Improvement of severe pulmonary hypertension in a patient with SLE

The development of pulmonary hypertension during the course of connective tissue diseases is a frequent clinical finding. In cases where the clinical course is characterized by no treatment, the progression of pulmonary hypertension is rapid. In such cases, however, the prognosis is very poor. Several reports have described the use of corticosteroids for the treatment of pulmonary hypertension, but the results have been disappointing. In the case presented here, a patient with SLE and pulmonary hypertension was treated with high-dose methylprednisolone and cyclophosphamide. The patient responded well to the treatment, and her pulmonary hypertension improved significantly. The patient's clinical course supports the use of high-dose methylprednisolone and cyclophosphamide for the treatment of severe pulmonary hypertension in patients with SLE.

Our patient had several of the variables associated with poor survival rates in patients with pulmonary hypertension: New York Heart Association functional class IV, presence of Raynaud’s phenomenon, raised mean pulmonary arterial pressure, decreased cardiac index. Immunosuppressive treatment with cyclophosphamide and prednisone was initiated for 12 months followed by quarterly infusions, in combination with steroid treatment—resulted in prolonged decrease of pulmonary pressure together with dramatic clinical improvement. Our patient might have resulted from treatment with high dose corticosteroids or cyclophosphamide, or both, and could not be attributable to cyclophosphamide only. The association of vasodilator and immunosuppressive drug treatment might have been helpful, even though the initial treatment with vasodilator alone was ineffective. A few cases of improvement with immunosuppressive drug treatment have been reported. Corticosteroids alone are rarely efficient. An initial but not sustained response to high dose methylprednisolone has been reported in a patient with mixed connective tissue disease. Goupille et al. reported the case of a lupus patient with precapillary pulmonary hypertension who was successfully treated with high doses of corticosteroids, with an improvement of 18 months. A woman with mixed connective tissue disease and pulmonary hypertension improved after sequential administration of cyclophosphamide and cyclosporin A over a period of 10 years. Green et al. reported a prolonged—but only partial—improvement with low dose prednisone and quarterly cyclophosphamide infusions in a woman with SLE and pulmonary hypertension. In conclusion, the prolonged and excellent outcome seen in our patient supports treatment with immunosuppressive drugs associated with vasodilator agent in precapillary pulmonary hypertension arising in SLE, before considering heart-lung transplantation. Controlled trials of immunosuppressive drug treatment in patients with SLE and precapillary pulmonary hypertension are needed.
Antibodies to ribosomal P proteins and hepatic damage in undifferentiated CTD

Ribosomal antibodies were first detected by immunofluorescence in the serum of a few patients with systemic lupus erythematosus (SLE) in 1974 by Hengen et al.1 Presently, it is well known that most ribosomal antibodies recognize a conserved sequence of 22 aa at the carboxy terminus of three ribosomal phosphoproteins P0, P1, and P2 with molecular weights 38, 19, and 17 kDa respectively (antibodies to ribosomal P proteins).2 These antibodies have been described in about 10% of patients with SLE and their presence in serum is considered a marker of this disease. Various reports have shown an association between ribosomal antibodies and the development of lupus psychosis,3 whereas others found a correlation with lupus activity.4 Recently, an association between antibodies to ribosomal P proteins and liver or renal complications, or both, in SLE has been suggested.5,6 We would like to comment on an interesting case in which a relation between the development of liver disease and the titres of antibodies to ribosomal P proteins was found in a patient with undifferentiated connective tissue disease.

In March 1992 a 9 year old girl was referred to Asturias Central Hospital with high fever, polyarthritis, oral ulcers, Raynaud's phenomenon, generalised hand swelling, conjunctivitis. Laboratory studies showed a normal total and differential white cell count, an erythrocyte sedimentation rate of 88 mm/1st h, and serum C reactive protein of 5.1 mg/l (normal values (NV) < 6 mg/l). Blood chemistry showed slightly raised levels of the liver enzymes aspartate aminotransferase (AST) and alanine aminotransferase (ALT) (fig 1). Immunological studies disclosed increased levels of serum IgG to 24-4 g/l (NV 5.6-17.6 g/l), a rheumatoid factor test of 126 IU/ml (NV < 30 IU/ml), and normal complement levels. Immunofluorescence on Hep-2 cells showed positive staining of the cytoplasm and nucleoli; no other nuclear staining patterns were observed. The patient's serum strongly stained the cytoplasm of the chief cells of rat stomach, which is characteristic of the presence of ribosomal antibodies. The serum was titrated for the presence of ribosomal and nucleolar antibodies on rat tissue sections (liver, kidney, and stomach) (fig 1). At the starting dilution (1/40) all normal serum samples were negative. The Western blot test, using rat ribosomes as a source of antigen, disclosed the presence of antibodies reacting with a 38 kDa ribosomal P0 protein (ribosomal antibodies) (fig 2). Tests for other autoantibodies (dsDNA, SS-A, SS-B, Sm, and nRNP) were negative.

Despite the presence of antibodies to ribosomal P0 protein, which is considered as a marker of SLE, the diagnosis was un-differentiated connective tissue disease because the patient did not fulfil the American Rheumatism Association criteria for the diagnosis of SLE. She was treated with prednisolone (20 mg/day). The acute manifestations resolved rapidly, and the patient left hospital three weeks later in a good condition. The dose of prednisolone was tapered gradually.

In February 1993, while the patient was receiving a daily dose of 2 mg of prednisolone and 500 mg of the non-steroidal anti-inflammatory drug naproxen, a high increase in the seric concentration of the liver enzymes was observed (AST 334 U/l, ALT 438 U/l; NV < 31 U/l for both enzymes). She had no hepatomegaly and serological tests for the Epstein-Barr virus, cytomegalovirus, and viral hepatitis were all negative. The increased liver enzyme levels were accompanied by a parallel increase in the titres of cytoplasmic and nucleolar antibodies. Owing to the possibility of drug induced liver damage, naproxen was discontinued and the dose of steroids reduced to 1 mg on alternate days. However, the levels of liver enzymes and the titres of ribosomal antibodies and nucleolar antibodies remained abnormally high.

In April 1994 the patient was readmitted with an acute episode of severe asymmetrical polyarthritis. High dose prednisolone treatment was reintroduced (0.75 mg/kg daily), and treatment with antimalarial drugs (3 mg/kg daily) was started. Interestingly, despite the relapsing of her articular process the titre of autoantibodies decreased as well as the levels of liver enzymes, which normalised by June 1994. In September 1994...
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doi: 10.1136/ard.55.8.561

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