Tacrolimus-induced posterior reversible encephalopathy syndrome presenting as left upper limb monoplegia, convulsions, and sudden blindness: case report

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Abstract

Background: To report a case of sudden onset left upper limb monoplegia, convulsions, and bilateral blindness in a patient receiving tacrolimus for immunosuppression following living donor liver transplantation (LDLT) consistent with posterior reversible encephalopathy syndrome (PRES).

Case presentation: We report a case of a 64-year-old male patient on tacrolimus treatment following LDLT. On day 11, during his post-operative routine follow-up. The patient developed sudden onset of left upper limb monoplegia associated with attacks of convulsions and sudden bilateral blindness. MRI revealed multiple, bilateral cortical, and subcortical areas of high T2 and FLAIR signal intensity that did not show restricted diffusion. Findings were suggestive of posterior reversible encephalopathy syndrome (PRES). After the cessation of tacrolimus, vision was completely regained and all other neurologic symptoms were resolved, and follow-up MRI was normal. This case represents an uncommon presentation of tacrolimus toxicity.

Conclusion: Tacrolimus toxicity may present with PRES. Neurological deficits may be fully reversible with discontinuation of the drug; therefore, the early recognition and prompt management of this condition are of utmost importance.

Keywords: Tacrolimus, Left upper limb monoplegia, Convulsions, Sudden blindness, MRI brain, Posterior reversible encephalitis syndrome
other possible causes. There are also characteristic MRI and CT white matter lesions, but these are not always present as CT finding.

The aim of this case presentation is to raise the awareness of rare tacrolimus-induced side effects such as sudden bilateral blindness and serious neurological symptoms consistent with PRES.

Case presentation

A 64-year-old male underwent living donor liver transplantation for recurrent hepatocellular carcinoma (HCC) within the Milan criteria. He was not known to have a history of diabetes or hypertension. His donor was related (his sister), 40 years old, no past medical history, BMI = 27, liver biopsy showed 10–12% steatosis; graft to recipient weight ratio (GRWR) was 0.8%. PET scan was normal 1 month before transplantation.

On day 11, following liver transplantation and during regular daily assessment, painless left upper limb weakness (grade 0) was observed. Shortly after, an attack of status epilepticus started and followed by loss of consciousness (GCS less than 8). The patient was readmitted to ICU, sedated, and needed mechanical ventilated for 3 days due to his current conscious level and the state of status epilepticus. Convulsions were controlled with anticonvulsant treatment and a continuous infusion of midazolam; after that, the patient progressively regained normal conscious level and was weaned from the mechanical ventilation. Following regaining consciousness, the patient developed bilateral blindness. The neurological assessment revealed bilateral complete loss of vision with left upper limb monoplegia, other neurological examination was normal. Ophthalmologic examination revealed bilateral complete loss of vision up to no light perception. Pupils were non-reactive and pinpoint. Eye movements, intraocular tensions, fundus examination, and anterior slit-lamp examination were normal.

The patient’s initial blood work-up included a complete blood count, chemistry panel including electrolytes, creatinine, liver function tests, and thyroid function tests and were all within normal ranges.

His medication included tacrolimus 2 mg twice a day since day 1 of transplantation. Tacrolimus blood level was 8.12 ng/ml (target therapeutic level in blood is 10–15 ng/mL) [7].

CT brain with contrast was normal. Magnetic resonance imaging (MRI) demonstrated bilateral, multifocal, cortical and subcortical areas of bright T2 and FLAIR signal intensity in the occipital and fronto-parietal regions. They show no diffusion restriction on DWI and ADC map. Those changes were consistent with atypical radiological features of posterior reversible encephalopathy syndrome (PRES) (Fig. 1). Also, atypical MRI findings that may be found with PRES could include diffusion restriction on DWI, post-gadolinium contrast enhancement on T1W images, and hemorrhage [8].

