Upsala Journal of Medical Sciences. 2014; 119: 50–54

informa
healthcare

CASE REPORT

An uncommon cause of acutely altered mental status in a renal transplant recipient

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Abstract

Introduction. Neurological complications are quite frequent in patients after solid organ transplantation presenting with focal or generalized neurologic symptoms as well as altered mental status. Posterior reversible encephalopathy syndrome is a rare cliniconeuroradiological entity characterized by headache, altered mental status, cortical blindness, seizures, and other focal neurological signs and a diagnostic magnetic resonance imaging.

Case report. We present a case of a 57-year-old woman with one episode of seizures and sudden onset of altered mental status (time and person perception) accompanied with headache at the thirtieth postoperative day after renal transplantation.

Conclusion. Posterior reversible encephalopathy syndrome, although an uncommon post-renal transplantation complication, should be considered in these patients, as several factors surrounding the setting of transplantation have been implicated in its development. Thus, physicians should be aware of this condition in order to establish the diagnosis and offer appropriate treatment.

Key words: *Depression, end-stage renal disease, hypertension, posterior reversible encephalopathy syndrome, tacrolimus*

Introduction

Neurological complications may present in patients after solid organ transplantation, mostly affecting the central nervous system presenting with focal or generalized neurological symptoms as well as altered mental status (1). The differential diagnosis in these cases typically includes stroke, ischemic or hem`orrhagic, meningitis, and encephalitis (Table I). We present an unusual multifactorial syndrome causing acutely altered mental status in a renal transplant recipient. The so-called posterior reversible encephalopathy syndrome (PRES) is a proposed cliniconeuroradiological entity characterized by headache, altered mental status, seizures, and a diagnostic magnetic resonance imaging (MRI) picture (2).

Case report

We report a case of a 57-year-old female with sudden onset of altered mental status (time and person perception) following an episode of seizures, without any kind of hallucinations, and accompanied by headache. She was a kidney transplant recipient, and the above episode occurred on the thirtieth postoperative day after transplantation. She had been diagnosed with end-stage renal disease (ESRD) and had been on hemodialysis for 5 years before she received a graft from a deceased donor in our center. She was also hypertensive and treated with beta-blockers, namely bisoprolol.

Physical examination revealed no focal neurological signs such as paralysis, cortical blindness, or Babinski's sign. After the described episode, the patient was generally stuporous with rare incidence

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(Received 10 May 2013; accepted 4 September 2013)

ISSN 0300-9734 print/ISSN 2000-1967 online
DOI: 10.3109/03009734.2013.842618

Table I. Literature summary of neurological complications after solid organ transplantation.

Author (most recent publication)	Year	Number of patients	Immunosuppression	Organ	Results
Zierer et al. (10)	2007	200	Calcineurin inhibitors	Heart	The most common complication is ischemic stroke, reported in 3%–10% of the patients followed by drug toxicity
Shigemura et al. (11)	2013	759	Calcineurin inhibitors	Lung	Neurological complications are common after lung transplantation, affecting 92% of recipients within 10 years, presenting with symptoms such as seizures, followed by encephalopathy, headache, depression, and focal neurologic etiologies
Dhar et al. (12)	2008	101	Calcineurin inhibitors	Liver	Neurological complications of liver transplantation are more common than with other solid organ transplants, ranging from 4% to 70%, due to the complexity of the surgical procedure, the unfavorable conditions of patients awaiting transplantation (malnutrition, ionic disorders, coagulopathy), and hepatic encephalopathy before the transplant. Encephalopathy is the most common central nervous system complication, followed by seizures
Senzolo et al. (13)	2009	54	Calcineurin inhibitors	Intestine	Neurological complications of intestinal transplantation seem to be more common than with other solid organ transplants, ut are similar in the spectrum of signs and symptoms
Carrasco et al. (14)	2009	668	Calcineurin inhibitors, corticosteroids	Kidney	Central nervous system complications after kidney transplantation are reported in 6%–21% of recipients. Stroke may occur in 8% of renal transplant recipients and may be facilitated by hypertension, diabetes, and accelerated atherosclerosis, which may be acquired during dialysis
Senzolo et al. (13)	2005	15	Calcineurin inhibitors	Pancreas	Major central nervous system complications of pancreas transplantation include hypoxic encephalopathy, cerebral and spinal-cord infarction, and seizures
Kiok (15)	1988	15		Pancreas andkidney	

