CASE REPORT

Post Renal Transplant Posterior Reversible Encephalopathy Syndrome

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Abstract

Posterior reversible encephalopathy syndrome is commonly associated with factors like hypertension, immunosuppression, uraemia, volume overload and electrolyte disturbances in post renal transplant patients. We report a case of (posterior reversssible encephalopathy syndrome) PRES in young post renal transplant patient where all these common associations were absent. High index of suspicion, clinical course and characteristic MRI finding was the key to the diagnosis.

Case Summary

A 18 yr old male, renal transplant recipient, on third post-operative day of renal transplant surgery developed acute onset bilateral headache with visual disturbance followed by an episode of generalised tonic clonic seizure for 1-2 min and postictal confusion followed by continuous irritability. The physical examination revealed afebrile status, pulse rate of 84/min., blood pressure of 140/84 mm Hg, no pedal oedema, no focal neurological deficit, no papilloedema, and no neck rigidity.

After collecting blood sample for Serum Tacrolimus level, tacrolimus was stopped and intravenous Phenytoin loading dose was given followed by maintenance dose. MRI brain revealed bilateral symmetric vasogenic oedema mainly involving the subcortical white matter in the parieto-occipital, posterior temporal, and posterior frontal lobes. The MR angiography of the vertebrobasilar system was unremarkable without any area of stenosis or vasospasm. Possibility of venous infarct was ruled out by MRI venogram. CSF was normal and rest biochemical tests (sr. creatinine – 1.04, sr. potassium - 4, BUN - 08, sr. calcium - 7.9) and graft function were unremarkable.

For uncontrolled, recurrent seizures despite being on IV Phenytoin (serum Phenytoin level of 14 mg/l) and Midazolam infusion @ 5 mg/hr. He was shifted to ICU. He was electively put on volume control mode ventilation and additionally sedated with fentanyl and started on IV levetiracetem 500 mg twice a day. On this regimen he remained seizure-free for next 36 hrs. He was weaned off the

Fig. 1: MRI Brain showing signs of cerebral oedema in occipito-parietal lobes

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Post-recovery MRI Brain showing complete recovery of cerebral oedema

ventilator and was shifted to renal transplant unit. There was complete recovery of the vision. Repeat MRI brain after a week showed significant decrease in cerebral oedema (Figures 1 and 2). Initially tacrolimus was stopped considering a possibility of calcineurin inhibitor toxicity, and restarted in small doses after confirmation of serum tacrolimus levels which was 12.3 ng/ml (normal-5-15 ng/ml). His blood pressure was never elevated, urine output was adequate and there was no pedal oedema or signs of fluid overload throughout this stormy post-transplant period. Afterwards there was no further episode of seizure or any other focal neurological deficit. Based on the clinical presentation, imaging appearances and complete restoration of neurological function, a diagnosis of PRES was made. Later patient was discharged in stable condition on oral antiepileptics and transplant medicines (tacrolimus, mycophenolate mofetil and steroids).

Discussion

Posterior reversible encephalopathy syndrome is a clinico-radiologic entity characterised by headache, altered sensorium, seizures, and visual disturbances, it is associated with white matter vasogenic oedema predominantly affecting the posterior occipital and parietal lobes of the brain. PRES can be associated with many diverse clinical entities, other than the commonly seen entities like hypertension or immunosuppression. Recognition of the characteristic imaging findings by radiologists is the key to diagnosing this syndrome, so to prevent deleterious work-ups or therapies the suspicion of PRES should always be kept by clinicians.

The pathophysiology of PRES is under debate, but it is related to disordered cerebral autoregulation. Two pathophysiologic mechanisms have been proposed regarding cerebral autoregulation - cerebral vasospasm, which results in cytotoxic oedema, and vasodilatation, which results in vasogenic oedema. The pathophysiology of PRES also implicates endothelial dysfunction, especially in cases without severe hypertension, such as pre-eclampsia or cytotoxic therapies. Patients with PRES in the setting of longstanding hypertension may have markedly elevated blood pressures, while less severe elevations, even normal blood pressures, are associated with PRES in other settings. Children appear particularly vulnerable to PRES at lower blood pressures than adults.

The most characteristic imaging pattern in PRES is the presence of oedema involving the white matter of the posterior portions of both cerebral hemispheres, especially the parieto-occipital regions, in a relatively symmetric pattern that spares the calcarine and paramedian parts of the occipital lobes. However, other structures such as the brain stem, cerebellum, and frontal and temporal lobes may also be involved, and although the abnormality primarily affects the subcortical white matter, the cortex and the basal ganglia may also be involved.

Recently, studies with diffusion-weighted sequences and diffusion-tensor sequences have shown increased apparent diffusion coefficients (ADCs) in the involved regions accompanied by anisotropy loss, which suggests reversible vasogenic oedema as an underlying pathophysiology. Therefore, early diagnosis and treatment is essential for the patients’ prognosis.

MRI findings of hyper-intense signals on DWI and restricted diffusion on ADC mapping suggest cytotoxic as opposed to vasogenic oedema; these findings seem to be predictive of irreversible infarction and in turn a worse prognosis. More extensive brain involvement, particularly in the brainstem also correlates with a worse prognosis.

The neurotoxic effects of immunosuppressants are well known but still poorly understood. Toxic levels of medications are not required for the development of PRES, and prior exposure to the drug does not appear to be protective. While cyclosporine use is most commonly reported in relation to PRES, other agents including tacrolimus, sirolimus, cisplatin, interferons and bevacizumab (a monoclonal antibody directed against vascular endothelial growth factor) have also been implicated. The mechanisms are thought to be similar. Reduction in drug dosage or prompt removal of the cytotoxic drug is usually recommended in cases of PRES associated with cytotoxic agents. However, cases are reported in which symptoms resolve while the medication is maintained.
immunosuppressive agent is substituted, patients must be followed closely for recurrence of PRES. It is not recommended that agents known to induce PRES be reintroduced, as recurrence has been reported in this setting. Most case series and case reports suggest that posterior reversible encephalopathy syndrome (PRES) is usually benign. In many cases, PRES seems to be fully reversible within a period of days to weeks, after removal of the inciting factor and control of the blood pressure.1,6

In our case abrupt onset, quick recovery and MRI lesions were characteristic of PRES but few things were unusual like this case was normotensive throughout the stormy course, though most of the reported cases have shown hypertension, being a common association, but a few case reports involving children, patients on immunosuppression and pre-eclamptic women have also shown to be associated with normal blood pressure. In Post-transplant PRES case reports, Calcineurin toxicity is common association which was in our case too but serum Tacrolimus level was never more than the desired therapeutic level. However just as in case of cyclosporine it may be necessary to study the optimal blood levels of Tacrolimus in Indian subjects by doing proper multicentric studies as safe optimal levels may differ considerably from population to population. There were no signs of fluid overload or peripheral oedema or electrolyte disturbance, with normal urine output, graft function was fine and normal creatinine levels. The abrupt onset of symptoms and characteristic MRI picture made us think of PRES at all the stages of disease course but at the same time because of absence of usual associations we had to exclude other possibilities. In the end complete clinical and radiological recovery confirmed our suspicion of PRES.

References