Systemic sclerosis and porphyria cutanea tarda

Sir: The appearance of sclerodermoid changes in porphyria cutanea tarda is well known; cases of porphyria cutanea tarda associated with systemic sclerosis have rarely been described, however. A further case of this association is reported here. Repeated phlebitomy led to a slight improvement in the cutaneous sclerosis, but visceral involvement remained unchanged.

A 48-year-old woman was admitted for study of generalised cutaneous thickening. She was a heavy smoker and drinker. He had received no drugs and had not been in contact with toxic products. Outbreaks of vesicular lesions on the back of his feet, soles of his feet and intermittent dark urine had been evident for the past three years. Generalised skin thickening, particularly on his hands, and Raynaud's phenomenon had developed nine months before admission. Other clinical data included constitutional symptoms, pyrosis, impotence coeundi of six months' duration, and diffuse cutaneous hyperpigmentation lasting at least three months before admission.

Physical examination showed erosions, crusts, scars, and milium cysts in areas exposed to the sun and on the soles of his feet. There was diffuse hyperpigmentation with vitiligo-like patches. Skin thickening of the chest, back, abdomen, face, and arms were pinching impossible and greatly limited articular function. The legs were relatively unaffected. The finger tips showed pitting scars. There were no telangectasias or subcutaneous calcifications. The remainder of the physical examination, blood and urine analyses were unremarkable. A Feto protein, carcinoembryonic antigen, cortisol, and adreno corticotrophic hormone were normal; iron 10 μmol/l (normal 10–28 μmol/l), transferrin 1.7 g/l (normal 1.6–2.7 g/l), saturation index 22% (normal 20–40%), ferritin 350 μg/l (normal 18–300 μg/l), the urinary uroporphyrin level was 940 ± 270 μmol/24 h (normal <48 nmol/24 h) with presence of faecal isocoproporphyrin; unanitary alcohol titre was 1/160 homogenous pattern and 1/10 240 speckled pattern; and ScI-70 and other antitissue antibodies were negative.

A chest radiograph showed slight emphysema. Functional respiratory tests showed slight restrictive ventilatory disturbance, with impairment of both the transfer factor of the lung for carbon monoxide and the transfer coefficient. Pulmonary gammagraphy with gallium-67 was normal. A hand radiograph disclosed lysis of the distal phalanges. Nailfold capillaroscopy showed capillary dilatation in several fingers. Abdominal echography showed slight liver enlargement. Liver biopsy showed moderate hepatic siderosis, but no needle-like inclusions in the hepatocytes cytoplasm were seen under polarised light microscope. Skin biopsy disclosed epidermal hyperpigmentation of the basal layer, a thickened basement membrane positive for periodic acid-Schiff reagent, superficial perivascular hyalisation, and an increase in dermal collagen. Oesophageal manometry showed hypotension of the lower oesophageal sphincter and severe hypomotility of the distal two thirds of the oesophagus.

The patient was diagnosed as having porphyria cutanea tarda and systemic sclerosis. Alcohol abstinence was recommended and treatment with repeated phlebitomy (300 ml every two weeks) was started. At six weeks of treatment urinary porphyrins were normal. A slight improvement in the cutaneous and oesophageal manifestations was seen, with several months. Oesophageal manometry results after six and 24 months of treatment remained unchanged.

Our patient had porphyria cutanea tarda before the clinical onset of systemic sclerosis. We wonder whether this was a chance coexistence of two admittedly different pathogenic entities or whether there is a causal relation between them.

Sclerodermoid lesions may develop in 18 to 27% of patients with porphyria cutanea tarda. They are usually late lesions, which appear in patients with untreated porphyria cutanea tarda of several years' duration and tend to have a characteristic appearance and location. The face may take on a systemic sclerosis-like appearance and the fingers may show sclerodermoid changes not usually associated with Raynaud's phenomenon.

Experimental studies have shown that uroporphyrin I increases collagen synthesis in human skin fibroblasts, that urat or skin fibroblasts are coupled to the skin fibroblasts of patients with porphyria cutanea tarda, and that the tissue shows a characteristic appearance of porphyria cutanea tarda. Although in most cases sclerodermoid changes in porphyria cutanea tarda are confined to the skin, some cases with visceral involvement suggestive of true systemic sclerosis have been reported.

Friedman and Doyle believe that it is reasonable to think that porphyria cutanea tarda may be associated with systemic sclerosis as with other connective tissue diseases, improvement in most cases of sclerodermoid changes with normalisation of uroporphyrin concentrations suggests more than simple coexistence. In this case only a slight improvement in cutaneous sclerosis, but not in visceral involvement, was achieved with treatment. We believe that when systemic sclerosis is associated with porphyria cutanea tarda, treatment of the latter does not modify the former, at least not the visceral involvement. In view of the small number of reported cases there is for the moment no answer to the question posed earlier.

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Increased concentrations of soluble interleukin-2 receptor in the serum of patients with systemic sclerosis

Sir: The extent to which the immune system is important in the pathogenesis of systemic sclerosis is still poorly understood. In a recent issue of the Annals Gustafsson and colleagues showed the presence of increased numbers of HLA-DR positive T lymphocytes in the peripheral blood of patients with systemic sclerosis compared to healthy controls. Expression of HLA-DR antigens as well as of the interleukin-2 receptor on a cellular surface is acquired by T cells after stimulation by antigens or mitogens.

It has been reported that a soluble form of interleukin-2 receptor is released in culture supernatants by activated lymphocytes, derived mostly from T cells, and that it can be measured in the sera of patients with various clinical disorders in which the immune system is activated. Therefore, the soluble form of interleukin-2 receptor has been regarded as a new marker of T cell activation; increased concentrations have been noted in sera of patients with systemic autoimmune diseases, including systemic lupus erythematosus, rheumatoid arthritis, and Sjogren's syndrome.

We evaluated the concentration of the soluble form of interleukin-2 receptor in the sera of patients with systemic sclerosis by an enzyme linked immunosorbent assay (ELISA) based on the sandwich principle (Cellfree, T Cell Science, Cambridge, MA). Results are expressed in units/ml relative to a set of standards supplied with the test kits.

Twenty eight patients (27 women, one man; median age 52 years) were studied. The American Rheumatism Association preliminary criteria for the classification of systemic sclerosis 11 had typical sclerodematous skin changes proximal to the metacarpophalangeal joints. Twenty eight patients (76%) had concentrations of the soluble form of interleukin-2 receptor more than 3 SD above the mean concentration of the controls. Patients with the CREST syndrome had non-significantly lower concentrations than those with diffuse scleroderma (679 ± 148 U/ml vs 902 ± 427). We data agree with those of previous studies showing the presence of activated lymphocytes in systemic sclerosis.

Our findings of Gustafsson et al., however, as we did not note a significant inverse correlation between disease duration and the marker of T cell activation (R = 0.14; Spearman's test).


8 Six cases of systemic sclerosis and porphyria cutanea tarda of systemic sclerosis have rarely been described, however. A further case of this association is reported here. Repeated phlebitomy led to a slight improvement in the cutaneous sclerosis, but visceral involvement remained unchanged.

9 The presence of increased numbers of HLA-DR positive T lymphocytes in the peripheral blood of patients with systemic sclerosis compared to healthy controls. Expression of HLA-DR antigens as well as of the interleukin-2 receptor on a cellular surface is acquired by T cells after stimulation by antigens or mitogens.

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