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Autoimmunity Reviews 5 (2006) 125–128
AUTOIMMUNITY REVIEWS
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Digital ulcers in patients with systemic sclerosis

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Available online 13 September 2005

Abstract

Digital ulcers (DU), defined as necrotic lesions located at distal digits or overlying bony prominences, occur in up to 50% of patients with limited or diffuse systemic sclerosis (SSc). These lesions are extremely painful and lead to substantial functional disability. The pathogenesis of DU differs depending on their location. DU located at distal aspects of digits are thought to be related to tissue ischemia from several processes, including vasospasm secondary to Raynaud's phenomenon, intimal fibroproliferation, and thrombosis of digital arteries. DU located over bony prominences, such as the phalangeal joints and elbows, are thought to be due to repetitive microtrauma and difficulty healing due to atrophic, avascular tissue overlying the joints. Management of DU include non-pharmacologic and pharmacologic modalities. This review summarizes the current available and investigational therapies for the treatment and prevention of DU in patients with SSc.

Keywords: Raynaud's phenomenon; Digital ulcers; Systemic sclerosis

Contents

1. Introduction

Systemic sclerosis (SSc) is a connective tissue disease characterized by cutaneous and visceral fibrosis, as well as vascular disease involving arterioles, and small and medium arteries of the peripheral circulation. Raynaud's phenomenon (RP), defined as color changes of the digits induced by cold exposure and other stimuli, is the most common manifestation of vascular abnormalities in SSc [1]. Digital ulcers (DU), defined as necrotic lesions that occur either at distal aspects of digits or

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doi:10.1016/j.autrev.2005.08.004

over bony prominences [2], occur in up to 50% of patients with limited or diffuse SSc [3]. These lesions are exquisitely painful, heal slowly, and lead to substantial functional disability. Other complications associated with DU include scarring and loss of distal tissue, infection, and progression to gangrene requiring amputation. This review summarizes the current information regarding pathogenesis, management, and investigational treatments of DU in patients with SSc.

2. Pathogenesis of DU in SSc

The pathogenesis of DU is thought to differ depending on whether the lesions are located at distal digits or overlying bony prominences [2]. DU that develop at distal aspects of digits (Fig. 1A) are thought to be due to progressive tissue ischemia with resultant injury induced by oxygen free radicals [2]. Persistent vasospasm secondary to RP is a contributing factor to impaired tissue oxygenation and to the development of DU [4]; however, the frequency and duration of RP attacks has not been shown to correlate with the presence of DU [5].

The underlying vasculopathy in patients with SSc is another factor leading to ischemic tissue damage of distal digits. Histologic evaluation of digital arteries from patients with SSc demonstrates intimal proliferation with fibrosis, resulting in greater than 75% luminal narrowing [6]. In addition, endothelial cell injury, possibly mediated by antiendothelial cell antibodies in some patients, results in an increased production of vasoconstrictors such as endothelin, and a decreased production of vasodilators such as prostacyclin and nitric oxide [2].

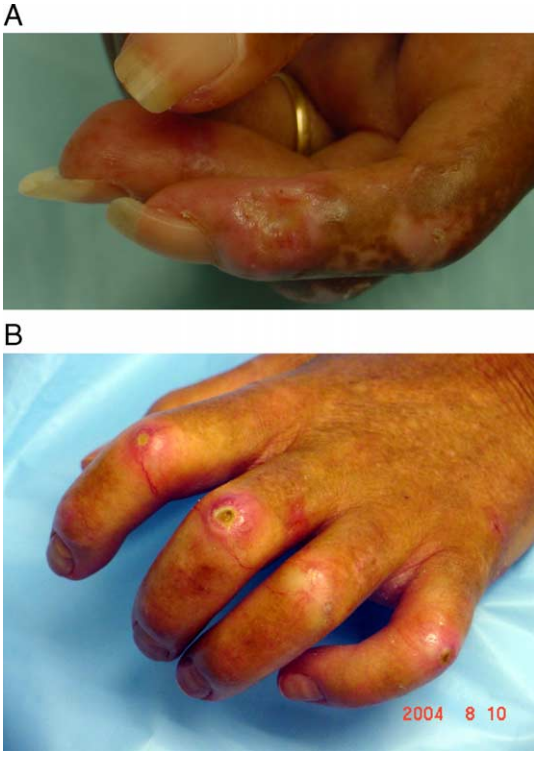

Fig. 1. (A) Digital ulcer located at distal aspect of a digit. (B) Digital ulcers overlying contractures at the proximal interphalangeal joints.

Another factor that may play a role in the development of ischemic ulcers at distal digits is intraluminal thrombosis [4]. Platelet activation has been shown to be a prominent feature of sclerodermatous vasculopathy, leading to clot formation as well as release of vasoconstrictors such as thromboxane [7].

In contrast to DU located at distal digits, the development of DU located over bony prominences (Fig. 1B), such as the phalangeal joints and elbows, is thought to be related to repetitive trauma at sites of chronic contractures [2]. The avascular, atrophic nature of the tissue overlying these sites results in vulnerability to injury and impaired healing [2]. These lesions are thought to be less affected by vasodilating therapies than DU located at distal digits.

3. Management of DU in SSc

Management of DU in SSc involves non-pharmacologic and pharmacologic modalities for treatment and prevention of these lesions (Table 1). Non-pharmacologic therapies include avoidance of triggers of RP such as cold exposure, emotional stress, or vasoconstricting drugs [2]. Although smoking has not been shown to be directly correlated with the frequency of RP attacks [8], avoidance of nicotine exposure in patients with SSc is essential to prevent accelerated vasculopathy and resultant ischemic tissue injury. Patients should also make every effort to avoid trauma to sites prone to ulceration. Occlusive dressings may be helpful in both protecting areas from recurrent trauma as well as promoting healing of lesions. Topical hydrocolloid dressings have been shown in a randomized controlled trial to promote healing of DU, however, they are difficult to secure effectively and require frequent dressing changes [9].

Several pharmacologic therapies for the treatment and prevention of DU are currently available for clinical use. Supportive therapies such as pain medications and antibiotics are critical in the treatment of DU. Patients commonly require narcotics for pain control and multiple courses of systemic oral antibiotics are frequently necessary to treat superinfected DU. Persistent infections can spread to underlying bone with resultant osteomyelitis, requiring prolonged courses of intravenous antibiotics [4].