Acute renal failure due to gabapentin. A case report and literature review

Nefrologia 2012;32(1):130-1
doi:10.3265/Nefrologia.pre2011.Nov.11087

To the Editor,

Gabapentin is an anticonvulsive that is widely used for a number of indications at present: diabetic neuropathy, neuropathic pain of other causes, epilepsy, etc. Some of its most common side effects include the following: ataxia, nystagmus, drowsiness, headaches, diplopia, fatigue and myoclonic twitches.[1] All of these effects appear quite often in patients with chronic kidney disease, especially if they are undergoing dialysis and their doses are not adjusted to their glomerular filtration rates.[2] We describe a new case of rhabdomyolysis and acute renal failure due to gabapentin in order to raise awareness of the importance of monitoring creatine kinase (Ck) and renal function, and of being on the alert for side effects every time this drug is used.[1,3]

The patient, aged 49 years, was taken to the Emergency Department due to delirium, deteriorating condition and myalgias evolving over 48 hours. The patient had visited the Emergency Department two days before due to lumbosacral pain, was diagnosed with mechanical low back pain, and began treatment with 600mg gabapentin every 8 hours.

Relevant medical history included smoking 1 packet/day, active use of multiple substances (alcohol, heroin, cocaine, etc.) and a recent hospital admission. Arterial hypertension treated with eprosartan and bisoprolol. Anxiety-depression syndrome. No relevant nephrological or urological history. Ten days prior to being admitted, he underwent laboratory testing at the clinic. Tests showed normal renal function (creatinine 0.9mg/dl, urea 30mg/dl and no pathological findings in urinary sediment.

His normal treatment consisted of paroxetine, mianserin, disulfiram, eprosartan, bisoprolol, and, during the last 48 hours, gabapentin.

The physical examination showed acceptable general condition, no fever, and low blood pressure (90/60mmHg). The patient was conscious, disoriented and drowsy, with myoclonic twitches. Eupnoea at rest. Normal breath sounds; no oedema in lower limbs, with mucous membrane dehydration. The neurological examination found no focal dystonia or neck stiffness, and the significant finding was that the patient trembled when at rest.

Due to the patient history mentioned above, we screened urine for toxins, and it was positive for cocaine, heroin and morphine. We also ran a full blood and urine analysis which provided the following relevant results:

- Blood: glucose: 146mg/dl; GOT: 246IU/l; GPT: 231 IU/l; bilirubin: 0.8mg/dl; LDH: 2520 U/l; C-reactive protein: 258; Ck: 14911 U/l; creatinine: 13.5mg/dl; urea: 273mg/dl; Na: 136mmol/l; Ki: 6.8mmol/l; Ca: 6.1mg/dl; Pi: 16mg/dl; pH 7.2; bicarbonate: 12mmol/l.
- Urine: specific gravity 1020; pH 5; proteins 30mg/dl; glucose negative; ketone bodies: present; leukocytes 70; erythrocytes 200/μl (after catheterisation).

Given these findings and oligoanuria, doctors requested a kidney ultrasound that showed kidneys of normal size, shape and ecogenicity and no ureteral dilation. Medical treatment for hyperkalaemia and metabolic acidosis was initiated as well as plasma volume expansion. As oliguria, severe metabolic acidosis and delirium persisted with only minimal improvements after administration of 0.5mg flumazenil, we decided to place a femoral catheter and perform an emergency dialysis session. In order to avoid imbalance syndrome, we used a low cut-off dialyser with a flow of 200ml/min during 2 hours 30 minutes and neutral-pH Balance solution. Under this treatment, the patient improved partially from a clinical standpoint; diuresis resumed at 60ml/hour and the metabolic acidosis resolved.

As the patient had a history of multiple drug use in addition to the delirium and the abnormal laboratory results described here, we performed a differential diagnosis to rule out other causes of delirium, such as Wernicke encephalopathy, neuroleptic malignant syndrome and sepsis. The biochemical study was expanded to measure thyroid hormones, vitamin B_{12} and folic acid; results were normal. Serological analyses for hepatitis B and C and HIV were negative. Cultures from blood and urine samples were negative. A cerebral MRI found non-specific demyelinating lesions in pale nuclei and the pyramidal tract that were not compatible with Wernicke-Korsakoff syndrome. Neuroleptic malignant syndrome was effectively ruled out by the absence of high fever and rigidity, in addition to the clinical response following the first dialysis session. We gathered information from family members, who confirmed that the patient had ingested at least 6 gabapentin tablets in the 24 hours prior to admission, along with the drugs cited above.

After discontinuing gabapentin and providing hydration and an additional dialysis session in the following 12 hours, the patient's encephalopathy improved progressively. The electrocardiogram taken at 72 hours showed no pathological findings, renal function became normal (creatinine: 1mg/dl; urea: 55mg/dl in 48 hours and 0.9mg/dl in 36 hours) and Ck values decreased progressively (7327 at 48 hours and 555 at 96 hours).

Gabapentin toxicity and side effects are well-known among nephrologists and fully described in the literature as myoclonic twitches, myopathy, neurotoxicity, etc., particularly in dialysis patients.[2,4]

Rhabdomyolysis with associated acute renal failure is an uncommon side effect, but it has been described in earlier cases.[1,3]

The aetiology of rhabdomyolysis varies greatly. Its most frequent causes include trauma, intense physical exercise, infections, and drugs such as statins, fibrates, neuroleptics, colchicine and proton pump inhibitors.[5,6] It is also

associated with cocaine use, but unlike the case described here, rhabdomyolysis tends to be associated with hypertension and malignant nephrosclerosis. While our patient did use cocaine, this is unlikely to be the root of the problem[7] given that the patient was originally hypotensive and experienced early renal function recovery.

