Chapter 10
Digital Ulcers

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Introduction

Digital ulcers (DU) are common (Fig. 10.1) in patients with SSc and are a major non-lethal complication associated with the disease. Around half of patients report a history of DUs [1, 2]. Common sites for DUs include the fingertips and over the dorsal aspect of the fingers [2]. They can also occur on the lower limbs/toes [3]. Fingertip DUs are ischaemic and driven by the progressive vasculopathy observed in SSc. Whereas, dorsal aspect DUs are driven by the progressive thinning of the skin/contractures and recurrent trauma to these exposed surfaces. DUs can also develop from existing digital pitting scars and in relation to underlying calcinosis [2]. They can also occur on the lateral aspects of the digits and at the base of the nail (Fig. 10.1).

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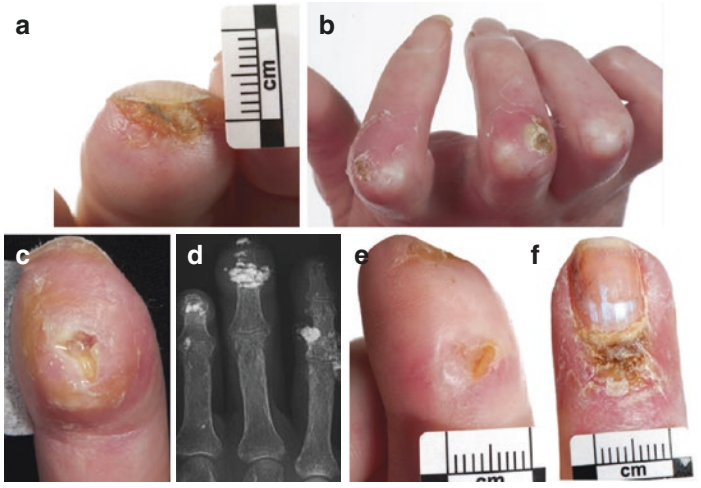

Figure 10.1 SSc-DUs. Fingertip (**a**), extensor (**b**), overlying subcutaneous calcinosis as seen on a plain radiograph (**c** and **d**, respectively), and on the lateral aspect (**e**) and the nailbed of the fingers (**f**). Reproduced with permission [10]

Microvascular and Microvascular Assessment

Both microvascular and macrovascular involvement are implicated in SSc-DUs. The progressive microangiopathy (e.g. enlarged capillaries with areas of avascularity) which characterises the SSc disease process is easily appreciated by nailfold capillaroscopy. Although videocapillaroscopy (magnification ×200–600) is considered the 'gold standard', capillaroscopy can also be performed using a number of other lower-magnification techniques such as the dermatoscope [4] or USB-microscope. A number of authors [5–7] have reported that nailfold capillaroscopic abnormalities are highly predictive of the development of future DU (and in their absence are reassuring to the clinician). Thermography which measures surface temperature can differentiate between patients with primary and secondary Raynaud's

phenomenon (RP) [8], however, at present its use is limited to a number of specialist centres. A key point is the need to distinguish between primary ('idiopathic) and secondary RP (i.e. due to an underlying medical condition such as SSc) because patients with PRP do not develop ischaemic tissue damage such as DUs. Macrovascular involvement is a very important feature that must not be neglected including abnormalities of the digital and ulnar arteries. An increased risk of cardiovascular disease has also been reported in patients with SSc [9]. The peripheral pulses should be assessed in all patients with digital ischaemia. Arterial Doppler scanning should be performed early if there is any clinical suspicion of proximal (large) vessel disease and confirmed by large vessel imaging [10]. Large vessel disease should be identified early as this potentially could be amenable to successful therapeutic intervention.

Pain Evaluation and its Management

SSc-DUs can be exceptionally painful and disabling, and therefore the evaluation of pain is mandatory. A simple method to evaluate pain is to perform a visual analogue scale using a 10 cm long line in which the patient indicates their level of pain (the left being the lowest possible and the right representing the highest). Such an approach can be used to track DU progression/healing and to inform changes in pain management. Patients not uncommonly require strong (i.e. opioid-based) analgesia. Nocturnal pain can be very disabling and can significantly disturb sleep. A key approach is to consider and identify DU infection early and to treat with appropriate anti-microbial therapy, as this may contribute to the patient's pain generation. Severe pain and tenderness are a potential indication for surgical intervention which can suggest the collection of pus and/or necrotic material [11]. This should be suspected where palpation of the DU is associated with significant pain [11].