of hyperactivity. Her body temperature was normal, blood pressure reached 203/147 mmHg, and the heart rate was 123 bpm. Her Hct at admission was 31.4%, C-reactive protein 1 mg/dL, Hb 9.3 g/dL, and WBC 4794 leukocytes/mm^3. TSH, T4, T3, FT3, and FT4 were within normal ranges, and C-reactive protein at episode was 7 mg/dL.

Her blood pressure was controlled by intravenous esmolol infusion, with no improvement of the clinical status. Her immunosuppression regimen included tacrolimus, corticosteroids, and mycophenolate mofetil, according to our immunosuppression protocol. Serum tacrolimus concentrations were measured continuously and were between 6.5 and 7.5 ng/dL. Although these tacrolimus concentrations are generally considered satisfactory and not capable of triggering a tacrolimus-related encephalopathy, the dose of the drug was further tapered after the episode just to keep serum creatinine within preferred ranges (1.3 mg/dL; eGFR >60 mL/min/1.73 m^2).

At the same time, a set of examinations was applied, due to the wide spectrum of differential diagnoses mentioned above. Fundoscopic examination and cerebrospinal fluid analysis including cultures and PCR analysis for HSV 1 and 2 showed no abnormalities. Brain computerized tomography (CT) scans showed no hemorrhagic or ischemic lesions. Electroencephalography analysis was not suggestive of epilepsy. MRI of the central nervous system showed signal abnormalities in the pons and the parietal and occipital lobes. More specifically, fluid-attenuated inversion recovery (FLAIR) MRI (Figure 1) revealed high-signal areas in

