan shows normally perfused LV myocardium with normal size LV cavity and LVEF of 65% with no wall motion abnormality. Prognostically it was a good study with low probability for annual risk for major cardiac events.

Patient was on oral steroids for more than 20 years, in addition to anti-hypertensive, thyroxin and cardiac medications. Family and genetic history was unremarkable.

After discussing with anesthesia team and the patient, decision was taken to proceed with open reduction and internal fixation with plate under spinal anesthesia. Intraoperative spinal anesthesia was difficult and took longer than usual. She underwent uneventful plating of the right femur with MIPO (minimally invasive plate osteosynthesis) technique. Surgery was performed by a senior orthopedic consultant. Only stat dose of IV Hydrocortisone 100 mg was given on immediate postoperative period and was put on IV Clindamycin and Ciprofloxacin until discharge. She was given subcutaneous enoxaparin 40 mg QD. She tolerated the procedure and remained comfortable on intravenous analgesics which were switched to oral as we faced difficulty in her cannulation. Patient was mobilized bed to chair non-weight bearing on first postoperative day (POD). Her hospital stay was uneventful and she was discharged on 5th POD.

On 14th POD, wound was ok and stitches were removed in clinic. On same day she presented in ER because of wound dehiscence and serous discharge. Wound was washed with normal saline and pyodine and tagging sutures were applied and advised alternate day dressing. She was also discharged on Table Augmentin 1Gm Q12H.

On 3rd postoperative week she had foul smelling discharge from surgical site and culture swab showed moderate growth of Acinetobacter species. She underwent wound debridement and arthrotomy under spinal anesthesia. About 20 ml of frank pus was drained and CS showed Acinetobacter species sensitive to ciprofloxacin and meropenem. It was yellow in color and was clear. Urine culture showed Enterococcus species and she was put on linezolid and meropenem. Subsequently relook debridement was done in addition to antibiotic cement beads insertion. In this surgery anesthetist faced difficulty in spinal anesthesia and had to convert it to general anesthesia. She was put on meropenem, gentamycin and

doxycycline after consulting the infectious disease (ID) team. She was also given Inj. Hydrocortisone 100 mg IV stat and Inj. Enoxaparin.

Postoperatively she was shifted to special care. Multiple teams were involved in postoperative care including the physician, ID team, cardiologist, pulmonologist and endocrinologist. She was diagnosed with atrial fibrillation with low ejection fraction of 15%, pulmonary edema and type II respiratory failure necessitating her admission in ICU. Patient dropped GCS to 5/15 and she was intubated and put on ventilator. Second day in ICU patient's condition improved, successfully extubated and shifted out of ICU.

Her health status deteriorated again with low cardiac output, acute kidney injury, not maintaining oxygen saturation and she was put on Bi-level Positive Airway Pressure (BiPAP). The patient and family refused the intubation and patient developed cardiopulmonary failure and expired.

## 3. Discussion

According to the criteria for diagnosis of scleroderma established by the Subcommittee for Scleroderma Criteria of the American Rheumatism Association (ARA), the patients should have either:

- Scleroderma proximal to the digits, affecting limbs, face, neck or trunk- this is the single major criterion; or
- At least two minor criteria, consisting of:
  - Sclerodactyly (localized thickening and tightness of the skin of fingers and toes causing them to curl and limit their mobility)
  - Digital pitting scarring (DPS)
  - Bilateral basal pulmonary fibrosis

These criteria have 97% sensitivity and 98% specificity [11].

Systemic sclerosis is an often fatal disease that affects skin and internal organs with variable degrees. Many factors, including environmental factors, can lead to immunologic system disturbances and vascular changes. It is important to realize that this widespread disease does not involve all organs in any patient; in certain cases it may be limited to one or two organs. Even when changes are present in any one organ, they are not uniform [12]. From a systematic perspective patients with scleroderma may have the following manifestations:

### 3.1. Vascular

The earliest feature of SSc is usually, but not invariably, Raynaud's phenomenon. It may precede cutaneous changes by years, this interval can be shorter in males –usually under a year- than in females, in whom it is approximately 5 years, but may be as long as 30 years. Patients may have digital ulcers and be unable to use their hands to perform activities of daily living [12].