Disability and Functionality Assessment and its Management

As previously described, DUs are associated with significant disability including all of the activities of daily living and occupation. In routine practice it is very important for the clinician to actively ask about function including the activities of daily living/occupation during their consultation. The impact of SSc-DU on personal relations including emotional health, sexual relationships and social participation should also be examined. There is no disease-specific patient reported outcome instrument to assess the severity and impact of SSc-DUs. In general, there is a reliance of legacy instruments to assess the patient experience of SSc-DUs [12]. Patients should be managed as part of a dedicated multidisciplinary team including (but not limited to) physicians, nurses and physiotherapists who understand the challenges of caring for patients with SSc [13]. The goal is to identify any associated disability and functional impairment early so that patients can receive prompt intervention. For example, specialist input from colleagues in physiotherapy and occupational therapy for issues relating to physical function and the activities of daily living.

Complications and Their Management

Infections are a frequent complication of SSc-DUs, and are often caused by *Staphylococcus aureus*, *Pseudomonas aeruginosa* or faecal pathogens. As previously discussed, infection can cause significant pain and is associated with the presence of the signs of inflammation [14].

Although rare, fistula can develop from infection, representing a communication between the DU and a deeper layer of the skin (in particularly in calcinosis induced DU) [15]. Fistulae can be suspected in the case of the appearance of a second satellite lesion, depression of wound edges or, when aboundant exudate is present [15].

Infections can spread to the surrounding soft tissues, causing cellulitis, or to the bone, resulting in ostomyelitis. While elevated acute phase reactants and/or an increase in the neuthrophil count may raise the suspicion of presence of infection, radiographs and MRI are considered the first line and confirmatory tests for osteomyelitis, respectively. Osteopenia and periosteal reactions on radiography guide the clinician to request a MRI scan, showing the presence of bone oedema if there is bone Infection [14].

Gangrene represents the most severe DU complication. This should be suspected when a line of demarcation appears, representing the inflammatory reaction dividing dead and living tissues [16]. Gangrene can present as a dry, dark coloured area, evolving into dehydration and rarely mummification, otherwise as wet, when bacterial infecion determine purulent liquefaction [16]. The latter is frequently associated with soft tissue oedema, maceration and a characteristic odor. In the case of gangrene, it is mandatory to evaluate macrovascular blood flow, in order to exclude vascular stenosis/large vessel disease (.e.g. by performing Allen's test and Doppler ultrasound) [16].

Local Treatment: Wound Bed Preparation

The principles of local treatment of DUs are derived from the "Wound bed preparation" algorithm from diabetic ulcer care, which includes all the possible intereventions which favour lesion healing. All these concepts are included in the acronym "TIME" [17]: "T" for tissue management, which includes a deep agitation to remove dirt, necrotic tissue and remnants of previous dressings, and allows tissue evaluation [18]. This is followed by evaluation of "I", including both inflammation/infection, which should be suspected in the case of redness and swelling of surrounding skin and in case of exudate/purulent slough in the wound bed [18]. Once washed, DU should undergo debridement to remove all necrotic tissues which may prevent the lesion from promot-

ing self-healing. Debridement requires adequate anesthesia to be perfomed physically with a scalpel [19, 20], otherwise this can be done chemically, using autolytic dressings, such as alginate for exudating wounds or hydrogels and hydrocolloids for dry or poorly exudating wounds. The general status of "M", the moisture balance of the wound, is of pivotal importance: as both excessive dryness or exudation are not efficient in promoting wound healing, and an appropriate dressing choice should help in restoring a correct hydration status [21]. Finally, DU edges ("E") evaluation is important, as it reflects the attempt and the evolution of healing, from periphery to centres and from bottom to top: hyper-proliferation or undermining of the edges should always be checked and locally treated [18].

Systemic Treatment: Healing and Prevention

Systemic medical treatment (Fig. 10.2) is of pivotal importance and aims at both preventing and healing DUs [22]. Prevention includes education of the patient in cold exposure and trauma avoidance and pharmacological treatment of Raynaud's phenomenon, which commonly includes calcium-channel blockers. DU vasodilating and vasoactive treatments targets the three main pathways of SSc vasculopathy: prostanoids, in particular intravenous Iloprost over 3–5 days, which compensates for prostacyclin deficiency, and have proven efficacy in DU healing and preventing DU recurrency when administered chronically [23, 24]. Similarly, phosphodiesterase 5 inhibitors restore the lack of nitric oxide. The SEDUCE trial showed a trend for higher DU healing rate, in particular when used in combination with Bosentan [25]. Endothelin 1 receptor antagonists, i.e. Bosentan, have a vasoactive effect, promoting vasodilation and vascular-remodelling. Both the RAPIDS-1 and RAPIDS-2 studies showed beneficial effect in DU prevention, and this was more significant in those patients with more than 3 DUs [26, 27].

