Systemic sclerosis: clinical features and management

Ariane L Herrick

Abstract

Systemic sclerosis (SSc) differs from other multisystem connective tissue/autoimmune diseases in that its clinical features result mainly from a combination of fibrosis and vascular abnormality (rather than from inflammation). This has major implications for management. SSc is associated with high morbidity and mortality, and is often very painful and disabling. There are two major subtypes, defined on the basis of the extent of skin involvement: limited (often previously referred to as CREST) and diffuse cutaneous. The two subtypes have very different natural histories, autoantibody associations and prognoses, and require different approaches to management, at least in their early stages. The two most characteristic features of SSc are Raynaud's phenomenon (which can be very severe) and skin thickening ('scleroderma'). Although both cause troublesome, often disabling symptoms, it is the internal organ involvement of the disease that can be life-threatening. This article discusses recent advances in early diagnosis, clinical features and the approach to investigation and management. It is an exciting time for clinicians with an interest in SSc, because following on from the development of new treatments for several organ-based complications (e.g. pulmonary arterial hypertension, digital ulceration), several promising 'disease-modifying' therapies (including antifibrotics) are currently being studied in clinical trials.

Keywords MRCP; pulmonary fibrosis; pulmonary hypertension; Raynaud's phenomenon; scleroderma; scleroderma renal crisis; systemic sclerosis

Key points

- Systemic sclerosis (SSc) carries high morbidity and mortality, but advances in treatment are leading to improved quality of life and increased survival
- The two main subtypes (limited cutaneous, diffuse cutaneous) have very different natural histories and prognoses
- The clinical features of SSc result mainly from a combination of fibrosis and vascular abnormality (rather than from inflammation), with implications for management

Introduction

Systemic sclerosis (SSc) is a multisystem connective tissue disease (Figure 1) associated with high morbidity and mortality. Many different specialists are involved in the care of patients with SSc, and may make the initial diagnosis. This is because although the most common presenting feature of SSc is Raynaud's phenomenon (RP), the diagnosis may not be suspected until the patient develops another problem; examples include breathlessness caused by interstitial lung disease or pulmonary arterial hypertension, heartburn and/or dysphagia owing to oesophageal dysmotility, or (rarely but life-threateningly) a scleroderma renal crisis.

SSc is therefore an exemplar of a disease requiring good general medical knowledge and skills to make the diagnosis and provide best practice clinical care. This article provides a brief overview of epidemiology, pathology and disease subtyping, and then discusses diagnosis (highlighting the importance of early diagnosis), clinical features and the approach to investigation and management.

Definition and terminology

SSc is sometimes used interchangeably with 'scleroderma' (= hard skin), but strictly speaking this usage is incorrect: scleroderma is one of the clinical features of SSc (albeit the most characteristic) and has a differential diagnosis (see below).

The term 'CREST', often used in the past to mean the limited cutaneous subtype of SSc (lcSSc), has fallen out of favour. CREST is essentially an acronym for five of the clinical features of SSc (Calcinosis, Raynaud's phenomenon, oEsophageal dysmotility, Sclerodactyly (scleroderma of the fingers), Telangiectases), and all of these five features can occur in both the lcSSc and diffuse cutaneous (dcSSc) subtypes of SSc, described below.

Epidemiology

SSc is an uncommon disease, with a prevalence of around 100–250 per million and an incidence of around 10–20 per million per year[1]; it is estimated that approximately 10,000 people in the UK are affected. Women are more commonly affected than men (around 7:1).

In contrast, RP (with which SSc often presents) is very common, affecting around 5% of the population. RP is usually primary (idiopathic) and is then 'benign' – a purely functional vascular abnormality (an exaggeration of the normal physiological response to cold) that does not progress to irreversible tissue injury. Therefore, in the vast majority of patients, RP does not progress to SSc, so patients can be reassured.

Pathology

Unlike most autoimmune connective tissue diseases, SSc is not primarily an inflammatory disease. Its clinical features result

Ariane L Herrick *MD FRCP is Professor of Rheumatology at the University of Manchester, and Honorary Consultant Rheumatologist, Salford Royal NHS Foundation Trust, UK. Her main clinical and research interests are Raynaud's phenomenon and systemic sclerosis spectrum disorders, including assessment of the microvasculature. Competing interests: ALH has done consultancy work for Actelion, served on a Data Safety Monitoring Board for Apricus, and received research funding and speaker's fees from Actelion, and speaker's fees from GSK.*

Please cite this article in press as: Herrick AL, Systemic sclerosis: clinical features and management, Medicine (2017), https://doi.org/10.1016/j.mpmed.2017.11.007

