

LETTER TO THE EDITOR

A possible explanation for the high frequency of contact sensitisation in chronic venous ulcers

Dear Editors,

A 62-year-old woman was referred to our department for an itchy eruption on the left leg that had appeared 2 weeks into a bandage treatment with Iruxol ointment (a mixture of collagenase clostridiopeptidase A and proteases) (Figure 1A). Based on patient history and vesicular appearance of lesions, a diagnosis of contact dermatitis to Iruxol, confirmed by patch testing (Figure 1B), was made. Suspension of the causative ointment and a 2-week therapy with topical corticosteroids induced remission of the condition (Figure 1C).

Allergic contact dermatitis is a T-cell-mediated inflammatory reaction (delayed-type hypersensitivity reaction) to a contact allergen (hapten), occurring at the site of challenge in sensitised individuals. Classically, its pathophysiology consists of two distinct phases: the sensitisation and the elicitation phases, which are considered to be temporally and spatially dissociated (1).

Patients with venous ulcers are often treated with a large variety of dressings and ointments to which they frequently acquire contact sensitisation. A high incidence of allergic contact dermatitis in patients with venous ulcers or even with simple stasis dermatitis has been well-documented (2). These patients often have multiple sensitivities to a large series of medications, including lanolin and rubber, although the pattern of allergens appears to be changing, and this change is likely to be determined by local wound care practice (2).

Many influencing factors have been hypothesised to be involved in the pathogenesis of this phenomenon: intrinsic genetic predisposition, lipophilic galenics, use of occlusion and the disrupted skin barrier, with an increased permeability

and inflammation of the skin upon which the wound care products are applied (2). Although interesting, these hypotheses fail to give a unified pathogenic view capable of explaining this common incidence of contact dermatitis in patients with venous leg ulcers.

Allergic contact dermatitis is more frequently observed in patients with a long history of venous ulcer therapy, indicating an overactivation of local immune response in phlebolympoedematous legs. Zmudzinska *et al.* hypothesised that high frequency of contact sensitisation in patients with venous ulcers has a pathogenic relationship with chronic venous insufficiency (3). Signorelli *et al.* (4) found increased levels of tumour necrosis factor α (TNF α), interleukin (IL)-1 β and IL-6 in monocyte cultures obtained from patients with venous hypertension, which are considered the most powerful immunity activators.

As recently hypothesised by Ruocco *et al.*, phlebolympoedema could be considered as a cause of immunocompromised district (ICD) (5), that is, a cutaneous site particularly susceptible to subsequent outbreaks of opportunistic infections, tumours and immune-related disorders, confined to the district alone (3). Many different causes have been recognised as capable of inducing an ICD and thereby predisposing patients to harbouring opportunistic disorders (6): chronic lymphoedema, herpetic infections (Wolf's isotopic response), vaccination, physical injuries (ionising or UV radiation, thermal burns and traumas) and also neurologic disorders such as carpal tunnel syndrome (7) and hemiplegia (8). The term 'immunocompromised' refers to a generic alteration of the immune response, and not necessarily a reduction

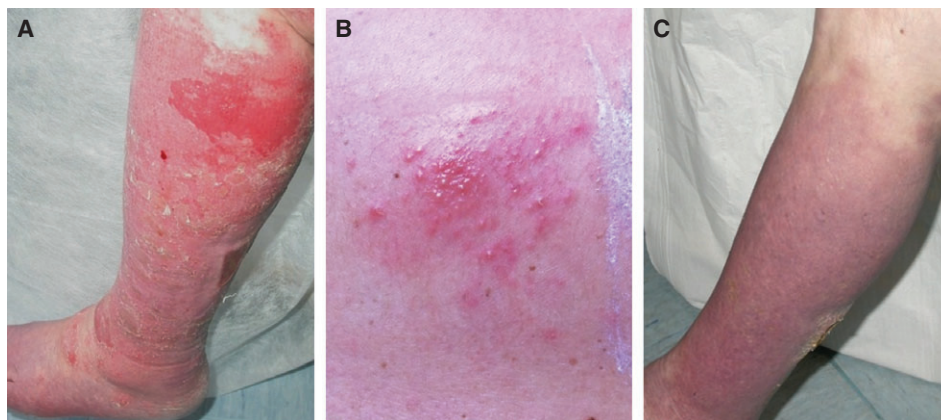


Figure 1 (A) Erythema, oedema and vesicles on leg skin treated with Iruxol ointment. The ulcerous lesion is visible on the back of the leg. (B) Patch test for Iruxol showing the vesicular reaction (++). (C) Aspect of leg skin after topical corticosteroid treatment. Hyperpigmentation follows healing of contact dermatitis.

of it (6–8). An imbalance between immune-suppressive and immune-stimulating neuropeptides could explain the variegated immune response possible in ICD, either defective (infections and tumours) or excessive (immune-mediated diseases such as pemphigus, bullous pemphigoid and contact dermatitis) (5–8).

On the basis of the pathogenic theory explained above, contact dermatitis in patients with venous leg ulcers thoroughly fulfils the criteria of ICD in which there would be an excessive immune response, favouring the sensitisation to products used for wound care.

In conclusion, the application of this pathomechanism to address the high frequency of contact dermatitis in patients with venous leg ulcers enlarges the wide and expanding spectrum of ICD. Moreover, it indicates how an alteration of the complex and delicate equilibrium between local immune cells and neuropeptides could produce such a variegated group of disease.

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