### 3.2. Cutaneous

Skin over the face and hands is most frequently involved, but changes may extend proximally to forearm and upper arm, upper chest, abdomen and back. Lower extremity changes are not uncommon. Changes in the dermis show hyalinization of collagen, often with associated abnormalities in elastic tissues and reticulin. In one study, no increase in skin thickness or its collagen content was found. The thickness and collagen content of the clinically affected forearm skin were usually decreased and with a normal collagen density. It is concluded that the clinical impression of thickness and toughness is due to binding down of the skin to deeper structures [13]. Dermal thickening can result in flexion contractures, ischemic



**Fig. 1.** X-ray of right knee antero-posterior and lateral shoot through views showing comminuted fracture at the diaphysis-metaphysis junction.

ulcerations, and resorption of distal phalanges (Sclerodactyly and microstomia). Calcium deposits occur in the skin of fingers and hands that may break down to discharge chalky white material (calcinosis cutis). Telangiectases are often seen over the involved skin as well as oral mucosa; these may cause excessive bleeding when traumatized during intubation.

### 3.3. Musculoskeletal

Notable bone changes seen in SSc are resorption of terminal phalanges (Acro-osteolysis) associated with calcinosis. Approximately 70% of the patients show absorption, which may be minimal and only involve one terminal phalanx or be gross and involve several phalanges up-to proximal phalanges. Erosive arthropathy with “pestle and mortar” deformity of the distal interphalangeal joints may also be seen. Other changes include increased intraosseous deposition of calcium [12]. Arthritic pain is often seen in early stages of systemic sclerosis, and initial radiographic changes seen are reminiscent of rheumatoid arthritis but less destructive. One study showed the presence of radiological abnormalities including

periarticular osteoporosis, joint space narrowing, and erosions [14]. Avascular necrosis of head of femur, presumably resulting from vasculitis, has been described [15]. Muscle weakness may occur. Muscles of the forearms and hands are often affected as well as the proximal muscles. Electromyography is abnormal in 50% of the cases early in the disease and reaches up to 93% in late disease [12].

### 3.4. Pulmonary

Pulmonary involvement frequently includes diffuse fibrosis associated with diffuse disease or pulmonary hypertension that is associated with the limited disease or CREST syndrome [12]. Interstitial lung disease is reported to occur, in up to 80% of patients with scleroderma. Although, in the majority of the patients, the interstitial lung involvement is sub clinical and asymptomatic in the early stage; clinically significant interstitial lung disease is observed in approximately 40% of patients with systemic sclerosis and is a leading cause of morbidity and mortality [16]. Pulmonary function is frequently abnormal while chest radiography shows no pathology [17]. Most experts rely on a combination of pulmonary function

tests for diagnosis of interstitial pulmonary disease. Pulmonary hypertension and right-side heart failure have become the leading cause of death in patients with SSc [18].

3.5. Gastro-intestinal

Esophageal dysmotility, gastro-paresis and intestinal bacterial overgrowth are some of the most common gastrointestinal manifestations seen in patients with systemic sclerosis. Esophagus is involved in about 75% of all patients; making it the most frequently affected part of gastrointestinal tract. Patients often complain of dysphagia and gastric reflux. Stricture of the lower end of esophagus is seen in 10% of the cases which is not necessarily associated with gastro-esophageal reflux or hernia. Esophageal mucosal thinning occurs, with fibrotic thickening in the remaining layers. There may be extensive mucosal ulceration and marked esophageal dilation. Carcinoma of the esophagus has also been reported [19].

3.6. Cardiac

The resting ECG is abnormal in approximately 50% of the cases along with presence of cold-induced changes [20]. Other findings include arrhythmias, partial or complete heart block and sclerosis of coronary arteries. General enlargement of the heart; left ventricular hypertrophy or a triangular outline is the most frequent radiological abnormalities seen on radiography. Cardiac fibrosis has been demonstrated using MRI and CT scans [21].

3.7. Renal

Renal involvement was seen as proteinuria in 36%, hypertension in 24%, azotemia in 19% and malignant hypertension in 7% of one series [22]. Creatinine clearance is affected in about 40% of cases [12].

3.8. Endocrine

The thyroid and parathyroid glands may be involved in the fibrotic process and thymus may show cortical changes [12].

Summary of the difference between diffuse and limited SSc is shown in Table 1.

3.9. Drug therapy

Currently there is no standard treatment regimen for systemic sclerosis; the treatment depends on the presentation. Corticosteroids have largely been used for treating connective tissue disease, but their role remains controversial in treating SSc due to lack of evidence of effectiveness. Nevertheless, low-dose corticosteroids may reduce articular symptoms. Dexamethasone pulse

therapy has been claimed useful in some patients [12]. Of particular interest in this review is that long-term treatment with steroids poses an increased risk of osteoporosis, myopathy and delayed wound healing. Agents that have been used with varying efficacy are cyclophosphamide, prednisone [23].

Surgeons and Anesthesiologists managing patients with SSc must have experience and background about the pathogenesis, clinical manifestations, systemic involvement, surgical and anesthetic considerations. The fact that every aspect of surgical and anesthetic care may be altered or hindered by the pathogenesis of this disease should never be forgotten.