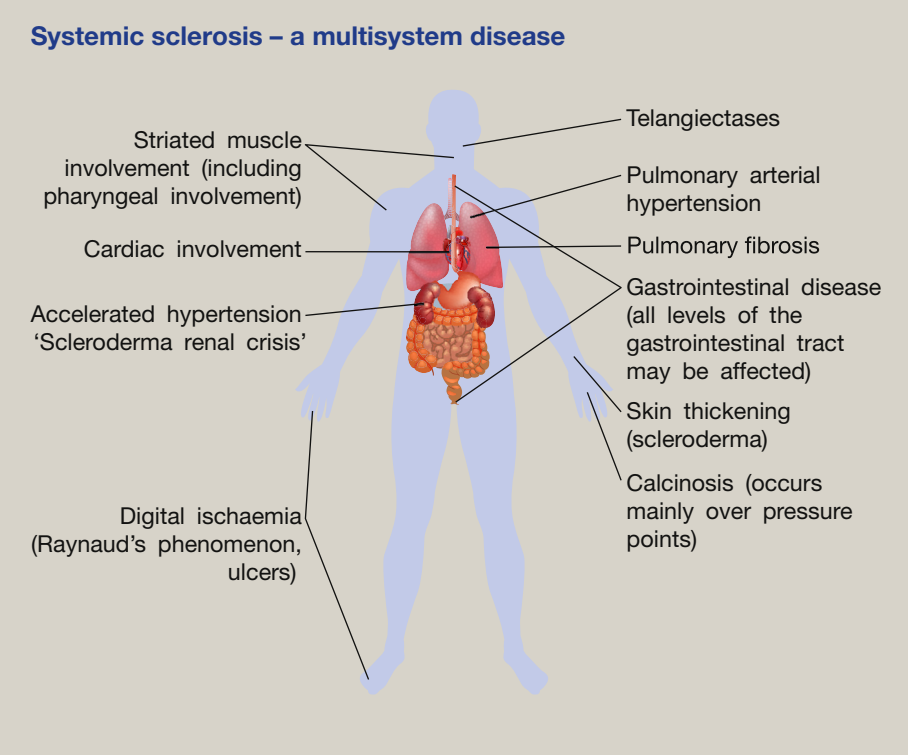

Figure 1

mainly from a combination of fibrosis and vascular abnormality. Although the fibrosis is typically seen in the skin (scleroderma), the internal organs can also be affected (e.g. pulmonary fibrosis). In addition, although the vascular abnormalities most typically affect the fingers and toes (SSc-related RP can be very severe and progress to digital ulceration and gangrene), again the internal organs can be affected (e.g. pulmonary arterial hypertension, which develops in 10–15% of patients, and scleroderma renal crisis).

Subtyping and course of the disease

The two main subtypes of SSc are defined on the basis of the extent of skin involvement.[2] In lcSSc, skin thickening is confined to the extremities, face and neck. Conversely, in dcSSc, skin involvement progresses (often rapidly) to proximal to the elbows and/or knees, so that the upper arms, thighs and/or trunk are involved. The two subtypes have very different disease courses, autoantibody associations and prognoses.

Increased recognition of the differences between these two subtypes has been a major advance because management is very different, at least in the early stages of disease. In lcSSc (the more common subtype), there is often a long history of RP before the development of other features, whereas patients with dcSSc often present with swollen, tight fingers (sometimes initially diagnosed as inflammatory arthritis), with rapid progression and a high risk of early internal organ involvement. Patients with dcSSc require close monitoring for the first 3–5 years, after which the illness tends to plateau.

Either subtype of disease can occur in overlap with other connective tissue diseases (overlap syndromes). Some patients with SSc have no skin involvement (SSc sine scleroderma).

Diagnosis

The diagnosis is based on a combination of symptoms, signs and investigation results. The 2013 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria for SSc are shown in Table 1.[3] Although these are classification rather than diagnostic criteria, they are pragmatic and helpful to clinicians in everyday clinical practice. For patients to fulfil the criteria, they must achieve a score of 9 or more. The diagnosis is often very obvious, for example in a patient with definite skin thickening including and commencing in the fingers. Skin thickening proximal to the metacarpophalangeal joints (in the absence of any other cause) is enough to make the diagnosis of SSc (Table 1).

In recent years, there has been a strong focus on early diagnosis, to allow early intervention and disease monitoring. Because RP is the most common presenting symptom, careful assessment of patients with RP provides a window of opportunity for early diagnosis, with increased recognition of the importance of testing for SSc-specific autoantibodies (Table 2), combined with increased uptake among rheumatologists of nail fold capillaroscopy (Figure 2). Puffy fingers, an SSc-specific autoantibody and abnormal nail fold capillaries are all early predictors of development of SSc in patients with RP. Although high-magnification video-capillaroscopy is currently the gold standard for examining the nail fold capillaries, lower magnification hand-held devices (e.g. dermoscopy) can also be used.

History and examination

A careful history and detailed physical examination are important in making the diagnosis, and in monitoring the patient for the different aspects of disease shown in Figure 1.

Please cite this article in press as: Herrick AL, Systemic sclerosis: clinical features and management, Medicine (2017), https://doi.org/10.1016/j.mpmed.2017.11.007