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Auto-Immune Haemolytic Anaemia and Thrombocytopenia in Scleroderma

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Auto-immune haemolytic anaemia and auto-immune thrombocytopenia are well-known manifestations of systemic lupus erythematosus (SLE), but occur much less often in the other connective tissue diseases. We report the case of a patient with scleroderma, who developed severe auto-immune thrombocytopenia, leucopenia and, later, fulminant auto-immune haemolytic anaemia.

In 1972, a 16-year-old man presented with polyarthralgia and Raynaud's phenomenon. Over the time he developed thinned lips and a narrowed mouth, ulcerations of the fingertips and atrophy of the soft tissue of his fingers, which became fixed in a claw-like position. These findings together with difficulties in swallowing, and facial teleangiectasia led to the diagnosis of scleroderma. Laboratory investigations revealed rheumatoid factor, anti-nuclear antibodies up to 1/10,000 with speckled pattern and anti-RNP antibodies, but no anti-Scl-70 antibodies, no anti-Sm antibodies and no increased levels of anti-dsDNA antibodies. The patient was treated with prednisone in small doses.

In 1981, the patient was admitted because of spontaneous bleeding and petechiae. He had a very low platelet count ($2 \times 10^9/l$), no anaemia, but a moderate leucopenia, with a normal differential count. A bone marrow aspirate contained an increased amount of megakaryocytes. Platelet antibodies were detectable in the patient's serum with an indirect Coombs' test. Treatment with 40 mg of prednisone daily resulted in normalization of the platelet count within a month.

Two years later, the patient presented with fever, jaundice, fatigue and dark urine. Laboratory examination showed a haemoglobin value of 73 g/l, reticulocytosis, neutrophilic leucocytosis and thrombocytopenia. A direct Coombs' test was positive with IgG, IgA, IgM, C3 and C4 on the surface of the erythrocytes. The plasma haemoglobin concentration increased to 2,033 mg/l (reference range < 50 mg/l). A test for

cold agglutinins was negative. A bone marrow aspirate showed erythroid hyperplasia.

Prednisone treatment (80 mg/day) and methylprednisolone pulse therapy (1 g intravenously for 3 subsequent days) had no effect on the haemolysis. On days 7–11 of hospitalization, intravenous immunoglobulin infusions (Sandoglobulin® 0.4 g/kg body weight/day) were given. The patient's need for erythrocyte transfusions, however, continued, his condition deteriorated and he became oliguric. In this situation, plasmapheresis treatment (performed with a membrane filtration technique) was started on day 9 of hospitalization. After the first plasmapheresis, the haemoglobin value stabilized, and began to rise 2 weeks later, after five plasmaphereses and an

exchanged plasma volume of 20 liters, totally. After the course of plasmaphereses, the patient was given azathioprine, but this medication was stopped 3 months later because of gastrointestinal side effects. During the last years, he has been maintained on a small dose of prednisone. There has been a slight progression of his skin changes but no relapse of the blood cytopenias.

Anaemia in patients with scleroderma is most often caused by complications, such as iron deficiency, intestinal malabsorption, renal failure and micro-angiopathic haemolysis [1, 2]. When thrombocytopenia develops during the course of scleroderma, micro-angiopathy or an overlap syndrome with SLE is considered [2]. Since the first report of auto-immune haemolytic anaemia in scleroderma by Fudenberg and Win-trobe [3] in 1955, only about 10 cases have been recorded [1,2, 4–9], and auto-immune thrombocytopenia seems to be even rarer. The combination of autoimmune haemolytic anaemia and auto-immune thrombocytopenia has previously been described in only 1 patient with scleroderma [6].

Most patients with auto-immune haematological disorders associated with scleroderma have been effectively treated with corticosteroids. Our patient's

180

Pettersson/von Bonsdorff

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thrombocytopenia responded excellently to corti- 3 costeroids, but his haemolytic anaemia was corti-costeroid-resistant. The reports on a beneficial effect of intravenous immunoglobulin infusions on autoimmune thrombocytopenia [10] encouraged us to try this treatment for the patient's auto-immune haemo- 5 lytic anaemia. The immunoglobulin infusions could certainly have modified the haemolytic process, but 6 seemed not to have any immediate effect. Our clear impression was that plasmapheresis was the treatment 7 which led to the patient's improvement. After the first plasmapheresis, the patient's requirement for erythro-cyte transfusions ceased and

his haemoglobin value then gradually normalized. That fulminant autoimmune haemolysis refractory to corticosteroids and intravenous immunoglobulin may be reversed by plasmapheresis has earlier been documented in selected cases with primary auto-immune haemolytic [10] anaemia [11].

Our case illustrates the possibility that severe antibody-mediated haematological disorders may be [12] associated with scleroderma and that plasmapheresis can be used to reverse the cytopenias when conventional therapy has failed.

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