

LESSON OF THE MONTH

Autologous skin transplantation for widespread cutaneous necrosis in secondary antiphospholipid syndrome

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Accepted 23 April 2001

Cutaneous involvement in primary and secondary antiphospholipid syndrome often is a therapeutical dilemma. Here we describe a case of widespread cutaneous necrosis due to thrombosis of the microvasculature, and cutaneous vasculitis in secondary antiphospholipid syndrome in a patient with systemic lupus erythematosus. Autologous skin transplantation was able to cover the skin defects but was only successful in the presence of immunosuppressive treatment with glucocorticoids and cyclosporin A.

Case report

A 34 year old women was admitted to hospital because of widespread necrosis of the skin and muscle of both legs. She had a two year history of seronegative non-erosive polyarthritits of the knees, proximal interphalangeal and metacarpophalangeal joints, which was successfully treated with methotrexate 10 mg by mouth once a week. She complained about Raynaud's

symptoms and dryness of the mouth but previously had no skin rash, fever, photosensitivity, ulceration of the oral or genital mucosa, or signs of pleuritis, pericarditis, or neurological abnormalities. She did not have children and had no history of fetal loss, thromboembolic events, or other disorders.

Four weeks before she was referred to us, she suddenly noticed blue patchy skin lesions on the extensor surfaces of her arms and legs. The skin lesions on the arms subsided, but on the legs the skin lesions became bullous, and sharp margined ulcers with a dark necrotic centre appeared which quickly covered large areas of the upper and lower legs (fig 1A). Laboratory evaluation showed positive antinuclear antibodies with a titre of 1/320 and a homogeneous pattern. An enzyme linked immunosorbent assay (ELISA) for anti-dsDNA antibodies was repeatedly positive with a maximum titre of 277 IU/ml. A radioimmunoassay test and *Crithidia luciliae* test for anti-dsDNA antibodies was not performed at this time. Decreased



Figure 1 (A) Cutaneous necrosis of the legs. (B) Maximal extension of the skin ulceration, now completely covered by skin autografts.

complement C3c (0.7 g/l; normal value 0.70–1.4 g/l) and C4 (0.1 g/l; normal value 0.2–0.4 g/l) was found. Anticardiolipin antibodies (IgG) were detected in a qualitative assay, but the titre was not determined. Lupus anticoagulant was positive and a prolonged partial prothrombin time of 60 seconds (normal value 27 seconds), mild thrombopenia with 122 platelets/nl, and anaemia with haemoglobin 95 g/l was detected. Rheumatoid factor, extractable nuclear antigen screening, antineutrophil cytoplasmic antibodies, and antimitochondrial antibodies, blood smear and urine sediment showed normal results. Lupus serology and anticardiolipin antibody determinations were repeated later in the presence of immunosuppressive treatment but then showed normal results. A skin biopsy of the affected areas of the legs and the arms showed multiple thrombosis of small blood vessels as well as necrotising inflammation of the dermis, subcutis, and muscular tissue. In the immunohistochemical staining of the tissue, complement C1q and C3d as well as IgM could be detected in the vessel wall of small vessels of the dermis.

Systemic lupus erythematoses with secondary antiphospholipid syndrome was suspected, methotrexate was stopped, anticoagulation with 15 000 IU heparin a day was started, and immunosuppressive treatment was changed to 20 mg prednisone and 150 mg azathioprine a day. Because of the widespread ulceration of the skin, which now affected about 24% of the body surface and covered the periost of the tibiae on both sides, the patient was transferred to a unit in our clinic in a unit which specialised in the care of severely burned patients.

After necrosectomy of the necrotic tissue in the ulcer ground, transplantation of a split thickness skin autograft taken from the belly was performed. However, after several days the transplanted skin graft was almost completely rejected. The patient now received prednisone 500 mg IV for three consecutive days and

cyclophosphamide 100 mg/day IV. However, as severe leucopenia appeared, the latter was stopped after only two days, and leucocyte counts recovered.

Figure 2 shows the further therapeutic procedure, including immunosuppressive treatment, skin transplants, and the rate of graft acceptance.

Discussion

Antiphospholipid syndrome mainly manifests with recurrent thromboembolic events, fetal loss, or thrombocytopenia, but it often also affects the skin.^{1–9} Beside livedo reticularis and thrombophlebitis, cutaneous ulcers are the most common cutaneous manifestation of the antiphospholipid syndrome. Altogether, about 7% of patients with positive lupus anticoagulant have skin ulcers.³ Ulcers are usually small, sharply marginated, and mainly affect the legs. Small necrotic areas are often seen in the base or centre of the ulcer, but widespread necrosis of the skin is a rare event and was seen only in two cases in a large survey of 295 patients with positive lupus anticoagulant.³

In the case described here, biopsy specimens showed the typical histological signs of cutaneous antiphospholipid syndrome with thrombosis of small vessels associated with signs of vasculitis.^{10–11} Initial trials for autologous skin transplantation after necrosectomy in the presence of anticoagulation with heparin and moderate immunosuppression with prednisone 20 mg/day and azathioprine 150 mg/day failed owing to graft rejection. However, in parallel with an intensification of the immunosuppressive treatment with high dose prednisone and, later, the addition of cyclosporin A, the rate of graft acceptance of the skin transplants did increase up to almost 100%. After a total of 31 autologous skin transplantations the skin defects were completely covered (fig 1B), and the patient could be discharged from hospital after seven months' treatment with oral anticoagulation, cyclosporin A, and low dose prednisone.

