

Reflex Sympathetic Dystrophy

Occurrence of Inflammatory Skin Lesions in Patients With Stages II and III Disease

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• Reflex sympathetic dystrophy is a poorly understood syndrome of posttraumatic pain and sympathetic nervous aberration. We have observed previously unreported cutaneous manifestations of reflex sympathetic dystrophy. Seven patients with reflex sympathetic dystrophy were referred to our institution because of skin disorders. Three had recurrent ulcerating papules, and two had reticulate hyperpigmentation. Xerosis was common, and cutaneous atrophy was infrequent. Cutaneous ulceration and reticulate hyperpigmentation are previously unappreciated aspects of reflex sympathetic dystrophy. Further investigation regarding neural influences on the skin is warranted.

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Reflex sympathetic dystrophy (RSD) is a well-described but poorly understood syndrome^{1,2} that most frequently follows peripheral trauma. It is a staged process that evolves over time. In stage I disease, there is most often clear overactivity of the sympathetic nervous system with hyperhidrosis, cutaneous vascular instability, swelling, and characteristic burning pain. In stage II of the illness, abnormal movements, spread of the process, and increasing burning pain are most prominent.^{3,4} Stage III disease is a combination of all aspects of the earlier stages, but autoimmune, inflammatory, and atrophic changes are noted in affected areas.⁵

Cutaneous changes may be prominent in any stage of RSD but are most often seen in patients with stage III disease. Detailed reports of skin abnormalities are few

and center around the vascular changes seen in the early stages of disease.^{3,7} Cutaneous atrophy or "dystrophy" is often listed as a common finding. We recently encountered seven patients with long-standing RSD and noted several unusual cutaneous findings.

PATIENTS

Each patient in the series was referred by his or her neurologist for treatment of the skin manifestations of RSD. Each patient fulfilled established criteria for a diagnosis of RSD.¹ The salient features of each patient are presented in the Table.

COMMENT

Patients with RSD usually present for medical attention with severe and unremitting pain following trauma or surgery. The onset may be sudden but usually occurs several weeks after the tissue injury. The pain has a burning quality, and the patient usually complains of dramatic hyperalgesia. After several weeks to months, neurovascular changes develop. The skin has a mottled appearance, and there is marked cold intolerance. Hyperhidrosis is common in the affected area. Pain persists and may involve larger areas of the body. Stage II disease usually begins within the first 2 years following the original trauma. The skin during this phase is smooth, cool, and dry, and the nails may be brittle. Although pain occasionally resolves, it is more often severe during this stage. Osteoporosis, especially of the involved bone, may be notable.^{1,2}

Each patient in our series had had RSD for a substantial period and was disabled to some degree by the disease. The skin findings in this group of patients could be divided into two broad categories: (1) inflammatory papules and macules that tended to ulcerate and (2) pigmentary alterations that were believed to be postinflammatory. Two patients had a reticulated hyperpig-

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Summary of Patients*						
Sex/Age, y	Duration of RSD	Skin Findings	Bopsy Findings	Immune Complex	Erythrocyte Sedimentation Rate, mm/h	ANA
F/31	3	Superficial ulcerations, erythematous papules, leg edema	Reactive perforating collagenosis, granular C3 in papillary dermis	Normal	Normal	Normal
F/27	2	Superficial ulcerations, xerosis, erythematous papules, mild atrophy, leg edema	Neutrophilic folliculitis, lymphohistiocytic perivascular, IgM and C3 at DEJ, C3 in vessels	Normal	22	Normal
F/24	2	Pruritic/burning papules mostly on extremities, excoriations, xerosis, edema	Neutrophilic folliculitis, dermal perivascular lymphohistiocytic, immunofluorescence negative	Slight elevation C1q binding, normal Raji cell	Normal	Normal
F/51	4	Reticulate erythema progressing to hyperpigmentation, xerosis	Postinflammatory hyperpigmentation, immunofluorescence negative	Slight elevation Raji cell C1q normal	Normal	Normal
F/48	1-2	Reticulate hyperpigmentation and erythema	Sparse perivascular lymphocytic infiltrate, weak and IgM and C3 in papillary vessels	Normal	Normal	Normal
F/58	20	Edema and stasis dermatitis, postinflammatory hyperpigmentation	Postinflammatory pigmentation, immunofluorescence negative
F/29	2-3	Telangiectasia, petechiae	Immunofluorescence negative	Normal	Normal	Normal

