Physical injury as a provoking factor in three patients with scleroderma

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ABSTRACT

A 51-year-old female developed linear-like scleroderma in the left thigh following a linear wound caused by a car accident. 27 years later she also developed a typical diffuse cutaneous systemic sclerosis with extensive skin involvement and bibasilar pulmonary fibrosis. The second case is a 39-year-old female who had a history of Raynaud’s phenomenon since early childhood. She developed a morphea following a burning injury of the left thigh. 17 years later she also developed a typical limited cutaneous systemic sclerosis with sclerodactyly, skin ulcers and subcutaneous calcinosis. The third case is a 43-year-old female who developed a typical morphea of the right elbow around the site of a previous local corticosteroid injection. The two remarkable points of these 3 cases are the possible role of physical injury in the provocation of localized scleroderma and in the first 2 cases the unusual later development of a systemic form of scleroderma.

Introduction

Certain physical effects, including limb immobilization (1), spinal cord injury (2) and radiation therapy (3, 4), may provoke scleroderma. Other forms of physical injury, including local injection, have also been described as possible provoking factors of localized scleroderma (5-8). In the present study 3 patients are described who developed localized scleroderma following mechanical injury (wound formation following a traffic accident, thermal injury, and the effect of a local injection).

Case histories

Case 1

A 51-year-old female patient suffered a 20 cm longitudinal elongated wound, on the left thigh during a traffic accident in 1973. Six months following this local physical injury, a linear, scleroderma-like lesion developed on the site of the former lesion. The histological investigation proved the typical signs of scleroderma (Fig. 1). No other sites of the skin were involved. The patient was a chronic alcoholic with a possible intake of between 10-50 g/day. No signs of liver or biliary cirrhosis were found on ultrasound examination.

In 1975, plaques characteristic of lichen ruber planus appeared on both buttocks following several intramuscular injections. In 1983, symmetric polyarthralgia in the metacarpophalangeal and proximal interphalangeal joint lines were detected without any classical signs of inflammation. A positive LE test, a homogeneous antinuclear antibody staining pattern (on rat liver section), and a moderately elevated Waaler-Rose titer were also found. In 1985, a bronchopneumonia with a septic-toxic state was detected and cured. In the following years, apart from polyarthralgia, the patient was healthy and asymptomatic. The local skin involvement of the thigh remained stable. Regarding the laboratory findings, a permanently elevated ESR (between 50-80 mm/hr) and a polyclonal increase in the IgG level were detected.

In 1990, skin symptoms characteristic of rapidly progressive diffuse cutaneous systemic sclerosis were detected, involving the trunk, face, and the extremities. The skin involvement which was histologically confirmed by a skin biopsy from the forearm, was accompanied by extensive hypo-hyperpigmentation and a bibasilar lung fibrosis with restrictive ventilatory failure. No other internal organ involvement, myositis, or Raynaud’s phenomenon were detected. No anti-Borrelia, anti-Rnp, anti-topoisomerase I, anti-centromere, and anti-nucleolar antibodies were found. A homogeneous staining pattern of antinuclear antibody (on HEP-2 cells) was found without the presence of anti-dsDNA antibody.

In 1990, a combination of D-penicillamine (300-450 mg/day), pentoxyfyllin (800 mg/day), and nifedipine (30 mg/day) therapy was introduced. The progression of the skin symptoms stopped 10 months later. The patient’s condition became stable without any fluctuation in the following years. No signs of serious liver disease have been observed.

Case 2

A 39-year-old female had a history of Raynaud’s phenomenon involving symmetrically both hands since her early childhood. In 1980, at the age of 21, she spilt boiling water on the extensor sur-
face of her left thigh. Months later a lesion of typical morphea appeared in the affected area. Although the skin involvement was not confirmed by biopsy, the lesion was described as morphea several times. In the following years the lesion became atrophic and some hypopigmentation appeared and this condition remained stable. In 1982, while the previous sites of morphea became more pronounced, the lower left quadrant of the abdominal skin became slightly hyperpigmented and indurated lesions appeared. The abdominal skin was not previously affected by the thermal injury. In 1983 several tests were performed, including: chest x-ray, barium swallow, hand and feet x-rays, Schirmer’s test and nailfold capillary microscopy. At that time none of the investigations or laboratory data showed any signs of systemic scleroderma. In 1986 a skin ulcer appeared over the left lateral ankle. Since that time repeated skin ulcers have appeared in that area. Both the arterial and the venous circulation of this extremity were found to be normal.

Since 1990 antinuclear antibody positivity was reported on rat liver sections. The antibody showed homogeneous nuclear staining on HEp-2 cell cultures without anti-dsDNA positivity. Nailfold capillary microscopy described isolated apical widening of the capillary loops, but no abnormalities diagnostic of scleroderma were detected.

