Delayed-onset rhabdomyolysis related to olanzapine: a case report

Singapore Med J 2016; 57(5): 279 doi: 10.11622/smedj.2016094

Dear Sir,

Olanzapine is a widely used, atypical antipsychotic. Few reports on the association between regular dosage of olanzapine and rhabdomyolysis have been published to date. The present case report draws attention to delayed-onset rhabdomyolysis, a rare adverse effect of olanzapine therapy, and discusses its possible mechanisms.

The patient, a 62-year-old man, had a history of chronic schizophrenia, with his first episode of auditory hallucination and persecutory delusion occurring at 25 years of age. Between the ages of 30 and 60 years, the patient was repeatedly hospitalised due to psychotic exacerbations. About two years prior to the current presentation, he was receiving rehabilitation in a halfway house and treated with olanzapine 10 mg/day, valproate 500 mg/day, estazolam 2 mg/day and benzhexol hydrochloride 2 mg/day.

The patient was sent to our emergency department when he could not get up from the floor due to generalised weakness and paralysis. On presentation, he was conscious, and had decreased muscle power but no extrapyramidal symptoms. His creatine kinase (CK) level was high (13,046 U/L), but troponin, heart type creatine kinase isoenzyme, blood urea nitrogen, creatinine, complete blood count, electrolytes, C-reactive protein and glucose levels were all normal. Rhabdomyolysis was diagnosed.

On suspicion of its contribution to rhabdomyolysis, olanzapine was stopped. Following hydration, the patient's CK level fell to 11,407 U/L three days later and he was discharged back to the rehabilitation facility on the fifth day. At the one-month outpatient follow-up, his CK level was within normal limits.

The patient had no evidence of seizure on clinical presentation. He also did not have fever or muscle rigidity, making neuroleptic malignant syndrome unlikely. The causal relationship suggesting that olanzapine was the probable cause of rhabdomyolysis was supported by a score of 5 in the Naranjo Adverse Drug Reaction Probability Scale.[1] There have been previous case reports of olanzapine-induced elevation of serum CK level occurring within seven weeks of administration.[2,3] In our case, olanzapine 10 mg/day was administered for nearly two years without dose titration, which could have led to delayed-onset, olanzapine-related rhabdomyolysis. However, the combined effects of polypharmacy might also be a contributory factor, since olanzapine was used concomitantly with other medications like valproate, estazolam and benzhexol hydrochloride. The patient might have been vulnerable to some incipient muscle changes related to the use of olanzapine or the combination of medications over the two years, prior to the occurrence of drug-induced rhabdomyolysis.

Although unclear, the mechanism of olanzapine-related rhabdomyolysis might be drug-related myopathy. Olanzapine is an atypical antipsychotic with a high affinity for histamine-H1, 5-hydroxytryptamine 2A (5-HT2A) and dopamine D2. H1-receptor antihistamines, acting on the sarcolemma, may facilitate sodium flux into the cells, thereby depleting intracellular adenosine triphosphate (ATP) through the activation of energy-dependent Na+/K+ ATPase. Furthermore, an increased intracellular sodium concentration can elevate calcium and activate intracellular proteolytic enzymes, causing progressive rhabdomyolysis-related injury to muscle cells.[4] Also, the antagonist activity at the 5-HT2A receptors can block the uptake of glucose by skeletal muscles and increase its permeability to CK.[5]

In conclusion, even in patients receiving long-term olanzapine treatment, the possibility of delayed-onset rhabdomyolysis should be considered. If clinical manifestations such as muscle weakness, fever or alternations in consciousness occur, monitoring of serum CK is required.

Yours sincerely,

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