While gabapentin levels were not measured, the rapid resolution of the delirium and recovery of renal function after only two sessions of low cut-off haemodialysis seem to indicate that gabapentin caused the symptoms. In fact, gabapentin is eliminated through renal excretion only, and since it does not bind to proteins, a single dialysis session will eliminate nearly 35% of the total.[8,9] In our case, this would explain the rapid improvement in symptoms. As in the other 2 cases of gabapentin-induced acute renal failure and rhabdomyolysis, the patients involved had multiple illnesses and were affected by multiple medications or other factors that might lead to rhabdomyolysis and renal failure. Another similarity was the rapid resolution of the condition and the improvement in Ck values after discontinuing the drug.

In summary, we can conclude that although it happens infrequently, gabapentin may cause myotoxicity, rhabdomyolysis and renal failure even in patients whose renal function was previously normal. This is why we must take special care with its dosage, with concomitant medications and the patient's co-morbidities, and why, after prescribing gabapentin, we must be watchful for any signs of muscle toxicity or kidney failure and quickly discontinue the drug if necessary.

Conflicts of interest

The authors declare they have no potential conflicts of interest related to the contents of this article.

1. Bilgir O, Calan M, Bilgir F, Kebapçilar L, Yüksel A, Yildiz Y, et al. Gabapentin-induced rhabdomyolysis in a patient with diabetic neuropathy. Intern Med 2009;48(12):1085-7.
2. Bassilios N, Launay-Vacher V, Khoury N, Rondeau E, Deray G, Sraer JD. Gabapentin neurotoxicity in a chronic haemodialysis patient. Nephrol Dial Transplant 2001;16(10):2112-3.
3. Tuccori M, Lombardo G, Lapi F, Vannacci A, Blandizzi C, Del Tacca M. Gabapentin-induced severe myopathy. Ann Pharmacother 2007;41(7):1301-5.
4. Lipson J, Lavoie S, Zimmerman D. Gabapentin-induced myopathyin 2 patients on short daily hemodialysis. Am J Kidney Dis 2005;45(6):e100-4.
5. Guis S, Mattei JP, Cozzone PJ, Bendahan D. Pathophysiology and clinical presentations of rhabdomyolysis. Joint Bone Spine 2005;72: 382-91.
6. Marinella MA. Rhabdomyolysis associated with haloperidol withoutevidence of NMS. Ann Pharmacother 1997;31:927-8.
7. Horowitz BZ, Panacek EA, Jouriles NJ. Severe rhabdomyolysis with renal failure after intranasal cocaine use. J Emerg Med 1997;15(6):833-7.
8. Bluma RA, Pharm D, Thomas J, Schultz RW, Keller E, Reetze P, et al. Pharmacocinetics of gabapentin in subjects with various degrees of renal function. Clin Pharmacol Ther 1994;56:154-9.
9. Wong MO, Eldon MA, Keane WF, Türck D, Bockbrader HN, Underwood BA, et al. Disposition of gabapentin in anuric subjects on hemodialysis. J Clin Pharmacol 1995;35(6):622-6.
10. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimatingthe probability of adverse drug reactions. Clin Pharmacol Ther 1981;30:239-45.

Eduardo Torregrosa-de Juan, Pau Olagüe-Díaz, Pilar Royo-Maicas, Enrique Fernández-Nájera, Rafael García-Maset

Sección de Nefrología.
Hospital de Manises. Manises, Valencia. Spain.

Correspondence: Eduardo Torregrosa de Juan
Sección de Nefrología.
Hospital de Manises, Av. Generalitat Valenciana, 50, 46940 Manises. Valencia. Spain.
torregrosa_edu@gva.es
etorregrosa@hospitalmanises.es

Haemorrhagic fever with renal failure syndrome: a case report

Nefrologia 2012;32(1):131-2
doi:10.3265/Nefrologia.pre2011.Dec.11225

To the Editor,

Haemorrhagic fever with renal syndrome (HFRS) is a clinical condition secondary to infection with a hantavirus (Hantaan, Seoul, No Name, Andes virus, Puumala and Dobrava); the latter two varieties are endemic in rural areas of Eastern Europe, and of the two, infection with the Puumula virus has a better long-term prognosis.[1]

Rodents are the natural carriers of hantavirus, which is transmitted to humans when they come into direct contact with rodent secretions (urine, faeces and saliva).

The natural evolution of the disease entails 4 successive phases following an incubation period of about 3 weeks. The first phase is characterised by fever, followed by a phase with shock and oliguria; patients who survive this phase enter a phase with polyuria, which in turn is followed by a convalescence period of variable duration.

Thrombocytopoenia is common and may produce haemorrhages at any location.

Renal symptoms include proteinuria, haematuria and decreased glomerular filtration rate. Direct vascular endothelial lesions and tubulo-interstitial nephritis mediated by cytokines have been proposed as the underlying physiopathological cause.[2]

Diagnosis is based on a strong clinical suspicion, and confirmed by specific serological methods.[3] Kidney biopsy is not necessary.[4] A renal ultrasound can show the increase in kidney size and in resistance indices. Perirenal fluid collection is also a common finding (in addition to pleural or pericardial effusion or ascites). No vaccine or specific treatment exists; supportive therapy is of vital importance. One double-blind study showed decreased mortality given early treatment with ribavirin.[5]