Ciclosporin Neurotoxicity Presenting as an Unilateral Foot Drop in a Renal Transplant Patient

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Sir,

Greizard et al. [1] reported acute myositis possibly due to ciclosporin toxicity. With growing interest in this subject, we describe here a case of ciclosporin neurotoxicity presenting as a unilateral foot drop in a renal transplant patient.

A 55-year-old male developed end-stage renal failure secondary to urolithiasis. After a short (2 weeks) stay on hemodialysis, he underwent renal transplantation on 25 April, 1989. The postoperative period was uneventful except for ciclosporin nephrotoxicity which was responsive to dose reduction (as serum creatinine decreased from 2.4 to 1.5 mg/dl). His body weight was 62 kg and BP was 150/90 mm Hg. Biochemistry including BUN, creatinine, electrolytes, calcium, liver enzymes and cholesterol were within the normal range. Six weeks later, while he was on ciclosporin 240 mg (3.9 mg/kg/day) and whole blood level by monoclonal RIA method was 272 ng/ml (normal therapeutic range 160–320 ng/ml), he developed sudden isolated left foot drop with power grade 0–1/5 in the dorsiflexion group of muscles. There were neither sensory losses nor other neurological deficits. Cerebral causes were excluded by clinical and normal CT examination. There were slightly reduced nerve conduction velocity and distal motor response amplitude of the left common peroneal nerve with no focal demyelination. Needle EMG revealed fibrillation in the distal muscles. These findings were suggestive of an axonal degeneration process. On dramatic reduction in the ciclosporin dose to 100 mg (1.6 mg/kg/day) blood level dropped to 90 ng/ml and the neurological deficit recovered completely within 4–5 days. Creatinine also decreased from 1.9 to 1.5 mg/dl.

Unilateral foot drop due to ciclosporin therapy was not previously described in the literature. Hypertension, concurrent high-dose methylprednisolone, state of aluminum overload and hypomagnesaemia seem to contribute to an individual's susceptibility to develop ciclosporin neurotoxicity [2]. However, none of these factors were present in our case. More interestingly, our patient had mononeuritis in spite of a normal therapeutic range of ciclosporin. This toxic effect, resulting from an abnormal metabolism of ciclosporin by liver cytochrome P-450 111A [3], remains one of the possibilities. However, the [14C] erythromycin breath test was not carried out. Fami-glio et al. [4] showed, in an experimental rat model, that central nervous system toxicity may be due to a direct toxic effect of ciclosporin; however, such

an effect would not explain the mechanism of foot drop in our patient. Thus, ciclosporin-induced unilateral foot drop is a new form of neurotoxicity, which physicians should be aware of.

References

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