Management of Systemic Sclerosis-Related Skin Disease

A Review of Existing and Experimental Therapeutic Approaches

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KEYWORDS

- Diffuse cutaneous systemic sclerosis (DcSSc)
- Limited cutaneous systemic sclerosis (LcSSc) • Modified Rodnan skin score (mRSS)
- Digital ulcers (DU) • Raynaud's phenomenon (RP) • Methotrexate (MTX)
- Cyclophosphamide (CYC) • Hematopoietic stem cell transplantation (HSCT)

KEY POINTS

- The hallmark of systemic sclerosis (SSc) is cutaneous sclerosis, affecting nearly all patients with this rare and debilitating autoimmune disorder.
- Patients with SSc are classified based on the distribution of cutaneous involvement (ie, limited vs diffuse), and this distinction has important clinical implications.
- Existing treatment options for diffuse cutaneous SSc-cutaneous sclerosis include methotrexate, cyclophosphamide, and hematopoietic stem cell transplantation. Less evidence exists for treatment of limited cutaneous LcSSc-cutaneous sclerosis.
- All SSc patients experience Raynaud's phenomenon. After general preventative measures are taken, calcium channel blockers, prostacyclin analogs, and phosphodiesterase type 5 inhibitors are often used.
- A paucity of evidence is available for the management of digital ulcers, cutaneous telangiectasias, calcinosis, and pigment changes.

Disclosure Statement: E.R. Volkmann has no disclosures. D.E. Furst reports the following disclosures: D.E. Furst is a consultant for AbbVie, Actelion, Amgen, BMS, Cytori, Janssen, Gilead, GSK, NIH, Novartis, Pfizer, Roche/Genentech, UCB.

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Rheum Dis Clin N Am 41 (2015) 399–417
http://dx.doi.org/10.1016/j.rdc.2015.04.004 **rheumatic.theclinics.com**
0889-857X/15/$ – see front matter

INTRODUCTION

Virtually all patients with systemic sclerosis (SSc) experience cutaneous sclerosis and Raynaud's phenomenon (RP), although substantial variability in the presentation and severity of these cutaneous manifestations exist. Moreover, many patients with SSc exhibit varying degrees of additional and often disabling cutaneous manifestations, such as digital ulcers (DU), cutaneous telangiectasias, calcinosis, and pigment changes. The inherent heterogeneity in these cutaneous manifestations complicates strategies for improving patient care, as well as clinical trial design.[1,2] This review examines skin changes in SSc and how to manage them.

SYMPTOMS

Skin Sclerosis

The hallmark of SSc is skin thickening and hardening.[1] Symptoms usually first develop in the fingers and hands. Many patients experience nonpitting edema, erythema, and pruritus before the development of skin induration. Subsequently, the skin becomes firm and taut, adhering to deeper structures and limiting movement (**Fig. 1**). The presence of skin thickening of the fingers extending proximally to the metacarpophalangeal joints is characteristic of SSc and alone is sufficient to classify a patient as having SSc.[2]

As the disease progresses, the epidermis of the skin atrophies, leading to impaired hair growth and decreased sweating (ie, anhydrosis). Normal skin creases vanish, and the skin can seem to be shiny and undergo pigmentary changes. The combination of atrophy and sclerosis overflexed joints combined with a vasculopathy and dermal inflammation can cause ulceration and a reactive hyperkeratosis. The majority of patients have facial skin sclerosis, producing characteristic changes around the mouth, including increased furrowing of the skin around the lips, recession of the lips, and decreased oral aperture.

The distribution of cutaneous involvement has been classically based on the maximum extent of skin involvement.[1] In patients with diffuse cutaneous SSc (DcSSc), skin thickening occurs proximally to the elbows or knees (as well as finger/hand involvement), and often involves the trunk, whereas in patients with limited cutaneous SSc (LcSSc), skin thickening is confined to the distal extremities, or may only affect the fingers (ie, sclerodactyly; **Fig. 2**). Facial involvement is common and contributes to

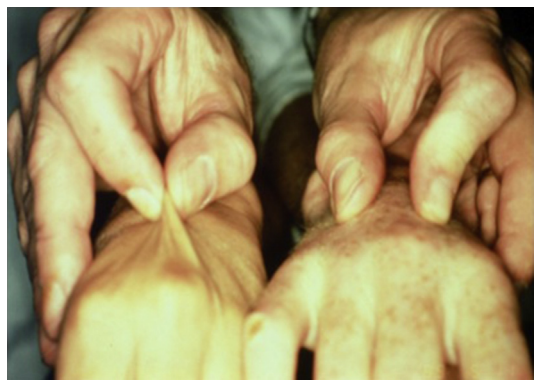

Fig. 1. Skin thickening. The left dorsal hand has normal skin thickness. The right dorsal hand has increased skin thickness. (*Courtesy of* P. Clements, MD.)