Hemolytic Uremic Syndrome/Thrombotic Thrombocytopenic Purpura in a Patient with Behçet's Disease Treated with Cyclosporin

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Dear Sir,

An increasing number of immunosuppressive drugs have been associated with the hemolytic uremic syndrome (HUS)/thrombotic thrombocytopenic purpura (TTP), including cyclosporin [1]. We report another patient who presented this severe disorder seemingly secondary to cyclosporin therapy.

A 32-year-old patient was admitted to hospital because of dyspnea and oliguria. The patient was known to be affected by Behçet's disease with prominent signs of neurological involvement; he had been taking cyclosporin (5 mg/kg/day) for almost 2 years.

On admission, the patient was somnolent, pale and afebrile; blood pressure was 110/70 mm Hg and pulse 110/min. Mild pretibial edema was present as well as palpable purpura of both thighs. A 2/6 systolic murmur was audible at the apex radiating to the axilla, and generalized rales were present in the lungs. The abdomen was normal. The urine output was minimal. Chest X-rays demonstrated pulmonary venous congestion and mild bilateral pleural effusion. An ECG demonstrated sinus tachycardia. Renal ultrasonography was normal.

Laboratory data included serum creatinine 6.1 mg/dl, blood urea nitrogen 99 mg/dl, sodium 134 mEq/l, potassium 5.1 mEq/l, chloride 94 mEq/l, bicarbonate 21 mEq/l, total proteins 5.1 g/dl (albumin 2.9 g/dl), hemoglobin 9.6 g/dl, hematocrit 26.6%, leukocyte count 9,100/mm³, platelet count 102,000/mm³. The erythrocyte sedimentation rate was 73 mm/h. Prothrombin time and partial thromboplastin time were normal, and fibrin degradation products were not detected. Urinalysis revealed specific gravity 1.013, proteins 300 mg/dl, numerous dysmorphic erythrocytes and occasional granular and hyaline casts. Cyclosporin level was 350 ng/ml; the drug was discontinued.

The day after admission, the patient's renal function deteriorated further with creatinine increasing to 7.5 mg/dl and blood urea nitrogen to 112 mg/dl; urine flow rate was 15-20 ml/h despite large doses of furosemide. Hemodialysis was started.

In the following days, purpura extended to the abdomen and upper extremities; thrombocytopenia worsened with the platelet count decreasing up to 40,000/mm³, hemoglobin

dropped to 6.2 g/dl and hemato-logical features suggestive of intravascular hemolysis became obvious: reticulocytes were 4%, serum haptoglobin was 11.3 mg/dl (normal values 30-150), serum lactic dehydrogenase was 1,410 IU/l (normal values 230-461), fragmented erythrocytes were demonstrated on blood smears. Results of direct and indirect Coomb's tests were negative. Coagulation studies remained normal throughout. Serum immunoelectrophoresis and complement levels were normal; rheumatoid factor, cryoglobulins, ANA and ANCA were negative. A biopsy of the involved skin demonstrated capillary lumina filled with finely granular material; there was no evidence of vasculitis.

Based on the above findings, HUS/TTP was diagnosed. The patient received multiple transfusions of packed erythrocytes and was treated with fresh-frozen plasma infusion, antiplatelet drugs (aspirin and dipyrid-amine) and steroids.

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Three weeks after admission, hemoglobin level was 9.7 g/dl, platelet count was 134,000/mm³ and indices of intravascular hemolysis had completely normalized. Renal function remained impaired; daily urine output ranged between 500 and 800 ml. The patient continued to be treated with hemodialysis. Kidney biopsy was not performed because of lack of consent.

In brief, we describe a patient with Behcet's disease who developed generalized purpura, acute renal failure, thrombocytopenia and microangiopathic hemolytic anemia while on treatment with cyclosporin. Although histopathologic data are lacking, the above clinical picture does suggest the diagnosis of HUS/TTP.

Two similar patients have recently been reported by Beaufils et al. [2]. Both patients developed irreversible renal failure with he-

molytic anemia and thrombocytopenia; renal lesions were consistent with the diagnosis of thrombotic microangiopathy. Since we could not find a case of HUS/TTP related to Behcet's disease in the literature, we hypothesized a causal role of cyclosporin, although the mechanism remains unknown (endothelium damage due to a direct toxic effect of the drug?). Interestingly, such a complication of cyclosporin therapy had previously been reported in renal-transplanted patients and was invariably associated with high blood levels of the drug [3].

We agree with Beaufils et al. [2] that patients treated with cyclosporin should be closely monitored. A rapid adjustment of excessive doses might prevent the development of the microangiopathic process in such patients.

References

Neild G: Haemolytic uraemic syndrome (including disseminated intravascular coagulation and thrombotic thrombocytopenic purpura); in Cameron JS, Davison AM, Grunfeld JP, Kerr D, Ritz E (eds): Oxford Textbook of Clinical Nephrology. Oxford, Oxford University Press, 1992, pp 1041-1060.

Beaufils H, de Groc F, Gubler MC, Wechsler B, Le Hoang P, Baumelou A, Chomette G, Jacobs C: Hemolytic uraemic syndrome in patients with Behcet's disease treated with cyclosporin A: Report of 2 cases. Clin Nephrol 1990;34: 157-162.

Neild GH, Reuben R, Hartkey RB, Cameron JS: Glomerular thrombi in renal allografts associated with cyclosporin therapy. J Clin Pathol 1985;38:235-238.

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