Cutaneous wounds in systemic sclerosis

KEY WORDS
- Raynaud's phenomenon
- Scleroderma
- Systemic sclerosis
- Ulcer
- Wound

Systemic sclerosis, also known as systemic or diffuse scleroderma, is an uncommon autoimmune connective tissue disease. Although not fully understood, the disease process is thought to involve immune dysfunction, vascular abnormalities and excess collagen deposition. Skin ulcers are reported to occur in up to 50% of patients and have a major impact on patients' quality of life (Khimdas et al, 2011). Specific problems include digital ulcers, ulcers over joint contractures or calcinosis, and lower limb ulcers, which can be severe and associated with gangrene. The authors describe cases of chronic wounds seen in patients with an underlying diagnosis of systemic sclerosis, highlighting the challenging nature of managing this condition for the wound specialist.

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Systemic sclerosis, or scleroderma, is an uncommon autoimmune connective tissue disease. One review article (Ingegnoli et al, 2018) estimated that the prevalence of systemic sclerosis was between 38 and 341 cases per million worldwide. The true prevalence is difficult to ascertain because of the rarity of the disease, and the small number of epidemiological studies relating to it, as well as the geographical variations in incidence and disease classification. Systemic sclerosis can affect many organs, for example, the heart, lungs, kidneys, and gastrointestinal tract, causing life-threatening complications. The mortality of the condition is high, and a review of observational cohort studies (Nikpour and Baron, 2014) found that the average life expectancy of a patient with systemic sclerosis is between 16 and 34 years less than age- and sex-matched controls.

Whilst progress has been made, the disease pathogenesis is still not fully understood. Denton and Khanna (2017) summarised the current knowledge of the aetiology and clinical features and there are both genetic and environmental factors involved. The main features in early disease involve immune dysfunction, microvascular abnormalities, and the deposition of excess collagen and other extracellular matrix components. The skin is almost always involved and is affected by progressive thickening and fibrosis, as well as pigment changes and pruritus. Diagnosis is usually based on the fulfilment of classification criteria defined by the American College of Rheumatology and European League Against Rheumatism Collaborative (van den Hoogen et al, 2013). The presence of skin thickening of the fingers on both hands, extending proximal to the metacarpophalangeal joints, is sufficient on its own to diagnose systemic sclerosis. However, there are other features which, if present in various combinations, may also indicate that the disease is present. These include organ diseases such as pulmonary artery hypertension and interstitial lung disease. Anticentromere antibody, anti-topoisomerase I and anti–RNA polymerase III are all listed as systemic sclerosis-related autoantibodies and are part of the classification system. Raynaud's phenomenon is another criteria which is commonly present and can be severe, with digital ulceration reported to occur in up to 50% of patients (Khimdas et al, 2011). This has a major impact on hand function and quality of life.

Systemic sclerosis patients can be subdivided depending on the clinical features present (Denton and Khanna, 2017). More than 95% of patients are affected by either limited cutaneous systemic sclerosis or diffuse cutaneous systemic sclerosis, with the remaining few affected by sine scleroderma. The features of each of these syndromes are described in *Box 1*. There is also

BOX 1. Subtypes of systemic sclerosis (adapted from Denton and Khanna, 2017)

Limited cutaneous systemic sclerosis (also known as CREST syndrome):

- Distal skin sclerosis (face and neck, and skin distal to elbows and knees)
- Pulmonary artery hypertension, severe gut disease, and a long history of Raynaud's phenomenon.

Diffuse cutaneous systemic sclerosis:

- Skin sclerosis of proximal limbs or trunk
- Short history of Raynaud's phenomenon
- Increased risk of renal or cardiac involvement
- Severe lung fibrosis common.

Sine scleroderma:

- Raynaud's phenomenon along with autoantibodies and other organ-based or other vascular manifestations of systemic sclerosis, but no skin changes.

systemic sclerosis overlap syndrome, which is when one of the three subtypes is found together with clinical and investigational features of another autoimmune rheumatic disease (Denton and Khanna, 2017).

The authors describe a series of patients with an underlying diagnosis of systemic sclerosis, referred to a specialist wound clinic, highlighting the challenging nature of managing this condition.