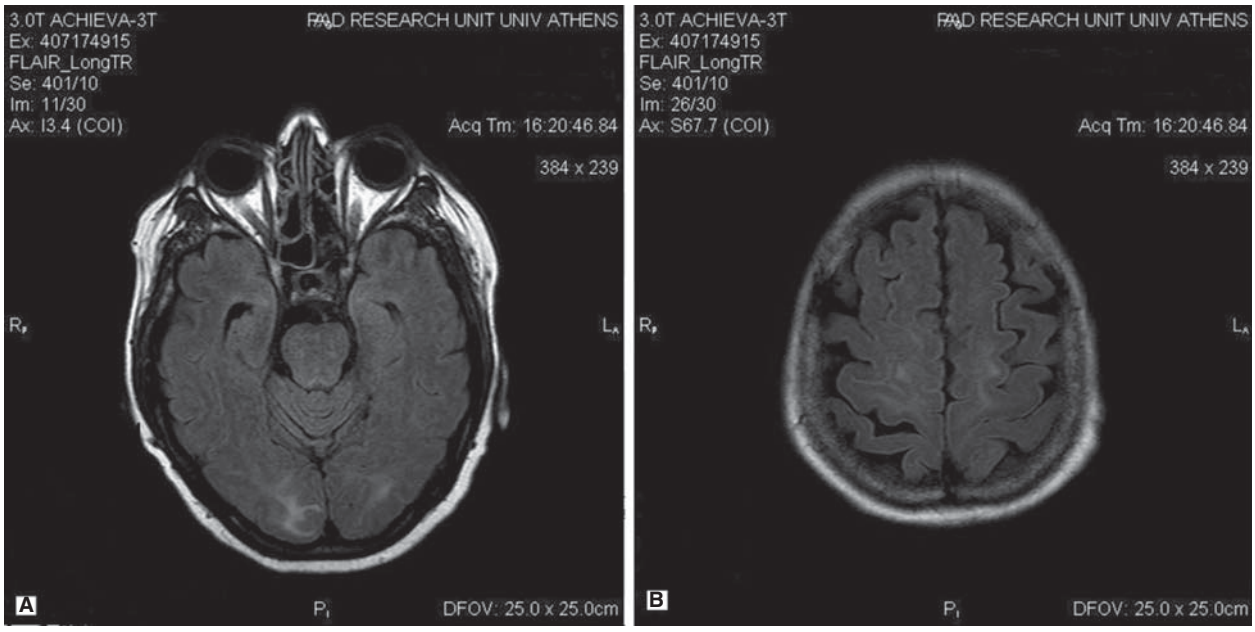

Figure 1. A: FLAIR MRI shows patchy gray areas of high signal in posterior brain within the cortical area and subcortical white matter of the occipital lobes (mainly right). B: FLAIR MRI reveals confluent gray areas of high signal in the parietal lobes, lesions indicative of mild subcortical vasogenic edema.

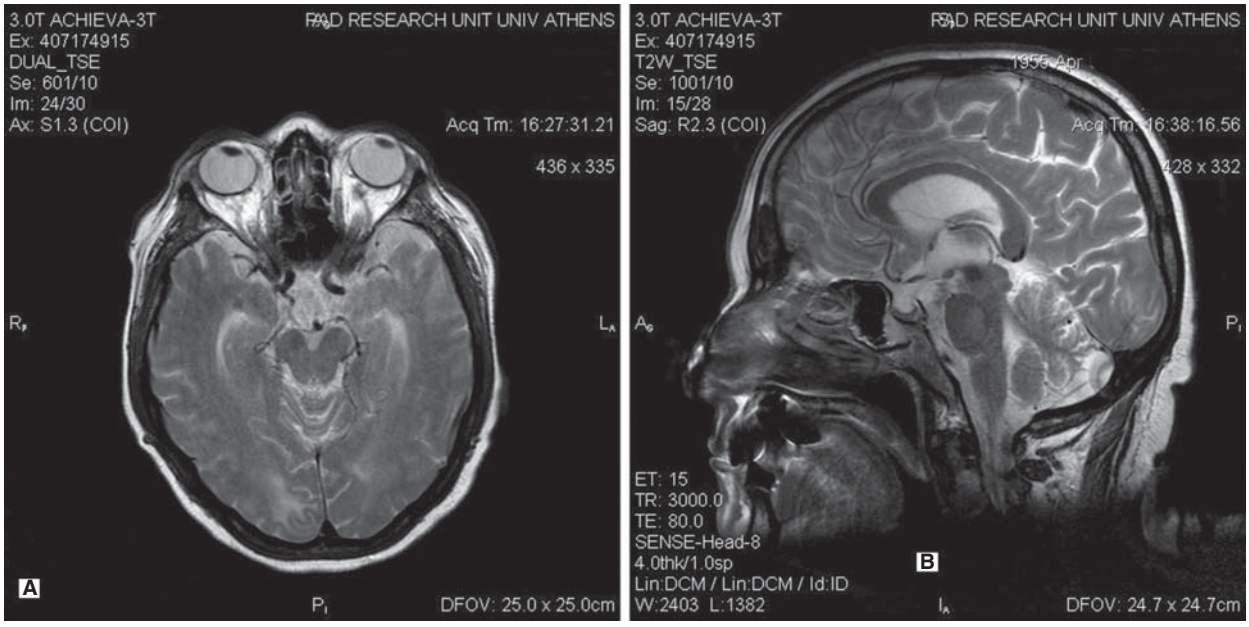

Figure 2. A: Dual turbo spin echo MRI shows patchy lesions in posterior brain, involving cortical and subcortical areas of the occipital and parietal lobes (mainly right) and also of the pons. B: T2W MRI reveals multiple patchy subcortical areas of hyperintense (white) signal involving the occipital lobe and pons, findings compatible with posterior reversible encephalopathy syndrome (PRES).

the occipital and parietal lobes (mainly cortical area and subcortical white matter of the right occipital lobe). Furthermore, T2-weighted (T2W) MRI (Figure 2) showed hyperintense signal involving the cortical and subcortical areas of the occipital lobes and the pons. These signal abnormalities were characteristic of vasogenic edema in the above-mentioned brain areas. These lesions were considered as indicative of PRES.

