Pregabalin Toxicity-Induced Posterior Reversible Encephalopathy Syndrome

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Abstract

Posterior reversible encephalopathy syndrome (PRES) is a neurological phenomenon in which vasogenic edema most commonly accumulates in the posterior parieto-occipital white matter. It was caused by some drugs such as opioids methadone or gabapentin.

Rare cases of PRES-related pregabalin were reported. It was typically used to treat neuropathic pain. We present a unique case of a 23-year-old patient without any previous history admitted to intensive care for quadriplegic paralysis with Guillain-Barre syndrome. His neuropathic pain was treated with pregabalin. He presented poorly balanced hypertension and a worsening of renal function due to colistin toxicity. On day 52, he presented a sudden drop in visual acuity without altering his consciousness. Cerebral MRI revealed subcortical white matter edema in the bilateral parietal and occipital lobes with T2 and Flair hyper signals without diffusion restriction suggestive of PRES. He was treated by controlling hypertension and by stopping pregabalin. The clinical course was favorable after 5 days, with a recovery of visual acuity.

This case indicates that physicians must be aware of potential PRES-related Pregabalin toxicity especially when increasing its doses in patients presenting worsening of renal function and in association with opioids.

Keywords: Pregabalin, Poisoning, Intensive care, Outcomes, Pres Syndrome

Introduction

The clinical radiographic syndrome known as posterior reversible encephalopathy syndrome (PRES) is characterized by diffuse structural changes in the cerebral white matter that are caused by bilateral vasogenic edema, which is usually observed in the posterior region of the hemispheres [1,2]. People at risk for presenting PRES have several risk factors including hypertension, preeclampsia, renal failure, kidney illnesses that cause secondary hypertension and hypovolemia, liver disease, exposure to cytotoxic or immunosuppressive medicines[2], autoimmune disorders, and sepsis [2,3]. Few cases had been reported to pregabalin [4,5]. We hereby report a rare case of pregabalin-induced PRES in a 23-year-old patient.

Case report

We report a pregabalin-induced PRES in a 23-year-old patient without any previous history admitted in intensive care with Guillain-Barre syndrome. He was quadriplegic, requiring invasive mechanical ventilation and tracheostomy. His neuropathic pain was treated with pregabalin 150 mg per day, and then increased to 300 mg per day, tramadol hydrochloride 200 mg per day, and morphine 3 mg per day. He also presented with poorly balanced hypertension up to even on nicardipine, clonidine hydrochloride, amlodipine, and methyldopa. He was tachycardic with a pulse of 120 and hypertensive with a blood pressure of 220/110 mm de Hg. It should be noted that the patient presented worsening renal function due to colistin toxicity following a nosocomial infection with creatinine at 200 µmol/l. On day 52, he presented a sudden drop in visual acuity without altering his consciousness. An emergency cerebral MRI revealed bilateral parietal and occipital areas with T2 and Flair hypersignals without diffusion restriction and enhancement after injection of Gadolinium (Figure). Because of hypertension and cerebral MRI findings, PRES was diagnosed. An antihypertensive drug by an electric syringe pump including nicardipine, isosorbide dinitrate, and clonidine hydrochloride was conducted. The blood pressure control was achieved with a target blood pressure of less than 140/90 mmHg. Pregabalin, tramadol hydrochloride, and morphine were discontinued. The clinical course was favorable after 5 days, with a recovery of visual acuity.

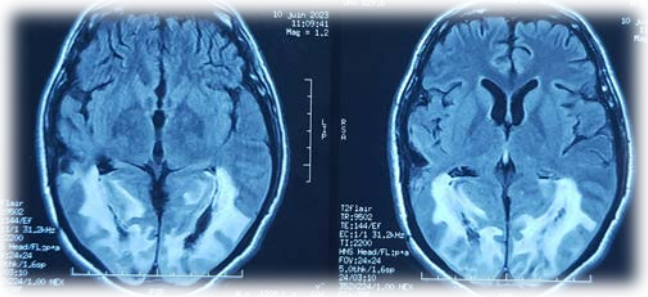

Figure 1 : MRI brain T2 flair: bilateral parietal and occipital areas with T2 Flair hyper signals without diffusion restriction and enhancement after injection of Gadolinium

Discussion

This case indicates that physicians must be aware of potential PRES-related Pregabalin toxicity especially when increasing its doses in patients presenting worsening of renal function and in association with opioids. Pregabalin is used as an adjuvant medication for partial seizures, and the treatment of diabetic neuropathy, fibromyalgia, and neuropathic pain [5]. Few cases have raised concern about the abuse potential of pregabalin

which has increased substantially over the last decade[6]. This medication can intensify the effects of opioids, methadone [5,7], and benzodiazepines leading to neurological disorders [8,9]. Pregabalin acute toxicity has been linked to several occurrences of neuropsychiatric symptoms [10,11]. Two cases study was described: an older patient who had a history of diabetic nephropathy and hypertension who inadvertently overdosed on pregabalin and a patient who developed prerenal azotemia and had years of pregabalin treatment experienced mental changes. In the two cases, the electroencephalogram shows continuous triphasic waves [4,11]. The most likely cause of intoxication in both cases was impaired renal clearance of pregabalin, and after stopping the offending medication, the patient's mental condition completely recovered [4,11] as in our patients who presented worsening renal function leading to a decrease in clearance of pregabalin. In the literature, PRES can occur with some neuromodulating medicines, such as gabapentin and duloxetine, but there is no documented documentation of PRES caused by acute pregabalin poisoning [12,13]. Because both pregabalin and gabapentin belong to the same class of medications called gabapentinoid medications, their pharmacodynamic profiles are similar. Since pregabalin is 2.5 times more effective than gabapentin and has a higher absorption. Uncertainty surrounds the physiopathology of PRES [5]. Hypertension is not always present in cases with PRES. It can cause endothelial injury, and flare vasogenic edema[14] leading to cerebral auto-regulation loss. Another theory holds that endothelial dysfunction is caused by a variety of factors such as infections, autoimmune illnesses, and chemotherapy, which compromises the blood-brain barrier's integrity and thus results in vasogenic edema [15].

The brain barrier is known to be compromised by prevalent drugs of abuse including cocaine,and opioids, which may account for reports of opioids, including methadone, causing PRESS [8,16]. Given his history of renal failure and the rather

large dose of pregabalin he had taken, our patient's toxicity was exacerbated by the opioids (morphine and tramadol hydrochloride). It is challenging to determine whether the acute pregabalin overdose that generated his clinical symptoms and MRI data suggesting PRES was due to the drug's pharmacological action or the potentiating effect of opioids [5,11].

Conclusion: We present a unique instance of pregabalin-induced PRES. Physicians should be mindful of the possibility of pregabalin-induced PRES, particularly when titrating the medication in patients who exhibit decreasing renal function and in combination with opioids.

Conflict of interest

All authors certify that they have no affiliations

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