Successful treatment of pure red cell aplasia associated with systemic lupus erythematosus with cyclosporin A

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We report the first case of a patient with pure red cell aplasia (PRCA) and systemic lupus erythematosus (SLE) failing to respond to corticosteroids and then being successfully treated with cyclosporin A (CyA), with no recurrence of the disease in the last 4 yr.

A 21-yr-old female was admitted to our ward with anaemia. Previously, she had had polyarthritis of the small joints of the hands, knees and ankles, photosensitivity, and a malar rash that responded well to non-steroidal anti-inflammatory drugs, which were used from October 1994 to April 1995. She was later seen in the emergency department and diagnosed with severe anaemia (haemoglobin 3.8 g/dl, haematocrit 11.1%, fatigue, tiredness, cephalalgia and low blood pressure), and she received two units of red blood cells. After initial improvement, her clinical condition worsened in the following 2 weeks. Her haemoglobin level and haematocrit fell to 2.8 g/dl and 8.8%, respectively. She was transfused again with two units of red blood cells and transferred to our service. She was dyspnoeic and semiconscious, with paleness and swelling of the metacarpophalangeal and hand proximal interphalangeal joints, knees and ankles. Her laboratory test results were as follows: haemoglobin 6.9 g/dl; haematocrit 20%; reticulocytes 0.2%; erythrocyte sedimentation rate 75 mm/h. Immunological studies showed a direct Coombs test result of 1:4, a speckled pattern of antinuclear antibodies at a titre of 1:320, DNA binding (radioimmunoassay) of 84.3% (normal value ≤52%), and IgG and IgM anti-cardiolipin antibodies 2.5 U (normal value <2.0 U) and 5.0 U (normal value <2.2 U), respectively. The following tests were normal: bilirubin, total proteins and albumin, prothrombin and partial thromboplastin; VDRL was negative. An additional search for serum IgG and IgM anti-B12 parvovirus antibodies was negative. Chest X-rays and computed tomography were normal.

A bone marrow sample revealed the absence of erythroid precursors cells, without significant abnormalities of the megakaryocytic, granulocytic or lymphocytic cell lines. A diagnosis of PRCA associated with SLE was established, and treatment with 60 mg prednisone (1 mg/kg) daily was started. Ten days later, her haemoglobin level was 5.9 g/dl, haematocrit 17.6% and reticulocyte count 0.4%; her clinical symptoms were unchanged. She was transfused for a third time with two units of red blood cells and treated with 1 g methylprednisolone intravenously for 3 consecutive days (Fig. 1). Haemoglobin rose to 9.2 g/dl and haematocrit to 27.1%; reticulocyte count remains without change. She continued with 60 mg of prednisone per day, but 4 weeks later (5 weeks after starting corticosteroids) symptoms reappeared and laboratory values dropped again (haemoglobin 6.2 g/dl, haematocrit 17.0%, reticulocyte count 0.4%). She was again transfused and started on CyA at a dose of 200 mg/day (3.5 mg/kg). Twenty-one days later, her clinical condition had improved significantly, as had her laboratory test values, with an increased reticulocyte count (haemoglobin 9.8 g/dl, haematocrit 31.6%, reticulocyte count 11%). Investigations during the following 6 months showed continuous improvement in her clinical condition and laboratory values. CyA was then stopped and azathioprine was introduced at a dose of 150 mg/day. Since then, the patient was followed for a mean of 4 yr; there was a favourable clinical outcome with remission of PRCA but with mild intermittent episodes of arthralgia and arthritis, which were treated with chloroquine. At the start of CyA, the patient’s serum creatinine value was 0.7 mg/dl and glomerular filtration rate 101.5 ml/min. Currently, her creatinine level is 1.0 mg/dl and glomerular filtration rate 112.0 ml/min. During follow-up, these parameters were monitored closely and remained within normal limits.

To date, 17 patients have been reported documenting the association of PRCA and SLE. In ten patients
Letters to the Editor

Response of PCRA in SLE to CyA during the first 6 months of treatment and 4 yr of follow-up. Haemoglobin (g/dl) (— ■ —), reticulocytes (%) (— △ —) prednisone (mg/day; values by 10) ( ) , CyA (200 mg/day) ( ).

Fig. 1. Response of PCRA in SLE to CyA during the first 6 months of treatment and 4 yr of follow-up. Haemoglobin (g/dl) (— ■ —), reticulocytes (%) (— △ —) prednisone (mg/day; values by 10) ( ), CyA (200 mg/day) ( ).

PRCA has been diagnosed within the initial 6 months of SLE [2, 5, 6, 8, 10, 12–14]. In three patients (17.6%), PRCA antedated the onset of SLE by 2–6 months and 4 yr [8, 13, 14]. In the remaining patients, PRCA occurred between 2 and 11 years after SLE diagnosis [1, 3, 4, 6, 9, 11, 13]. Although most patients have mild disease activity with associated skin, joint and haematological disease and serositis, as well as immunological abnormalities associated with PRCA, some also have more severe clinical manifestations (renal, neurological and/or pulmonary disease). At the time of PRCA diagnosis, some patients have active SLE [1, 3, 4, 6, 9, 12, 14] (predominantly haematological, renal and joint disease) and some have only immunological abnormalities [2, 5, 7, 8, 10, 11, 13].

Corticosteroids, the mainstay of treatment in PRCA and SLE, have proved efficacious in most cases (60%). Doses have ranged from 40 to 200 mg/day [2–5, 7–9, 13, 14]. However, there are some refractory patients [6, 10, 11–14]. Previous favourable results obtained with CyA in acquired PRCA [15] encouraged us to treat this patient with CyA. We found a remarkable response, with excellent safety with respect to renal function. The patient is currently off steroids. Thus CyA is a potential alternative in patients with PRCA and SLE refractory to corticosteroids.

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