

Local Reactions Associated with Subcutaneous Injections of Both β -interferon 1a and 1b

Sir,

Recombinant β -interferon 1a and 1b are used in the treatment of multiple sclerosis, amongst other pathologies. About 40% of multiple sclerosis patients develop cutaneous reactions at the injection site of β -interferon, but skin necrosis is rare (1, 2). These reactions have rarely been reported during treatment with β -interferon 1a (3). We describe here a patient who presented with cutaneous necrosis at the injection sites of β -interferon 1b and persistent infiltrated erythematous plaques after subcutaneous application of β -interferon 1a.

CASE REPORT

A 44-year-old woman, who had been diagnosed as having multiple sclerosis in April 1997, started treatment with β -interferon 1b, 8×10^6 IU s.c. on alternate days, in September 1998. From the first dose, she developed a local erythema at the injection sites, which resolved spontaneously in 1 or 2 days. After 6 months of treatment, persistent painful erythematous nodules appeared at the injection sites, some of which evolved into skin necrosis after 4 or 5 weeks, and then slowly cleared up leaving slightly depressed scars. When we first saw the patient, she presented with nodular indurated erythematous lesions on the buttocks, 2 necrotic lesions with erythematous borders on the thighs (Fig. 1) and some slightly depressed scars on the abdomen, buttocks and arms. The histological findings of a necrotic lesion and a nodular erythematous lesion showed thrombosis of deep vessels and a mild perivascular lymphocytic infiltrate, also localized within the vessel walls, without fibrinoid necrosis. Ischaemic fat necrosis with a mild lymphohistiocytic infiltrate was also present. A complete coagulation study searching for hypercoagulability states showed no abnormalities.

As a consequence of these cutaneous reactions β -interferon 1b was replaced with β -interferon 1a, 6×10^6 IU s.c. on alternate days. From the beginning, she developed painful nodular erythematous indurated lesions at the injection sites, which lasted for several weeks. She has not yet developed any necrosis. Biopsy of one of these erythematous lesions showed perivascular and peridnexal lymphocytic infiltrate in the superficial and deep dermis with mild oedema in the papillar dermis.

Patch and intradermal tests were performed with β -interferon 1a (Rebi) 12×10^6 IU/ml and the following dilutions in distilled water: 1/2, 1/4, 1/8, 1/16, 1/32, β -interferon 1b (Betaferon®) 8×10^6 IU/ml and in the same dilutions in CINA 0.45%, and the solvent of β -interferon 1b (CINA 0.45%) without interferon. Patch tests were all negative. Intradermal tests showed local erythema and infiltration with both commercial and diluted β -interferon 1a and 1b for all dilutions after 48 and 96 h, and no reaction to CINA 0.45%. Histological studies of the local reactions to both β -interferons showed similar results to the local reaction to β -interferon 1a described above. Intradermal tests in 8 controls also showed local erythema and infiltration to both undiluted β -interferon 1a and 1b after 48 and 96 h.

DISCUSSION

Local reactions after subcutaneous use of β -interferon are common, but they are usually moderate and disappear in 48–72 h (1). To our knowledge this is the first patient reported with skin necrosis after β -interferon 1b injections and persistent infiltrated erythematous plaques with β -interferon 1a, in whom hypersensitivity tests and histological studies of these tests were performed.

The pathophysiological mechanism, despite different

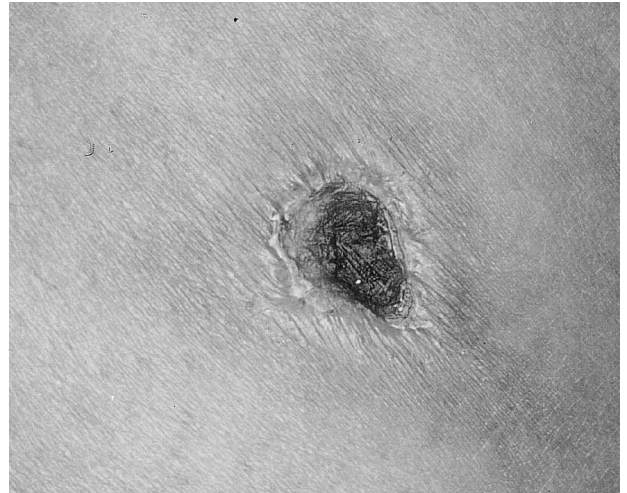


Fig. 1. Cutaneous necrosis on the right thigh after subcutaneous administration of β -interferon 1b.

hypotheses, remains unknown. Patch tests in this case and others (4) are not consistent with a hypersensitivity reaction and the fact that controls also showed a positive reaction in the intradermal tests points to a local toxic reaction to β -interferon. The histological findings of dermal vessel thrombosis suggest a procoagulant effect of interferon, direct damage to the endothelium, abnormality of platelet activation (5) or a coagulation disorder, which was not detected with the coagulation tests performed.

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