

Tacrolimus-induced cerebral blindness in a liver transplant patient

Sir,

We would like to describe a case of reversible posterior leukoencephalopathy syndrome (RPLS). An 18-year-old male underwent a liver transplant. On post-operative day 7, he complained of blurry vision. The blood pressure was between 134 – 161/74 – 91 mm Hg. Medications included mycophenolate mofetil 1000 mg twice daily, and tacrolimus 1 mg twice daily.

An examination revealed light perception vision with normal pupillary light responses, and normal optic nerve heads without swelling or pallor.

A cerebral basis for visual loss was suspected, and magnetic resonance imaging (MRI) revealed sub-cortical hyper-intense white matter lesions in the occipital lobes bilaterally consistent with RPLS.

Tacrolimus blood levels over the 7 days prior ranged between 6.1 - 13.5 ng/ml (therapeutic range 5-20 ng/ml). The dosage of tacrolimus was reduced to 0.5 mg twice daily. Mycophenolate was discontinued, and azathioprine, prednisone, and metoprolol were added. On follow-up examination 1 week later, the patient's vision had improved to 20/30 in his right eye and 20/50 in his left eye.

3 weeks after the patient's initial visual symptoms, he was re-admitted for altered mental status, respiratory failure, and sepsis. An MRI of the brain revealed a cerebellar abscess. Complete resolution of sub-cortical white matter hyperintensities in the occipital lobes was noted.

The patient's neurological status continued to deteriorate due to brain stem edema and cerebellar tonsillar herniation. He passed away 5 weeks status-post transplant following a catastrophic stroke.

Tacrolimus-induced RPLS should be suspected in the presence of neurologic symptoms and characteristic finding of sub-cortical white matter lesions on brain MRI.^[1] It is believed, that the breakdown of the blood-brain barrier may lead to delivery of high doses of the highly lipophilic calcineurin inhibitor to cerebral white matter, causing a direct neurotoxic effect.^[2] Factors reported to exacerbate tacrolimus neurotoxicity include hypertension, elevated tacrolimus blood levels, high-dose corticosteroid therapy, low serum cholesterol, magnesium and aluminum overload, and hepatic encephalopathy.^[2]

Although tacrolimus-induced RPLS is more commonly seen with elevated blood levels of tacrolimus, neurotoxicity may occur even at therapeutic levels,^[3] as seen in our patient. In our patient, visual loss was noted on postoperative day 7. Tacrolimus blood level was 10.6 ng/ml, mean systemic blood pressure was 184/92, and liver function tests were within normal limits. Reduction of tacrolimus dose and lowering of systemic blood pressure led to complete recovery of visual and neurological symptoms.

Although mycophenolate was also discontinued along with decrease in the dose of tacrolimus, one wonders about

the possibility of mycophenolate alone or a combination of mycophenolate and tacrolimus causing neurotoxicity. After literature search in PubMed and MEDLINE, we did not come across any confirmed reported cases of mycophenolate alone causing RPLS. We only found a single report speculating that the combination of mycophenolate and cyclosporin could cause neurotoxicity.^[4] To our knowledge, this is the second reported case of tacrolimus-induced RPLS in a liver transplant recipient without hepatic dysfunction who primarily presented with visual symptoms. Decreasing the dose or discontinuing the calcineurin inhibitor, lowering the systemic blood pressure, and correcting other metabolic derangements usually results in complete resolution of symptoms.

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