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Case Report

Phenytoin-Induced Rhabdomyolysis

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ABSTRACT

Background: A case of rhabdomyolysis, in which the etiology could be associated with phenytoin administration which was used as anti-epileptic drug in intensive care unit.

Case Description: 36-year-old female with disturbed consciousness level due to status epilepticus and post ictal state because of a prolonged attack of tonic-clonic convulsion that lasted for more than 30 minutes. She has no past medical history, drug ingestion or allergies. A phenytoin loading dose of 20 mg/kg was administer with ECG monitoring. After being stabilized in the Emergency room, brian CT scan was done and reported mild brain edema, otherwise unremarkable. Upon admission to ICU her Seizure was controlled .The level of consciousness gradually improved until she became fully conscious .The EEG performed illustrated no active epileptic foci. Plasma phenytoin levels were within the therapeutic range of 10-20mcg/ml with a phenytoin maintenance dose of 100 mg every 8 hours orally. Serum CPK level was 735 IU/L, higher than the expected reference interval of 170 IU/L on admission, and was increasing steadily after that .Despite no convulsion and improvement of Loss of Consciousness, it reached 30,182 IU/L in the second day while in the ICU, however the level increased further after phenytoin maintenance, and reached a peak value of 57,638 IU/L on her fourth day in the ICU. Phenytoin was suspected to have caused rhabdomyolysis when other differential diagnoses were ruled out, phenytoin was substituted with levetiracetam. Subsequently, the serum CK level promptly decreased.

Conclusion: The most likely cause of the rhabdomyolysis was phenytoin treatment due to the relationship between exposure to phenytoin along with symptoms appearance and rapid resolution after discontinuing phenytoin.

Keywords: Rhabdomyolysis; Phenytoin; Creatine phosphokinase; Status epilepticc

ABBREVIATIONS

ICU: Intensive Care Unit; ECG: Electrocardiogram; CT: Computerized Tomography; EEG: Electroencephalogram; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; MRI/MRV: Magnetic Resonance Imaging/Magnetic Resonance Venography

BACKGROUND

Phenytoin is commonly used as an anti-epileptic drug in an intensive care unit, and one of its rarely encountered significant side effects in case reports is phenytoin induced rhabdomyolysis. It has to be among differential diagnosis, so not to be forgotten, here we present a patient with status epileptics who suffers from rhabdomyolysis after being treated with intravenous phenytoin.

CASE DESCRIPTION

A 36 years old female presented to the Emergency room for a disturbed conscious level with a prolonged attack of tonic-clonic convulsion that lasted for over 30 minutes (status epilepticus), she has no past medical history and her relatives denied any drug ingestion or allergies. She recorded normal temperature, her blood pressure was 119/81 mmHg, heart rate 88/min, her clinical examination on arrival showed a Glasgow coma scale of 10/15, no meningeal irritation signs, and no focal neurologic sign. Hemoglobin reading of 12 g/dl, white cell count 8.5 /mm3, normal platelet blood count, sodium level was found to be below 115 mEq/l with high anion gap metabolic acidosis; PH: 7.22 PCO 2.32 HCO3 13 because of an elevated lactic acid level. Thyroid function tests and random cortisol readings were regular. AST and ALT increased to 384 U/L (from 16 U/L) and 256 U/L (from 21 U/L), respectively.

Upon arrival to the Emergency room, anticonvulsant therapy with intravenous diazepam were administered to the patient, followed by a phenytoin loading dose of 20 mg/kg with ECG monitoring. The patient was given a 1 mEq/hr hypertonic saline to correct her hyponatremia, untill her sodium serum level reached 130 mEq/l. After stabilization in the Emergency room, the brain CT scan was done and reported a mild brain edema, otherwise unremarkable. On admission to ICU, the seizure was controlled. The level of consciousness gradually improved until she became fully conscious. EEG performed illustrated no active epileptic foci. Plasma phenytoin levels within the therapeutic range of 10–20 mcg/ml with a phenytoin maintenance dose of 100 mg every 8 hours orally. An Imaging testing; MRI/MRV were performed on the patient with the results being unremarkable. Serum CPK level was 735 IU/L, higher than the expected reference interval of 170 IU/L upon admission, and was increasing steadily after that. Despite the absence of convulsions and improvement of consciousness; it reached 30,182 IU/L in the second day while in the ICU. Moreover, the level increased further after administrating the phenytoin maintenance dose, and reached a peak value of 57,638 IU/L on her fourth day in the ICU. Phenytoin was suspected to have caused rhabdomyolysis when other differential diagnoses were ruled out, phenytoin was substituted with levetiracetam. Adequate hydration and sodium bicarbonate were given to protect the kidney, which remained functioning normally throughout her stay in the ICU and the hospital course. Subsequently, the serum CK level promptly decreased (Figure 1). No more seizures were observed, and the patient was discharged home on day 8.