Fig. 1 MRI and MRA of the brain. a, b Axial T2 and FLAIR WIs demonstrate bilateral, cerebral, multifocal cortical, and subcortical areas of high signal intensity. c, d Axial diffusion WIs and ADC map at the same level showing no evidence of restricted diffusion. e, f MRA images showing normal appearance of the anterior and posterior circulation major vessels.
He was not hypertensive and his workup excluded any infectious or metabolic causes.

Tacrolimus toxicity was considered the most probable suggested cause and accordingly was discontinued. Immunosuppressive regimen of was changed into mycophenolic acid 1000 mg three times a day and prednisone 40 mg daily. All manifestations including weakness and loss of vision progressively improved with complete normalization in a couple of weeks.

The patient had not had any further deterioration of his vision, attacks of convulsions, or weakness. His follow-up MRI 2 weeks later was completely normal.

Discussion
Posterior reversible encephalopathy syndrome (PRES) or reversible posterior leukoencephalopathy syndrome is a syndrome of clinical findings with characteristic neuroradiological findings that was first described by Hinchey et al. [9]. It is a clinico-radiological syndrome that may present with one or a combination of headache, nausea, altered mental status, blurred vision, vision loss, and seizures. These symptoms were found in combination with neuroradiographic findings of edema of the posterior cerebral white matter. Although the exact pathophysiological mechanism is still unclear, numerous etiologies have been reported and include use of immunosuppressant medications, hypertensive encephalopathy, and eclampsia [8]; that is supposed to cause disruption in the BBB results in picture similar to that of vasogenic edema vs. cytotoxic edema [10].

Currently, there are no set diagnostic criteria for making the diagnosis of PRES; however, characteristic imaging findings in the setting of the above clinical presentations are consistent with the diagnosis. While changes may be present on CT, MRI is considered the best imaging modality to capture characteristic findings [11].

Our patient developed sudden onset of left upper limb weakness, convulsions, and blindness up to no light perception (symptoms consistent with PRES) while on oral tacrolimus therapy which promptly responded to discontinuation of accused medication. Although the patient did not have risk factors for optic neuropathy, the bilateral nature and concurrent PRES symptoms which resolved with the cessation of tacrolimus are consistent with tacrolimus-induced toxicity.

This can be explained by toxic effects of immunosuppressant medications on cells that may damage the endothelium of vessels and thus causing leakage of fluid into the brain parenchyma [12].

Tacrolimus is known to cause optic neuropathy and many mechanisms have been proposed including direct neurotoxic effect causing axonal swelling or a vascular mechanism [13].

It is important also to highlight that the tacrolimus toxicity can occur even within its therapeutic level [14] as occurred in our patient.

We find this association particularly important in an era of increased transplantation and immunosuppression use. Clinicians, including ophthalmologists, and neurologist should be aware of this association.

Herein, we portrayed a case of tacrolimus-induced side effect presenting with feature consistent of PRES.

Conclusion
It is important to raise the awareness of the possibility of tacrolimus-induced PRES as rare side effect following liver transplantation even within its therapeutic level. PRES generally has a good prognosis, prompt recognition, and management are important in preventing significant disease morbidity and mortality.

Abbreviations
LDLT: Living donor liver transplantation; PRES: Posterior reversible encephalopathy syndrome; HCC: Hepatocellular carcinoma; GRWR: Graft to recipient weight ratio

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Authors’ contributions
MS analyzed and interpreted the patient data regarding the liver disease and the transplant from the surgical point of view. AS analyzed and interpreted the patient data regarding the liver disease and the transplant from the surgical point of view. AA participated in revising the manuscript and general supervision of the research group. OA analyzed and interpreted the patient data regarding the radiological data. AG participated in writing the manuscript and general supervision of the research group. ME collected the data. AAA was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

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The study was approved by institution ethical committee and form review board of Kasr Al Ainy Hospital. Oral and written informed consents were obtained from the patient or from his eligible relatives.

Consent for publication
Oral and written informed consents were obtained from the patient or from his eligible relatives.

Competing interests
The authors declare no potential competing interests.

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