*RSD indicates reflex sympathetic dystrophy; ANA, antinuclear antibody; and DEJ, dermal-epidermal junction.

mentation reminiscent of a resolving livedo vasculitis or early erythema ab igne. One of these patients reported limited use of a heating pad, and all patients had some degree of xerosis. In this group of patients, atrophy was substantially less prominent than implied in the literature. One patient (patient 3) had notable localized atrophy and xerosis that dramatically resolved within 2 weeks following effective sympathetic blockade. Edema, usually in the lower legs, was present in four of the seven patients.

The areas of erosion or excoriation were distinctive. These lesions were largely limited to regions that were exposed to trauma and were accessible to the patient (Figs 1 and 2). The morphologic structure of the lesions was occasionally linear and was strongly reminiscent of a factitial lesion. In one case (Fig 3), similar lesions appeared at the site of prior lidocaine injection. Routine histopathologic examination showed nonspecific changes in the majority of patients with ulcerations. One patient had a histologic diagnosis of reactive perforating collagenosis that may be unrelated to the RSD. Only one patient had a mildly elevated erythrocyte

sedimentation rate, a prevalence substantially lower than the 78% previously reported.⁷ Direct immunofluorescence of lesional skin revealed weakly positive immune deposits predominantly in the vessels of the dermis in three of seven patients. This was interpreted as being consistent with but not diagnostic of an immune complex vasculitis but probably represented nonspecific deposition. Circulating immune complexes were identified in low titer in two of the seven patients, and cryoglobulins were present in one patient. In all cases, the erosions healed without scarring, leaving areas of quickly resolving postinflammatory hyperpigmentation (Fig 4).

The excoriations and erosions were resistant to treatment, and their course did not seem to be affected by treatment with topical and/or oral steroids, antihistamines, or oral and topical antibiotics. Emollients afforded some relief, as did light occlusive dressings. Topical capsaicin, which was previously reported to be effective,^{8,9} was not tolerated by either of the two patients for whom it was prescribed. In all cases, treatment of the patients was made more difficult by the



Fig 1. — Erosions on the trunk of patient 1.

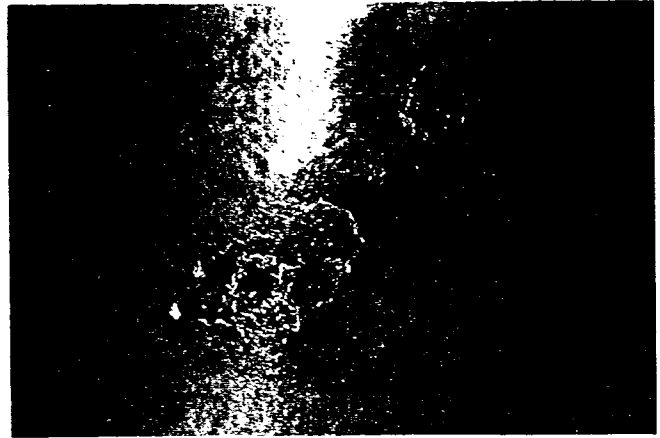


Fig 3. — Superficial erosions on the skin of patient 1. The three lesions in the center of the photograph represent a punch biopsy site flanked by two erosions at the site of prior lidocaine injection.



