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Unusual overlap of systemic lupus erythematosus and diffuse scleroderma

Sirs,

Patients with connective tissue disorders can often be classified into distinct entities by well-defined criteria. Occasionally, however, patients may have features overlapping between these conditions. One classical example is mixed connective tissue disease (MCTD) (1). Overlap syndromes usually include polymyositis with either scleroderma (SSc) or systemic lupus erythematosus (SLE). Coexistence of SLE with SSc is very rare. If this happens, the SSc is usually of the limited cutaneous type or scleroderma sine scleroderma (2). The antibodies found in SSc (e.g. anti-Scl 70, anti-centromere) are usually mutually exclusive from those typically found in SLE (e.g. anti-dsDNA, anti-Sm). We describe an unusual case of diffuse SSc that evolved into florid SLE with the simultaneous presence of anti-Scl-70, anti-dsDNA and anti-Sm antibodies.

A 27-year-old Chinese woman was admitted in June 1999 because of fever and ankle edema. She was a known patient with SSc diagnosed in 1994. Autoantibody screening at that time revealed positive ANA (1/1280, nucleolar pattern) and anti-Scl-70 (by immunoblotting). Anti-dsDNA and other anti-ENA antibodies (Ro, La, U1RNP, Sm) were

negative and serum complement levels were normal. She was treated with D-penicillamine (500 mg/day) and vasodilators with poor response. Her skin condition progressively worsened to involve the proximal parts of the limbs, face and trunk. Recurrent digital infarction resulted in auto-amputation of the terminal phalanges of the hands. The patient dropped out in September 1995, choosing to discontinue D-penicillamine because of ineffectiveness.

When she presented to us in 1999, she complained of fever, symmetrical polyarthralgia, oral ulceration, alopecia, weight loss and ankle edema lasting several weeks. She had not been taking any medications or herbal treatments since 1995. Physical examination revealed the typical features of diffuse SSc - microstomia, telangiectasia, skin depigmentation and tightening (modified Rodnan score (3) of 35/51), and resorption of the terminal phalanges of the digits. Bilateral ankle edema was present and the Schirmer's test was positive. Examination of other systems was unremarkable. Blood tests revealed Coombs' positive anemia, leucopenia (WBC $3 \times 10^9/L$), raised ESR (130 mm/hr) and hypoalbuminemia (18g/L; NR 35-50). Her muscle enzymes and platelet counts were normal. Urine microscopy showed red cell casts, and a 24-hour urine test for protein was 1.1 gram.

Repeat autoantibody testing revealed strongly positive ANA (1/2560, homogeneous pattern) but negative RF. Anti-dsDNA antibody had turned positive (Crithidia assay) and anti-ENA testing using immunoblotting showed positive bands for Scl-70, Sm, Ro and La. Anti-U1RNP was, however, negative. Her IgG and IgM anticardiolipin antibodies were grossly elevated but lupus anticoagulant was absent. Both serum C3 and C4 levels were markedly depressed. An echocardiogram showed small pericardial effusion but there was no pulmonary hypertension.

The evolution of diffuse SSc into an overlap of SSc/SLE was evident in the presence of a positive anti-dsDNA, oral ulcers, serositis, proteinuria, leucopenia, Coombs' positive anemia and hypocomplementemia. A renal biopsy was originally planned but the patient's condition suddenly deteriorated, with the development of tonic-clonic convulsions and a decreased conscious level. An emergency CAT scan revealed massive left parieto-occipital intracerebral hemorrhage with pressure effect. A magnetic resonance angiogram did not show any obvious aneurysms or arteriovenous malformations. An emergency craniectomy with clot evacuation was performed. Intravenous pulse methylprednisolone was also given for the

possibility of vasculitic hemorrhage. Unfortunately, the patient suffered further hemorrhage 4 days later and became vegetative. She finally succumbed to bronchopneumonia and multi-organ failure. Permission for an autopsy was refused.

SLE is an autoimmune disease characterized by a wide range of clinical manifestations. Features of other connective tissue diseases may be found. However, true overlap of SLE with diffuse SSc is rare. In a large series of 727 patients with SSc, only 2 (0.3%) had features of SLE (4). A review of 648 patients with SSc from 11 studies showed coexisting features of SLE in only 10 patients (1.5%) (5). A review of cases of SSc/SLE overlap revealed that the onset of SSc might precede, present concurrently or evolve from the diagnosis of SLE (5-8). Familial clustering of SLE and SSc may also occur (9). Our patient had an evolution from diffuse SSc into an overlap of SLE/SSc. She fulfilled the American College of Rheumatology's criteria for both conditions. As D-penicillamine had been stopped for several years, the possibility of drug-induced lupus was unlikely. In the absence of anti-U1RNP and myositis, the diagnosis of MCTD was also inappropriate. As anti-Scl-70 is present in 10-15% of SSc patients and anti-dsDNA and anti-Sm in 70% and 30%, respectively, of SLE patients, the simultaneous coexistence of these antibodies in the same individual is extremely unusual. Connective tissue disorders can overlap in various ways. Patients may present with features of several diseases without satisfying the respective diagnostic criteria but evolve into distinct entities afterwards. Alternately, a patient with a well-defined disease entity may develop new features that qualify for the diagnosis of another distinct disease. Occasionally, patients may fulfill simultaneously the diagnostic criteria of two or more diseases at presentation. The connective tissue diseases may be viewed as a continuous clinical spectrum and evolution into each other may occur during the disease course. Regular monitoring and surveillance for new clinical and serological features is necessary.

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Letters to the Editor

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