Ciclosporin A and Griseofulvin: Another Drug Interaction

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Sir,

The list of drug interactions with Ciclosporin A (CsA) in renal transplant patients is steadily growing [1, 2]. In this respect, antifungal agents, such as ketoconazole, have been associated with increasing CsA blood level, thus enhancing nephrotoxicity [3]. In this report, griseofulvin on the contrary, is accused, for the first time to our knowledge, to lower CsA blood level.

A 57-year-old male with hypertensive nephrosclerosis and diabetes mellitus received an HLA-identical renal allograft in January 1989. He did very well apart from onychomycosis which was resistant to local therapy, and thus was started on griseofulvin 500 mg once daily in December 1989. At that time, his immunosuppressive protocol consisted of daily CsA 2.8 mg/kg; azathioprine 75 mg, and prednisone 5 mg. He was also receiving nifedipine retard for mild systolic hypertension, and iso-niazid as a prophylactic measure because of a history of tuberculosis. His CsA trough blood level was maintained around 90 ng/ml (monoclonal whole blood RIA). Two weeks following griseofulvin, his CsA blood level dropped to around 50 ng/ml and continued to be in that range in spite of increasing the CsA dosage to 4.8 mg/kg. At 16 weeks of therapy, the fungal infection of the fingernails cleared, and griseofulvin was discontinued. CsA blood levels markedly increased shortly after that to above 200 ng/ml, and the dosage of CsA was readjusted accordingly. Serum creatinine continued to be stable around 1.2 mg/dl during this episode.

In our patient, the temporal relation between griseofulvin therapy and the drastic decrease in CsA blood level

was very impressive both at the start of therapy as well as at its termination. Although isoniazide, a medication which has been associated before with reduced CsA blood levels [4], was given, we still believe that griseofulvin was probably the causative agent, since there was no change in isoniazide dosage during that episode. Fortunately, these significant fluctuations in CsA blood level did not precipitate an episode of rejection thanks to the fact that our patient had received a very well-matched allograft and was on triple immunosuppressive regimen. Nevertheless, this case illustrates the need for close monitoring of CsA blood level each time a newer pharmacologic agent comes into use.

References

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