Fig 2. — Superficial erosions on the extensor part of the arm of patient 3

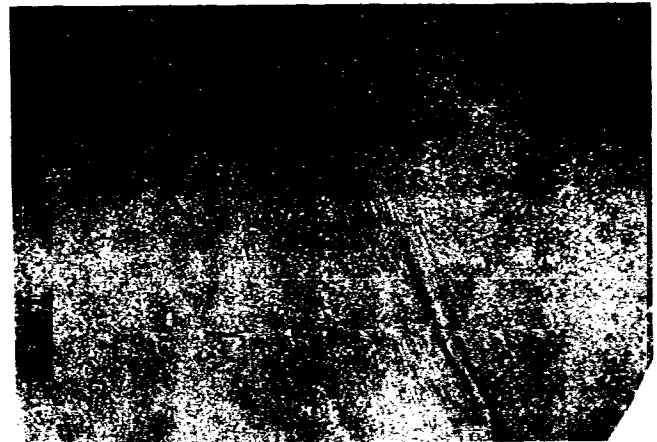


Fig 4. — Reticulate hyperpigmentation on the flank of patient 4.

presence of hyperalgesia in the involved area, which limited the ability of the patient to comply with topical therapy.

Most of the previously described skin manifestations of RSD involve the vascular reactivity seen early in the course of the disease.¹⁷ Stage I disease manifests signs of cutaneous vasodilation. The latter two stages, stages II and III, are primarily vasoconstrictive, with evidence of pallor and cyanosis. In contrast, we have found that patients who are diagnosed as having stages II and III RSD frequently have evidence of inflammatory changes in their skin. Two of our patients had skin changes suggestive of a livedolike syndrome, and three others had erythematous papules that progressed to ulceration, findings not previously described in RSD. The cause of these skin lesions is obscure. When considered on a case-by-case basis, it is hard to determine whether the erosions are factitial; however, a series of patients with RSD with strikingly similar lesions points to a common underlying mechanism. The presentation of the erosions argues strongly against skin fragility being central to the process, as the erosions are described as arising from tender erythematous macules

with no traumatic antecedent. There is no evidence of bullae or milia, and the lesions healed without scarring.

One potential explanation for some of these findings lies in an unusual response to trauma. A trivial insult might provoke sufficient inflammation to trigger a visible lesion, consistent with the observation in one patient that lesions appeared at the site of lidocaine injection (Fig 3). Potential mechanisms for this sort of inflammation might be linked to the presence of circulating immune complexes in these patients. Any cause of increased vascular permeability could result in the local deposition of immune complexes and in the onset of an inflammatory response. The somewhat archaic "histamine trap test," in which a small amount of histamine injected into the skin of a patient with circulating immune complexes results in immune complex deposition in the skin, could be considered a model for the lesions observed in these patients. Patients in this study were found to have evidence of deposition of immune complexes in the blood vessels of lesional skin. Two patients had mildly elevated circulating immune complexes. Despite these suggestions, definitive statements cannot be made based on these data, as inflammation of many

different causes can result in the deposition of immune reactants as an epiphenomenon.

An alternative mechanism for some of these lesions may be the phenomenon of reflex neurogenic inflammation. Animal studies have clearly demonstrated that injury to one hindlimb can produce swelling in the noninjured limb.^{9,10} Levine and colleagues⁴ have described a system in which inflammation can be detected in the limb contralateral to the traumatic stimulus. This inflammation can be blocked by denervation of either limb or by the application of capsaicin, which depletes substance P from small, thinly myelinated sensory fibers. A model of neurally mediated joint inflammation was recently found to involve mast cells, perhaps as an amplifier of inflammation.¹¹

Further study of patients with RSD will shed light on the interplay between the nervous and vascular systems in the maintenance of skin integrity. The reversible atrophy observed in patient 3 suggests that a neural influence on the skin may play an important role.

Immunofluorescence testing of biopsy specimens was performed by Immco Diagnostics, Buffalo, NY.

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