Autologous skin transplantation for widespread cutaneous necrosis in secondary antiphospholipid syndrome

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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 polyarthritis 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 marginated 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
addition of cyclosporin A.

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.

Discussion

Antiphospholipid syndrome mainly manifests with recurrent thromboembolic events, fetal loss, or thrombocytopenia, but it often also affects the skin. 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. Ulcers are usually small, sharply margined, 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.

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. 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.


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