DISCUSSION

Rhabdomyolysis is a life-threatening syndrome resulting from the rapid breakdown of skeletal muscle fibers, which causes an excessive amount of potassium, phosphate, myoglobin, and CPK to leak into the circulation. The syndrome is present when CPK level is above 1000 IU/L [1,2]. The most important complication is acute renal failure, which occurs in 14–46% of cases [2]. It happens due to an acute tubular necrosis resulting from an obstruction by myoglobin [3]. The known causes of rhabdomyolysis are trauma, epileptic seizures, muscle ischemia, hyperthermia, electrolyte disturbances and local infection with muscular invasion. Drug-induced rhabdomyolysis can occur by a primary direct toxic effect on the myocyte or a secondary indirect effect that predisposes the myocyte to injury [2-4].

In the case we are reporting, CPK was increasing consistently, although the convulsions were controlled as evidenced by an improvement in the level of consciousness, absence of clinical seizures, and normal EEG. On the second day of admission, CPK level was very high; 30,182 IU/L and peaked on day 4 to reach a level of 57,638 IU/L .Other causes of rhabdomyolysis were excluded; myocardial infarction was ruled out as the ECG and Troponin were normal. There was no clinical evidence of skeletal muscle damage or compartment

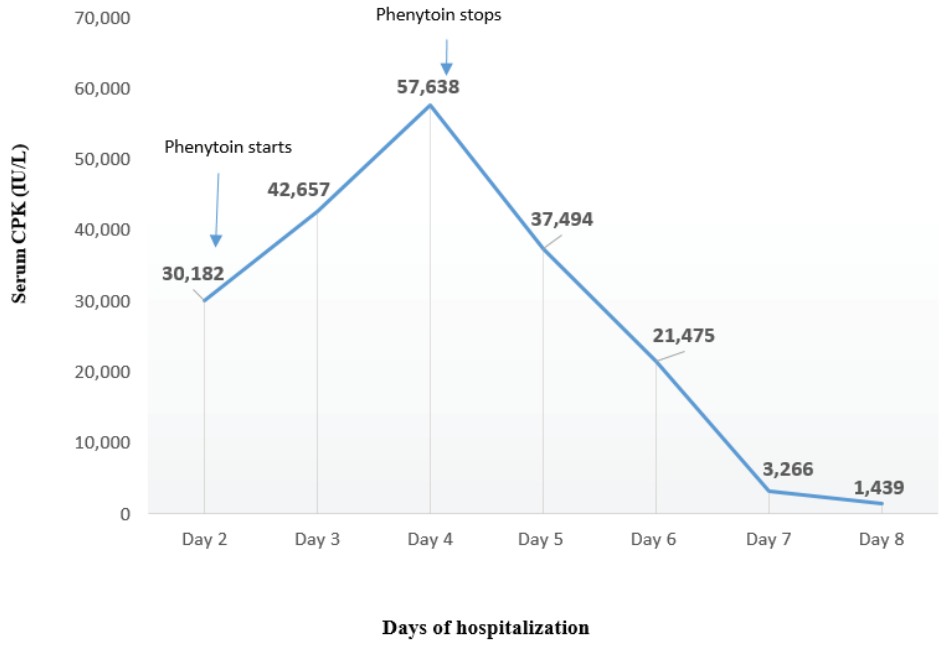

Figure 1: Serum creatine phosphokinase CPK and serum phenytoin concentration during hospitalization.

syndrome, and the drug screen for toxic ingestion was negative. Phenytoin was stopped, and a consistent reduction in CPK was noticed on the 5th day of her discharge. Phenytoin induced rhabdomyolysis might be associated with a phenytoin hypersensitivity reaction, which usually occurs after 3 weeks to 3 months post-exposure and is characterized by fever, rash, lymphadenopathy, and eosinophilia [5], manifestations that were all not present in this case. There are several case reports like this one that reported rhabdomyolysis occurring early and were not associated with hypersensitivity to phenytoin, but as per the reported cases, to the best of our knowledge, our case is the most severe one with a CPK level of 57,638 IU/L compared to 7,769 and 2,825 IU/L [5,6] showing that our case was the severest.

CONCLUSION

Phenytoin should be considered among the differential diagnosis of rhabdomyolysis in ICU, which can occur early and without hypersensitivity. It is a severe side effect and can lead to acute renal failure and death if it was not diagnosed and treated properly.

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