The lessons

- Autologous skin transplantation can be used to treat large skin defects in connective tissue diseases
- Immunosuppression might be a necessary condition for graft acceptance in these cases, and cyclosporin A seems to have favourable effects
- This case shows the possibility for a fruitful interdisciplinary cooperation between rheumatologists and plastic surgeons in the treatment of cutaneous manifestations of rheumatic diseases.

We thank Professor Dr Waldherr, pathologist, and Professor Dr Andrassy, nephrologist, for their help in the management of our patient.

- 1 Hughes GR. Thrombosis, abortion, cerebral disease and lupus anticoagulant. *BMJ* 1983;287:1088–9.
- 2 Hughes GR. The antiphospholipid syndrome. *Lupus* 1996; 5:345–6.

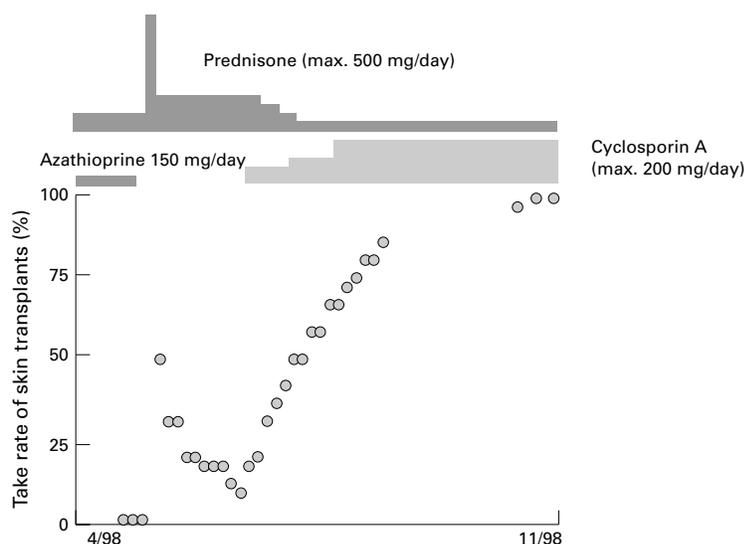


Figure 2 Repeated transplants were carried out with autologous split thickness skin grafts taken from the belly. In the presence of prednisone 20 mg/day and azathioprine 150 mg/day the grafts were completely rejected. However, the rate of graft acceptance (take rate of the skin transplants) did increase with high dose prednisone and approached 100% with the addition of cyclosporin A.

- 3 Alegre VA, Gastineau DA, Winkelmann RK. Skin lesions associated with circulating lupus anticoagulant. *Br J Dermatol* 1989;120:419–29.
- 4 Gibson GE, Su WPD, Pittelkow MR. Antiphospholipid syndrome and the skin. *J Am Acad Dermatol* 1997;36:970–82.
- 5 Naldi L, Locati F, Marchesi L, Cortelazzo S, Finazzi G, Galli M, *et al*. Cutaneous manifestations associated with antiphospholipid antibodies in patients with suspected primary antiphospholipid syndrome: a case control study. *Ann Rheum Dis* 1993;52:219–22.
- 6 Buhler-Singer S, von Hintzenstern J, Fartasch M, Hornstein OP. Anticardiolipin syndrome with only skin involvement. *Hautarzt* 1994;45:394–7.
- 7 Del Castillo LF, Soria C, Schoendorff C, Garcia Garcia C, Diez-Caballero N, Rodriguez Alen A, *et al*. Widespread cutaneous necrosis and antiphospholipid antibodies: two episodes related to surgical manipulation and urinary tract infection. *J Am Acad Dermatol* 1997;36:872–5.
- 8 Jou IM, Liu MF, Chao SC. Widespread cutaneous necrosis associated with antiphospholipid syndrome. *Clin Rheumatol* 1996;15:394–8.
- 9 Dodd HJ, Sarkany I, O'Shaughnessy D. Widespread cutaneous necrosis associated with the lupus anticoagulant. *Clin Exp Dermatol* 1985;10:581–6.
- 10 Goldberger E, Elder RC, Schwartz RA. Vasculitis in the antiphospholipid syndrome. *Arthritis Rheum* 1992;35:569–72.
- 11 Alegre VA, Winkelmann RK. Histopathologic and immunofluorescence study of skin lesions associated with circulating lupus anticoagulant. *J Am Acad Dermatol* 1988;19:117–24.



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