CASE ONE: LIMITED CUTANEOUS SYSTEMIC SCLEROSIS RESULTING IN BILATERAL LOWER LIMB ULCERATION

Figure 1 shows the ulcer on this patient's left medial malleolus. The other skin changes associated with systemic sclerosis can be seen; there is tightening of the skin over the foot due to fibrosis, and areas of dry scaly skin. The differential diagnosis for an ulcer with this appearance would include arterial disease, and it is important that other conditions that might result in delayed healing are considered and excluded.

CASE TWO: LIMITED CUTANEOUS SYSTEMIC SCLEROSIS RESULTING IN AN ULCER ON THE LEFT KNEE

Figure 2 shows the left knee of a patient with limited cutaneous systemic sclerosis. Fragments of calcium are visible at the base of the wound, and there were further deposits visible on X-Ray. Calcinosis (deposition of insoluble calcium salts within or beneath the skin) is a common feature in systemic sclerosis, particularly in the limited subtype.

CASE THREE: DIFFUSE SYSTEMIC SCLEROSIS RESULTING IN DIGITAL ULCERATION, SCLERODACTYLY, AND CALCINOSIS IN THE HANDS

Figure 3 shows the hands of a patient with diffuse systemic sclerosis. A number of skin manifestations of her disease can be seen here. There is sclerodactyly, or thickened and tightened skin distal to the metacarpophalyngeal joints. This is causing significant restriction in hand function. There is evidence of calcinosis in the skin around the interphalyngeal joints. There are multiple areas of ulceration, which are secondary to the calcinosis in places, but also the typical painful ischaemic ulcers caused by Raynaud's phenomenon. This can be treated with a vasodilator, such as Sildenafil. In cases where treatment is unsuccessful, digital amputation can be required to treat gangrene.

CASE FOUR: LIMITED CUTANEOUS SYSTEMIC SCLEROSIS RESULTING IN PRE-TIBIAL ULCERATION WITH CALCINOSIS

Figure 4 shows the right leg of a patient with limited cutaneous systemic sclerosis. There is obvious calcinosis which was contributing to this wound. Where possible, superficial pieces like this can be debrided in clinic, to increase healing and reduce the risk of infection. It can also be seen that the circumference of the leg is small, indicating a low body mass index. Dysphagia (difficulty swallowing) is common in limited systemic sclerosis as a result of oesophageal stricturing and dysmotility. Inadequate nutrition is a further challenge to successful wound healing.

DISCUSSION

Systemic sclerosis can result in severe skin problems, presenting a challenge to the wound care practitioner. As with any ulcer, the management needs to be holistic and the underlying diagnosis

A REVIEW OF 4 CASES FROM A COMPLEX WOUND CLINIC

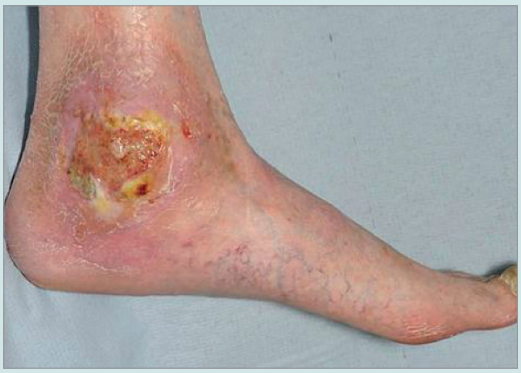


Figure 1. Case one: medial malleolus ulcer

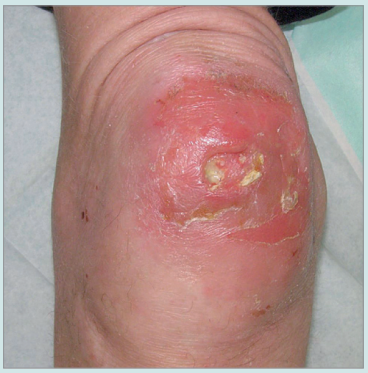
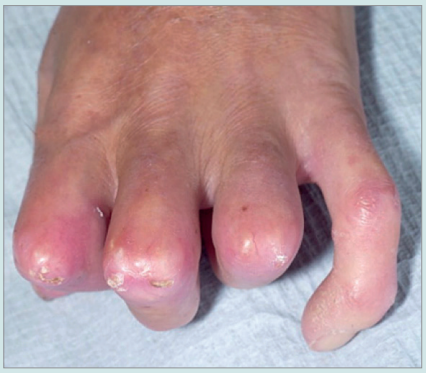