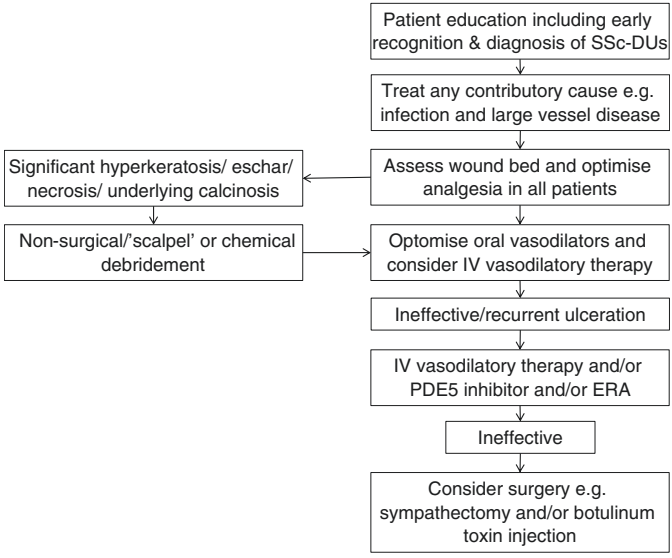

FIGURE 10.2 The management of SSc-DUs. Adapted from the UK Scleroderma Study Group Best Practice Recommendations on the management of DUs in patients with SSc [10]. ERA: Endothelin receptor antagonist. IV: Intravenous. PDE5: Phosphodiesterase type-5

In the case of non-resolving local infection when treated with topical anti-septic dressings or systemic infection, then systemic antibiotic treatment is of pivotal importance. This can include empirical treatment with broad-spectrum drugs, obtaining a swab sample with microbiologic isolation, and then targeted antibiotic therapy (Fig. 10.3). Hospitalisation for intravenous treatment is indicated for cases of septic/ osteomyelitis evolution [28].

In the case of medical treatment failure, then surgical options should be considered. Botulinum A toxin injection is a mini-invasive procedure, promoting local arterial vasodilation [29]. The same effect can also be obtained with a deep-surgical peripheral sympathectomy [11]. As a promising rescue treatment, a single injection of autologous fat tissue derived stem cells has proven to be effective in DU healing [30].

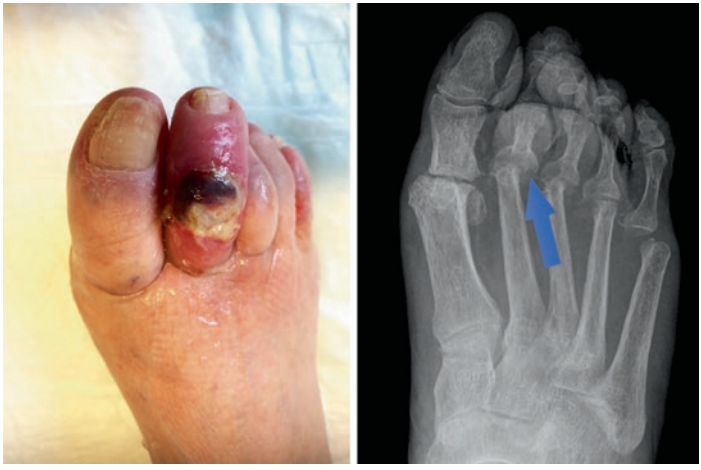

Figure 10.3 Management of SSc-DU. A 55 years old female patient with limited SSc and overlap with anti-phospholipid syndrome presented with a painful ulcer on the second toe of the right foot. Despite common vasodilating and vasoactive treatments, combined with wound bed-preparation and local dressings, the ulcer remained very painful and did not tend to improve. When radiography was performed, an area of bone reabsorption was seen at the basis of the proximal phalanx of the second toe (blue arrow), and was later confirmed by MRI as compatible with ostomyelitis. Treatment with Ciprofloxacine and Trimetoprim-Sulphametoxazole was used in association with the above mentioned treatment, with final ulcer healing

Conclusion

DUs are common and represent a serious complication of SSc. Different types of DU exist based upon the underlying pathophysiology. Microvascular and macrovascular assesment is needed. Both medical and surgical options are available to treat SSc-DUs. Careful attention must be paid to wound bed management and the treatment of complications (e.g. infection). Associated pain and disability/impairment of function must be identified and managed appropriately.

Through prompt assessment and the initiation of targeted treatment for DUs, clinicians can preserve patients hand function and prevent the development of devastating ischaemic tissue loss.

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