Psychiatric evaluation, on the other hand, excluded delirium. Antidepressive therapy was administered due to previous history of depression. She was treated intravenously, and 2 days after the initiation of

therapy her condition improved significantly. However, her discharge was delayed as the clinical picture was also complicated by an episode of bacteremia, due to multidrug-resistant *Pseudomonas aeruginosa*, sensitive only to colistin. She was treated with this medication, given in a dose of 9×10^6 IU daily, intravenously for 25 days.

At a 6-month follow-up, the patient is in good shape, without presenting similar episodes of altered mental status.

Discussion

PRES is a proposed cliniconeuroradiological entity characterized by headache, altered mental status, seizures, and a distinctive MRI picture (2). MRI is the most sensitive imaging test to detect PRES. It was initially described by Hinchey et al. (3) in 1996. Many potential predisposing factors have been proposed, including abrupt increases in blood pressure (4), preeclampsia/eclampsia, cyclosporine or tacrolimus (5) neurotoxicity, uremia/ESRD, porphyria, and severe infection or sepsis (2,6,7). With early diagnosis and prompt treatment, the syndrome is usually, but not always, fully reversible. Bilateral parietal and occipital subcortical vasogenic edema is classical and well-established imaging finding of PRES. MRI findings of increased T2W and FLAIR signals, predominantly involving the posterior regions of the cerebral hemispheres, should alert the clinician to the possibility of this diagnosis (4).

As experience of PRES grows, varied and atypical presentations become more frequent (8), such as frontal lobes or even pons involvement (9). For this reason it is thought that PRES is rarely limited to the posterior regions of the brain, and often located in the gray matter and cortex as well as in the white matter (5).

Recently, more assiduous and focused studies have shown that the term posterior reversible encephalopathy is a misnomer as the condition is not always reversible, is not necessarily confined to the posterior regions of the brain, and can affect both white and gray matter (4). Atypical imaging findings should not dissuade the diagnosis of PRES in the appropriate clinical situation, and knowledge of these atypical findings of PRES allows the radiologist to make this diagnosis (8). Posterior reversible encephalopathy is reversible with early cessation of the offending agent, rapid control of hypertension, and treatment of the underlying disease. More specifically, rapid correction of mean arterial blood pressure, with the goal of treatment being its reduction to premorbid levels, should be aimed for. Intravenous antihypertensive drugs should be preferably used. Hydration using intravenous crystalloid fluids, maintenance of adequate arterial oxygenation, and correction of coagulopathies and electrolyte disturbances should be taken into consideration when the diagnosis of PRES is made or suspected. Attention should first be given to monitoring airways and ventilation. Intubation may be initially avoided, but it is necessary to maintain adequate oxygenation if aspiration, hypoxemia, or pulmonary edema occurs. Insertion of a central venous catheter may be sometimes required to guide treatment if cardiac dysfunction is present.

We have described a unique case of PRES in a kidney transplant recipient with the patient's medical history including many potential triggers for the development of the syndrome such as ESRD, tacrolimus therapy, hypertension, and sepsis. However, the patient's condition was rapidly improved with the administration of antidepressive drugs.

Physicians in the transplant community should be alert about this unusual condition, since transplant patients usually present with post-transplantation neurological complications and carry many potential triggers associated with this syndrome. High suspicion of its atypical presentations and variance of clinical and radiological images will result in prompt appropriate management of these patients.

Acknowledgements

Study concept and design: D.M. and S.V. Acquisition of data: S.V. Analysis and interpretation of data: D.M. Drafting of the manuscript: D.M. and S.L. Critical revision of the manuscript for important intellectual content: D.M., S.V., and G.D. Study supervision: G.Z. D.M. and S.V. contributed equally to this study.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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