Figure 2. Case two: ulcer with calcinosis over the knee joint



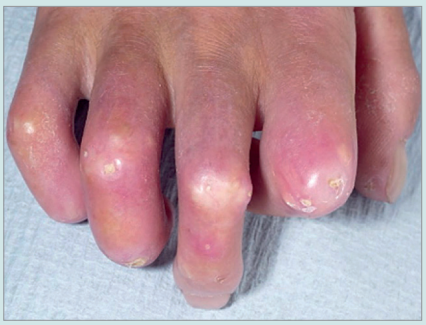


Figure 3. Case three: digital ulceration, sclerodactyly and calcinosis in the hands

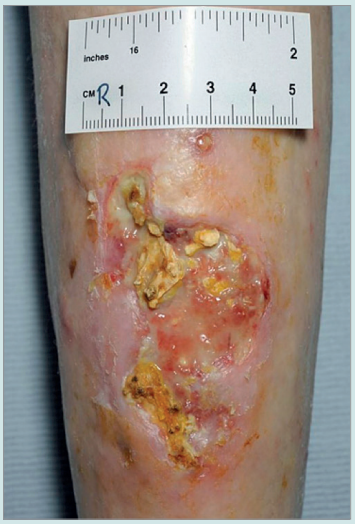


Figure 4. Case four: pre-tibial ulceration with calcinosis

is key. In cases of systemic sclerosis, early recognition, with referral for management by a specialist centre is important. As discussed, the disease is rare and has a heterogeneous course so a specialist team is likely to be best-placed to carry out diagnostic evaluation and oversee treatment. Internal organ involvement of the heart, lungs, kidneys, and gastrointestinal system needs to be monitored and treated. Additionally, there may be other medical problems pertinent to the wound aetiology. In terms of wound management, dressing choice should be made on the basis of local wound assessment, taking into consideration the wound base, edge, and surrounding skin, and the presence of factors such as infection. As Raynaud's phenomenon is exacerbated by the

cold, specialist warming gloves may be helpful. The evidence base varies for different aspects of care in systemic sclerosis. As might be expected in a rare condition, there is not always a randomised-controlled trial to guide management. There are a number of guidelines that provide consensus-based advice on the evidence available. The British Society for Rheumatology (BSR) and British Health Professionals in Rheumatology (BHPR) joint guideline for the treatment of systemic sclerosis (Denton et al, 2016) details some specific recommendations for skin care. In all cases, measures to ensure skin is adequately moisturised should be taken, and lanolin-based emollients are specifically recommended. Antihistamines may be used for itch. As illustrated by Case Two and and Case Four, calcinosis may be a feature. Calcinosis can be complicated by infection, and antibiotics may be required. If it is severe and refractory, and seriously impacting function and quality of life, then surgical intervention should be considered, however, the evidence for this is limited, consisting of case reports and small series.

There is a larger body of evidence to guide management of Raynaud's phenomenon and digital ulceration. This was summarised by the European League Against Rheumatism (EULAR) Scleroderma Trials and Research group (EUSTAR) in their recommendations (Kowal-Bielecka et al, 2009). For digital ulceration, integrated management by a multidisciplinary team is recommended. Oral vasodilators, such as Nifedipine or Sildenafil, and analgesia are the mainstay of medical treatment. In severe acute digital ulceration or refractory or recurrent ulcers, intravenous prostanoids or phosphodiesterase inhibitors or endothelin receptor antagonists may be required (under specialist supervision).

CONCLUSION

The cases illustrate the severity of skin complications that can occur in systemic sclerosis. The majority of patients with systemic sclerosis will have symptoms as a result of skin changes, and these often have a major impact on the patients' quality of life. The management strategies for skin problems are also described. Multidisciplinary input is important in patients with systemic sclerosis to ensure optimal care, however, management should be led by a specialist centre. WUK

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