In 1997, the patient was admitted with complaints of Raynaud’s phenomenon, slightly decreased maximal oral aperture, and facial telangiectasia. The skin of the fingers was tight, but not to the extent of sclerodactyly. X-ray studies revealed a subcutaneous calcinosis on the second phalanx of the left second finger and signs of mild bibasilar lung fibrosis. The latter was confirmed by high resolution computer tomography. No anticientromere antibody was detected. The findings described above were compatible with the development of limited cutaneous systemic sclerosis.

**Case 3**

A 43-year-old female received a periarticular corticosteroid injection to the lateral part of the right elbow in 1999, a few months before her first visit to our department. The indication for the administration of this therapy remained obscure; probably the presence of periostitis was presumed. A few weeks later typical morphea (confirmed by biopsy) was noticed around the site of the injection (Fig. 2). No other sites of the body were affected. We did not detect joint symptoms, and an x-ray of the right elbow did not show any abnormality. Regarding the investigation of the internal organs, mild bibasilar lung fibrosis was found on the chest x-ray and was confirmed by high resolution computed tomography. The latter did not show any signs suggesting the presence of alveolitis. Spirometry values were normal except a slightly diminished CO diffusion coefficient. The antinuclear antibody test on HEp-2 cells was negative.

**Discussion**

Several provoking factors may contribute to the development of scleroderma. We have previously described that exposure to certain chemicals including organic solvents, are important provoking agents of scleroderma among Hungarian cases (9). Regarding physical injury, limb immobilization (1), spinal cord injury (2), and radiation therapy (3, 4), have been reported as possible provoking factors for scleroderma. All 3 patients described above also developed a localized form of scleroderma (linear-like scleroderma and morphea) following a...
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local physical injury. Our first case is unusual for diffuse scleroderma because, in spite of the extensive skin involvement, a relative lack of internal organ manifestations was observed. Such a physical injury as a possible provoking factor of scleroderma skin lesions has not been previously described.

In the second patient the appearance of morphea was followed by the burns as physical injury and later a limited cutaneous systemic sclerosis developed. These 2 patients exhibit a certain similarity to the cases reported by Rahaman et al., who described 5 cases who developed systemic sclerosis shortly after episodes of trauma. But in these cases, the site of injury showed no signs of localised scleroderma (10). The difference is that in our 2 patients, besides the systemic scleroderma, the local trauma also caused localised scleroderma.

Regarding the third patient, an injection as a physical injury provoked the appearance of morphea, a phenomenon which has been previously described in only a few patients (5-8). Antitetanical vaccination, vitamin K1 and pentazocin were described as causing morphea following local injection (6-8). Similar to our case, a sclerodermaform linear atrophy following the administration of intralesional corticosteroids for periorbital hemangiomas has recently also been described (5).

In our case, the administration of local steroid may have also played a role in the provocation of morphea. Although it has been recently demonstrated that the coexistence of SSC and morphea may not be an entirely unusual event (11-13), patients with localized scleroderma rarely develop symptoms characteristic of systemic sclerosis (SSc) (14). Both autoantibodies as well as internal organs symptoms and microvascular injury can be observed in localized scleroderma, which is a well defined and strictly different disease entity from the diffuse form of SSc. In our 2 patients the localized SSc became combined with the systemic form of the disease. Furthermore, the third case also seems to have some systemic involvement, i.e. lung fibrosis. As we have previously described (15), internal organ manifestations including pulmonary fibrosis may occasionally occur in patients with localized scleroderma, but this seems to be a rather exceptional finding.

The vascular endothelial injury which is a hallmark of scleroderma, may be mediated by several mechanisms including decreased endothelial expression of the complement protective molecular system, white blood cell activation through the production of free radicals, and furthermore an altered production of neuropeptides (19-21). The exact neuronal-related mechanisms are not well characterised, but the development of scleroderma-like dermal changes following spinal cord injury suggests an important role for neuronal participation in the development of scleroderma.

Manual vibration exposure as a special form of mechanical injury can also induce Raynaud’s phenomenon and, occasionally, sclerodactyly (16-18). Vibration-induced direct damage of blood vessels causes a disturbed local microcirculation. Recent studies also indicate that the neuronal deficit formerly identified by immunohistochemistry in the digital skin of patients with vibration white finger (22) has a functional counterpart in vivo and is evident as a reduced ability to propagate an axon-reflex vasodilator response when challenged with histamine and endothelin-1 (23).

In our cases, mechanical injury may have caused vascular endothelial damage and neuronal injury which could be important contributing factors to the development of trauma induced scleroderma.

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