HyperCKemia induced by levetiracetam

Un cas d’hyperCKémie sous lévétiracétam

To the editor

We report the case of a 25-year-old Caucasian man with a history of epilepsy, diagnosed in 2013 after a first seizure which was treated by levetiracetam. Treatment compliance was poor. The patient was also an active cannabis and tobacco user and was known to exhibit self-destructive behavior. He was admitted to the intensive care unit (ICU) for generalized tonic-clonic seizure lasting for more than 30 minutes following recent sleep deprivation. He received clonazepam 1 mg twice, fosphenytoin 1.5 g and then thiopental for refractory seizures. Suxamethonium was used for orotracheal intubation. Because of status epilepticus, he was sedated with a continuous infusion of thiopental and sufentanil. At admission creatine kinase (CK) concentration level was 289 IU/L with normal renal function. Toxicology screening was negative. Levetiracetam was reintroduced at day 2 after admission (500 mg twice daily). The patient also received clonazepam (5 mg thrice daily on day 1, decreased to 5 mg twice daily on day 4, and stopped on day 5), esomeprazol 40 mg (stopped on day 4), propofol for one day, enoxaparin and crystalloid fluid expansion after intubation. He no longer presented signs of seizure and an electroencephalogram was normal. Propofol was stopped on day 2 and the patient was extubated on day 3. Despite a favorable neurological course, CK level increased (figure 1), reaching a maximum 5 days after admission (15,811 IU/L). The patient had no myalgia. Kidney function was normal but high-volume saline fluid therapy was required, with 7 L saline infused over 5 days. The usual causes of CK elevation were ruled out and a iatrogenic cause was suspected.

The regional pharmacovigilance center was contacted by the hospital pharmacists. Levetiracetam was incriminated and replaced by valproic acid 1 g/day on day 5. CK level decreased rapidly and markedly from day 6 (figure 1). Application of the Naranjo probability scale revealed possible causality between levetiracetam use and the hyperCKemia [1]. Levetiracetam is an antiepileptic drug, which inhibits neuronal hypersynchronization by binding to synaptic vesicle protein 2a (SV2A) in presynaptic membranes. Two cases of rhabdomyolysis and one case of CK exacerbated by levetiracetam therapy have been recently been reported [2–4]. The patients were young (13 to 29 years) with a history of seizures. CK elevation, with values above 29,000 IU/L, appeared one day to one week after levetiracetam introduction. In all cases, levetiracetam was discontinued, leading to rapid decrease in CK levels and rhabdomyolysis symptoms.

In our case, the usual causes of hyperCKemia were excluded: propofol infusion syndrome, sustained immobility, seizure recurrence, ischemia, sepsis, or metabolic disorders. Other drugs were also excluded. Moreover, chronological arguments supported the responsibility of levetiracetam: the seizure led to a first increase in CK levels, but levels rose markedly after levetiracetam was introduced and decreased rapidly after withdrawal. The responsibility of levetiracetam must be suspected in persistent hyperCKemia especially after its introduction for seizure. This case also demonstrates the value of close collaboration between pharmacists and ICU teams to improve patient outcomes [5].

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