Cyclosporine Neurotoxicity in a Renal-Transplant Recipient

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Dear Sir,

Cyclosporine A (CsA) has decreased the rate of allograft rejection, but its use is associated with multiple side effects [1]. CsA-induced neurotoxicity is often mild, and complex neurotoxicity manifesting as cerebellar syndrome and spinal motor dysfunction is rarely reported in bone marrow and liver transplant recipients. In this report, we wish to emphasize that severe cerebellar syndrome and psychiatric manifestations can occur due to CsA toxicity in renal-transplant patients who are profoundly immunosuppressed.

A 32-year-old male received a living-related renal allograft and was on conventional immunosuppression (Azoran 2.5 mg/kg + 10 mg prednisolone). He was also receiving antitubercular treatment (Isonex, ethambutol and pyrazinamide) for pulmonary tuberculosis. Eight months after transplantation, he had a rise in serum creatinine, oliguria and was detected to have acute cellular rejection on renal-allograft biopsy. He received antirejection treatment with 80 mg i.v. dexamethasone for 3 days but did not show satisfactory response. He was put on CsA (5 mg/kg body weight orally daily). His serum creatinine level was 3.0 mg%. After 2 days of CsA therapy, he complained of instability of gait, slurring of speech and inability to use his hands. On examination he was normotensive (blood pressure 130/80 mm Hg) and cooperative. He had cerebellar signs in terms of cerebellar gait, scanning speech, dysdiadochokinesia and titubation. Motor power and deep tendon reflexes in all four limbs were normal. CT scan and CSF examination did not show any abnormality. The fundus was normal. CsA was withdrawn as a presumptive diagnosis of CsA-induced neurotoxicity was made. This cerebellar syndrome lasted for 8 h. Similar symptoms developed 4 days later, when CsA was reintroduced (dose 3 mg/kg + 30 mg prednisolone) as he was leukopenic and was not able to take Azoran. The patient required intravenous haloperidol and diazepam to control psychosis followed by depression which persisted for 1 week. Blood biochemistry revealed serum creatinine 3 mg%, normal serum calcium, phosphorus, serum sodium and potassium and liver enzymes. Serum

cholesterol and serum magnesium levels were also normal. He had no prior history of psychiatric illness. CsA was withdrawn. The cerebellar symptoms and psychiatric manifestations disappeared fully 7 days after the discontinuation of CsA. On discharge neurological examination was normal. Speech was clear and gait had returned to normal. CsA can cross the blood-brain barrier as it is lipid soluble. A variety of CsA-induced neurological manifestations have been reported [2-4]. CsA-induced psychosis can also occur which manifests as hallucinations, paranoid delusions and violent behavior [2, 4] as was seen in the present case. CsA-induced neurotoxicity is a diagnosis of exclusion. Other factors like steroid toxicity, infections and other metabolic abnormalities could also be responsible for neurological abnormalities after transplantation. In the present case, there was no evidence of infection or any other metabolic CSF or CT scan abnormality. This patient had received intravenous steroids for antirejection therapy 4 days before the onset of neurological symptoms. Rechallenge with CsA again precipitated cerebellar and psychiatric symptoms implying that CsA was the responsible agent.

In our patient, blood CsA levels were not available. A correlation between blood CsA levels and neurotoxicity has not been found in many reports, and CsA can induce neurotoxicity even with therapeutic blood levels in the presence of structural damage and with high-dose steroid use [3]. In our patient, cerebellar and psychiatric symptoms were precipitated by oral CsA. This case highlights rarely reported psychiatric and cerebellar manifestations induced by CsA which disappeared after total CsA withdrawal.

References

- Kahn B, Flechner SM, Lorber MI, et al: Complications of cyclosporine therapy. *World J Surg* 1986;10:348-360.
- de Groen PC, Aksomit AJ, Rakela J, et al: Central nervous system toxicity after liver transplantation: The role of cyclosporine and cholesterol. *N Engl J Med* 1987;317:861-866.
- Palmer BF, Toto RD: Severe neurologic toxicity induced by CyA in 3 renal transplant patients. *Am J Kidney Dis* 1991;18:116-121.
- Koh MK, Habib N: Neurological complication following cyclosporine therapy – A case report. *Clin Transplant* 1993;7:216-217.