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TREATMENT OF CYCLOSPORIN-INDUCED HAEMOLYTIC URAEMIC SYNDROME WITH FK506

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Sir,—Haemolytic uraemic syndrome (HUS) is a well-recognised complication of cyclosporin therapy in organ transplantation.¹⁻⁴ It has usually been treated by a switch to azathioprine. We report the first use of FK506 in the management of this complication. A 33-year-old man had liver transplantation in January, 1989, for end-stage liver disease due to chronic active hepatitis. Recovery was complicated by acute tubular necrosis which required haemodialysis for 3 weeks. He was discharged 7 weeks postoperatively with normal liver function, normal haematological profile, serum creatinine 2.4 mg/dl, and blood urea nitrogen (BUN) 24 mg/dl. His daily medications were cyclosporin 600 mg, azathioprine 75 mg, acyclovir 200 mg, and trimethoprim 80 mg plus sulphamethoxazole 400 mg.

7 months postoperatively, he became anaemic with a haematocrit of 14.7%, platelet count of 29 000/μl, and white cell count 5800/μl. Total bilirubin rose to 5.7 mg/dl, creatinine to 5.0 mg/dl, and BUN to 69 mg/dl. His cyclosporin level, which was therapeutic, was 713 ng/ml (TDX method). A blood smear revealed microangiopathic haemolytic anaemia. The urine contained trace protein and the sediment had 1-3 hyaline casts per high-power field. The patient was afebrile and without major complaints. Because of the microangiopathic haemolytic anaemia, thrombocytopenia, and renal failure, cyclosporin-induced HUS was diagnosed.

When the platelet count and haematocrit continued to fall for 2 days after admission, azathioprine and cyclosporin were discontinued. FK506 was started at 8 mg daily (0.15 mg/kg) intravenously and changed to 16 mg per day orally after 3 days. Within 24 h of the start of FK506 the platelet count had increased to 130 000/μl, and by the seventh day it was 420 000/μl (figure). The haematocrit rose progressively, starting on day 6. Renal function initially worsened but also began to improve on day 7 of FK506 therapy. Dialysis was not required. Total bilirubin fell promptly (figure). The patient was discharged after a week, and a week after this his serum creatinine was 4.2 mg/dl and platelet count 420 000/μl.

After discharge, the dose of FK506 was arbitrarily halved. 4 weeks later HUS abruptly recurred with thrombocytopenia, hyperbilirubinaemia, and acute renal failure. The oral FK506 dose was restored to 16 mg daily, with resolution of the HUS within a few days and during the ensuing 6 weeks.

This patient quickly recovered from cyclosporin-induced HUS without the need for plasmapheresis or other ancillary therapy. Cyclosporin-induced HUS is often fatal¹⁻⁴ and poor control of graft rejection accompanies the discontinuation of cyclosporin. In our patient the offending immunosuppressive agent was replaced by a more potent one.⁵ Cyclosporin and FK506 both inhibit interleukin-2 production and binding and selectively suppress T-cell function. However, the two drugs have a completely different chemical structure, and this may explain the salutary effects of FK506 in cyclosporin-induced HUS.

Rapid recovery, as seen in this case, has been uncommon. Gradual improvement of the haematological picture has been the usual course as cyclosporin is cleared from the plasma with or without plasmapheresis. Cyclosporin-induced endothelial cell injury is the probable proximate event in the pathogenesis of HUS in most cases. However, autoimmune haemolytic anaemia has also been described.^{6,7} The ancillary manoeuvres used to treat cyclosporin-induced HUS are directed at immune mechanisms. FK506, the most potent immunosuppressant yet used clinically,^{5,8} may exert its effect not only by substituting for cyclosporin but also by treating the primary immunological origin of this disorder.

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1. . Hospital course of patient with cyclosporin-induced HUS

PLAT CT (○—○)=platelet count (1000s/μl) and BILI (□—□)= serum bilirubin (mg/dl).