Systemic Sclerosis (SSc)

63

Contents

Abstract

Epidemiological studies have underscored the incidence of SSc in the sixth, seventh and eighth decades of life. The pathogenesis of systemic sclerosis (SSc) is characterised by immune and endothelial activation, vascular dysfunction and overproduction of extracellular matrix. The late onset is clinically and immunologically different from the early onset. There are two subsets of SSc, diffuse cutaneous SSc (dcSSc) which is associated with progressive fibrosis of skin and internal organs and the other limited cutaneous.

Keywords

Systemic sclerosis · Late onset · Early onset · Diffuse cutaneous · Diffuse cutaneous · CREST syndrome

Introduction

There is evidence to suggest that the incidence of progressive SSc in the elderly is more common than in younger age group [1]. Most patients with SSc present in the third or fourth decade of life [2]. The incidence in patients over 75 years with systemic sclerosis is around 20 per million per year, and the peak incidence in white females is between 65 and 75 years and in white males over 75 years [3]. Epidemiological studies have underscored the incidence of SSc in the sixth, seventh and eighth decades of life [3–5]. Vascular dysfunction, overproduction of the cellular matrix and immune and endothelial activation constitute the pathogenesis of SSc [6, 7].

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Clinical Manifestations

Age of onset is commonly between the ages of 40 and 50 years [8]. There is however another subgroup with onset later in life. Some investigators have considered late onset as greater than 65 years [9] but others at or beyond 75 years [10]. There are two subsets of SSc, diffuse cutaneous (dcSSc) which is associated with progressive fibrosis of skin and internal organs [10] and the other limited cutaneous [10]. CREST syndrome is considered as limited cutaneous [11] and is characterised by calcinosis, Raynaud's phenomenon, oesophageal dysmotility, sclerodactyly and telangiectasia (Fig. 1). They have different disease courses and prognosis [2]. The skin becomes hidebound; the nose is pinched; the lips are thinned out resembling a fish mouth, telangiectasia (Fig. 2) and calcinosis (Fig. 3).

There is deformity of the terminal phalanges with contractures of the digital joints, sclerodactyly and hypo- and hyperpigmented skin (Fig. 4). A study of 123 patients with SSc 75 years and older showed that pulmonary hypertension occurred more frequently, and fewer patients had digital ulcers [10]. Older SSc patients are at greater risk for renal impairment, cardiac disease and muscle weakness [9]. Earlier reports indicated that late-onset SSc is a milder form of the disease with minimal skin and internal organ involvement and decreased mortality [1, 12], but subsequent data indicates that late-onset SSc is a more aggressive disease [13] and the risk of death increases for each year by 5% [14]. It is not always progressive and prognosis variable. Table 1 summarises the distinguishing features between late-onset and early-onset SSc.

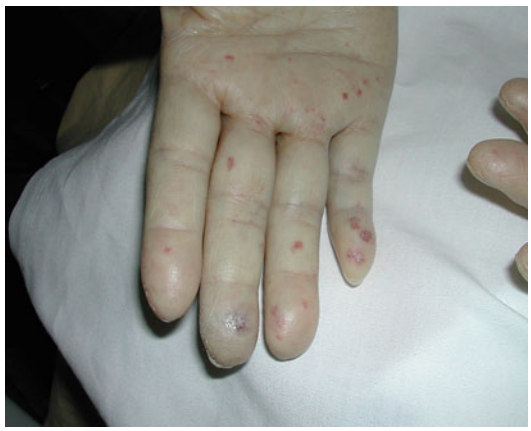

Fig. 1 Shows Raynaud's phenomenon, sclerodactyly and telangiectasia (Reproduced, with kind permission, from Professor Nicholas Manolios)

Diagnosis

Skin thickening with Raynaud's phenomenon with varying degrees of internal organ involvement provides the diagnosis of SSc. Raynaud's phenomenon may be the only early manifestation

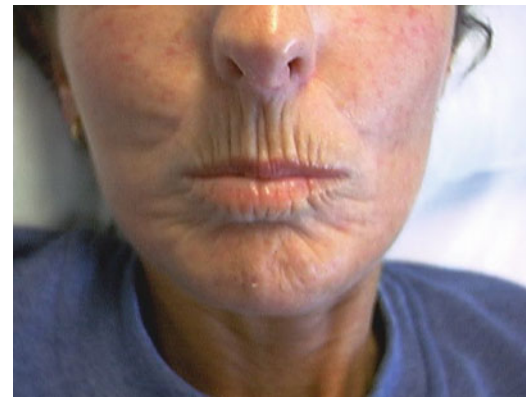

Fig. 2 Showing fish mouth, pinched nose and telangiectasia (Reproduced, with kind permission, from Professor Nicholas Manolios)

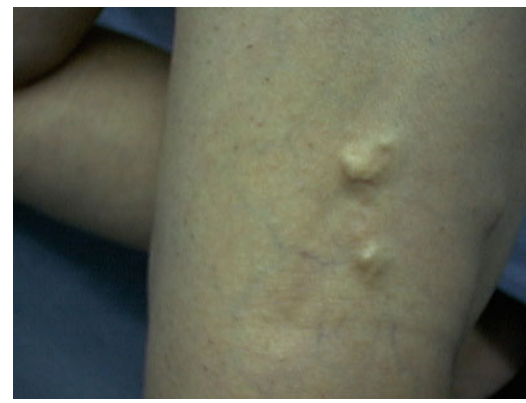

Fig. 3 Shows calcinosis cutis (Reproduced, with kind permission, from Professor Nicholas Manolios)