3.10. Pre-op preparation

Routine investigations should include a full blood count, urea and electrolytes, chest X-ray, ECG and clotting screen. Lung function tests, steroid cover and pretreatment with vitamin K may be necessary to avoid any events during or after surgery. Proper history should be taken for presence of dysphagia, regurgitation, weight loss and digital pallor.

Any anatomical changes should be assessed, such as skin tightening of the face, ability to open mouth (fibrosis of the temporomandibular joint, reduced oral aperture), neck mobility and presence of oral telangiectases in regard to the possibility of endotracheal intubation. Prior to arrival in the O.R, the patient should be treated with an antacid or H2-receptor antagonists to avoid regurgitation and aspiration. To minimize peripheral vasoconstriction the Operating room temperature should be maintained above 21 °C, and intravenous fluids should be warmed before administration [18]. Thickened skin, vasoconstriction and flexion contractures often pose difficulty in intravenous access and noninvasive BP monitoring. This situation may necessitate the need for ultrasonic blood pressure sensors or invasive monitoring and central venous access.

3.11. Intra-op considerations

The choice of anesthesia technique is variable and should be guided by identification of organ dysfunction. General anesthesia can lead to problems such as difficulty of intubation and insertion of an IV cannula or measuring blood pressure. Esophageal dysmotility and lower esophageal sphincter incompetence may increase the risk of aspiration [24]. In cases where general anesthesia is the only choice, awake fiber-optic intubation is preferred especially when mouth opening is limited [25].

Patients with Progressive Systemic Sclerosis (PSS) may require monitoring of cardiac performance, including cardiac output, con-

**Table 1**  
Difference between diffuse and limited SSc.

Diffuse cutaneous SSc	Limited cutaneous SSc
Short interval (<1 year) between the onset of Raynaud’s phenomenon and the development of skin changes	Long history of Raynaud’s phenomenon
Truncal and peripheral skin involvement	Limited skin involvement
Tendon friction rubs	Calcification, telangiectasia, late onset of pulmonary HTN
Pulmonary fibrosis, renal failure, gastrointestinal disease, myocardial involvement	Capillary dilation visible in the nail fold
Capillary drop-out visible in skin folds	Anticentromere antibody positive
Scl-70 antibody positive	
Anticentromere antibody- negative	

**Table 2**  
Common Features Associated with Progressive Systemic Sclerosis (PSS).

Common Features Associated with Progressive Systemic Sclerosis (PSS)	
Raynaud’s phenomenon	Dermal thickening, calcifications, contractures
Oral or nasal bleeding	Skin tightening, microstomia, decreased neck flexibility
Ventricular hypertrophy, diastolic dysfunction, conduction defects	Telangiectasias
coronary vasospasm	
Hypertension, decreased renal clearance	Esophageal dilatation, decreased LES tone
Anesthetic Considerations	Intestinal malabsorption
Peripheral vasoconstriction	Restrictive pulmonary disease
Peripheral IV difficulties	Myocardial fibrosis,
Difficult airway management	Renal disease
Aspiration	Decreased Vit K-dependent clotting factors
Increased positive airway pressure, increased oxygen concentration, extubation delays	

tractility, pulmonary arterial, and left ventricular filling pressures in the presence of myocardial fibrosis or pulmonary hypertension [18]. Common features associated with PSS in Table 2.

Many authors recommend regional anesthesia for elderly patients, those with severe SSc, and with severe pulmonary disease undergoing surgery. It should be kept in mind that owing to decreased circulation and fibrosis of tissue, the duration of action of local anesthetic may be prolonged. Review of literature has revealed that a smaller dose of local anesthesia is required [26].

#### 4. Conclusion

Patient with scleroderma presents a challenge to the surgical team and anesthetist and a multidisciplinary approach should be followed with all of these patients to avoid catastrophic results.

#### Conflicts of interest

No conflict of interest.

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#### Ethical approval

Ethical Review Committee ERC approval is taken.

#### Consent

“The head of the medical team/hospital or legal team has taken responsibility that exhaustive attempts have been made to contact the family and that the paper has been sufficiently anonymised not to cause harm to the patient or their family.”

#### Authors contribution

Obada Hasan: Design of the study, direct care of the patient and drafting the article and final approval

Muneeba Majeed Jessar: conception and design of the study, drafting the article and revising it and final approval to be submitted

Muhammad Ashar: conception and design of the study, drafting the article and revising it and final approval to be submitted

Shahryar Noordin: design of the study, acquisition of data, drafting the article, revising it and final approval for submission

Tashfeen Ahmed: design of the study, acquisition of data, drafting the article, revising it and final approval for submission

#### Guarantors

Obada Hasan and Tashfeen Ahmed.

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