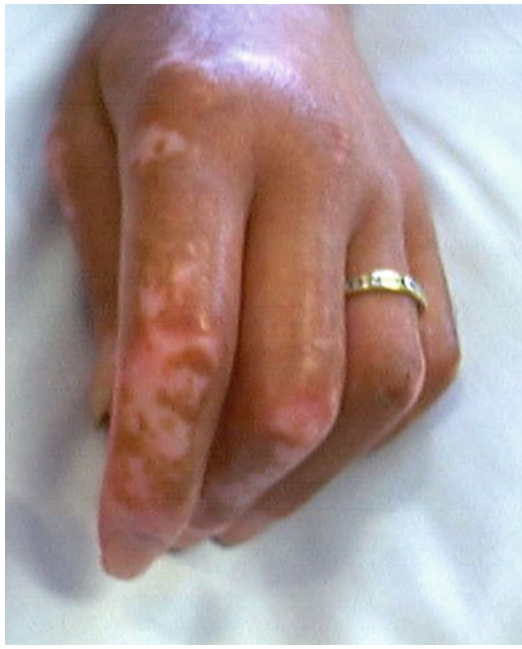

Fig. 4 Shows digital contracture of the digital joints, hidebound skin with hypo- and hyperpigmented areas (Reproduced, with kind permission, from Professor Nicholas Manolios)

of SSc. Nailfold capillary microscopy can help to determine primary Raynaud's disease from secondary Raynaud's (Raynaud's phenomenon) [18]. Most patients with dcSSc have one or more of the following autoantibodies positive, namely, auto-centromere antibodies (ACA), anti-RNA polymerase III and anti-topoisomerase I [18].

Treatment

Several therapies are available in the treatment of SSc, and the aim of treatment is to slow the progress of the disease, to improve vascular function and to provide supportive and symptomatic care [2]. The anti-inflammatory drugs, NSAIDs and corticosteroids, are useful in inflammatory states involving the joints, muscles, pericardium and pleura. They are of little use in inflammation of the skin and SSc-associated tissue injury [19]. Corticosteroids can increase the risk of renal crisis, and ACE inhibitors are known to reverse the vasospasm associated with SSc renal crisis [19]. The most effective vasodilators are the calcium channel blockers (e.g. nifedipine) and are the first-line agents to be used in Raynaud's phenomenon [20]. The immunosuppressive drugs include cyclophosphamide, mycophenolate mofetil, cyclosporine and methotrexate [19]. Cyclophosphamide is useful in patients with interstitial lung disease associated with scleroderma [21]. Aspirin in low dose has been recommended in Raynaud's phenomenon [2]. Bosentan, an endothelial receptor antagonist, has proved effective for the prevention of ischaemic digital ulcers [20, 22] and improved the blood flow to the lungs [20]. D-penicillamine has been used in patients with dcSSc in an effort to slow fibrosis [2]. Oral endothelial receptor antagonists, PDE5 inhibitors and parenteral prostanoids are included in the treatment of pulmonary hypertension [2].

Table 1 Distinguishing features between late-onset and early-onset systemic sclerosis (SSc)

Age of onset	<65 years	>65 years
Gender	Females	Females
Clinical expression		
Skin – diffuse	Present	Extensive
Digital ischaemia	Frequent	Less frequent
Renal	Frequent	More frequent
Muscle weakness	Frequent	More frequent
Pulmonary hypertension	Frequent	More frequent
Diastolic dysfunction		
and conduction deficits	Frequent	More frequent
Myositis	Frequent	Less frequent
Oesophageal involvement	Frequent	Less frequent
Raynaud's	Present	More severe
Relationship to		
Malignancy	Frequent	More frequent
Centromere antibodies (ACA)	Frequent	More frequent
Prognosis	Poor	Poorer

Information sources: Manno et al. [8]; Hugle et al. [10]; Manno et al. [9]; Derk et al. [15]; Czirjak et al. [16]; Albo et al. [17]

Impact

Late-onset SSc is associated with malignancy [15], severe Raynaud's phenomenon, cardiac and pulmonary complications and poor functional status [8]. The late-onset SSc is a poor prognostic indicator related to both severity and comorbidities [15]. Older patients have a greater risk of pulmonary hypertension, interstitial lung disease and renal impairment [8] and are common causes of death [22]. Other poor prognostic indicators are older age, male gender and involvement of internal organ system [2] (Box 1).

Box 1 Key Points: Systemic Sclerosis (SSc)

- The pathogenesis of systemic sclerosis (SSc) is characterised by immune and endothelial activation, vascular dysfunction and overproduction of extracellular matrix [6, 7].
- Age of onset is commonly between 40 and 50 years [8].
- There is another subgroup with onset later in life (late onset) [9, 10].
- There are two subsets of SSc, diffuse cutaneous associated with progressing fibrosis of the skin and internal organs and limited cutaneous [10].
- The late onset is clinically and immunologically different from the early onset.
- Renal, muscle weakness, pulmonary hypertension and relationship to malignancy are more frequent in the late onset (see Table 1).
- Digital ischaemia/ulcers, myositis and oesophageal involvement are less prevalent (see Table 1).

Multiple Choice Questions

1. The following are true of late-onset systemic sclerosis (SSc), except:
   A. SSc patients 75 years and older showed that pulmonary hypertension and digital ulcers occurred more frequently.
   B. There are two subsets of SSc, diffuse cutaneous and the other limited cutaneous.
   C. In the late onset, there is a higher prevalence of centromere antibodies.
   D. Raynaud's phenomenon is much more severe in the late onset.

MCQ Answers

1 = A

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