International Journal of Research in Medical Sciences
Çokal BG et al. Int J Res Med Sci. 2022 Jan;10(1):277-278
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20215066

Case Report

Phenytoin-induced rhabdomyolysis

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Received: 25 November 2021
Revised: 13 December 2021
Accepted: 20 December 2021

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ABSTRACT

Rhabdomyolysis is a potentially life-threatening syndrome that can develop from a variety of causes. The most common causes are muscle injury, alcohol abuse, drugs, toxins and increased muscular activity. Phenytoin is one of the drugs that rarely cause rhabdomyolysis. We present the case of a man who developed rhabdomyolysis following phenytoin treatment.

Keywords: Rhabdomyolysis, Phenytoin, Drug

INTRODUCTION

Rhabdomyolysis is a potentially life-threatening syndrome that can develop from a variety of causes. It is caused by skeletal muscle cell damage causing myoglobin and other intracellular material into the circulation. The most common causes are muscle injury, alcohol abuse, drugs, toxins and increased muscular activity.[1,2] Phenytoin is one of the drugs that rarely cause rhabdomyolysis. Phenytoin which is widely used in the treatment of partial seizures and generalized tonic-clonic seizures acts by blocking voltage-gated sodium channels in the neuronal cell membrane.[3] Phenytoin may cause dose related side effects or hypersensitivity reaction. Common side effects include gingival hyperplasia, coarsening of the facies and hursutism. Although rare, rhabdomyolysis associated with the use of phenytoin is a serious side effect. Acute renal failure, electrolyte disorders, such as hyperkalemia, which may cause cardiac arrhythmias and metabolic acidosis are the main complications of rhabdomyolysis.[1]

CASE REPORT

A 23-year-old male patient known for epilepsy was admitted with generalized convulsive status epilepticus. He had a history of generalized seizures since childhood due to perinatal hypoxic ischemic ensepalopathy He was taking levetirasetam 500 mg twice a day for seven years and he had no seizure during this period. He was not taking his drugs for 2 days. There was no finding in physical examination. His vital signs were stable. On neurological examination he was somnolent with Glasgow coma scale 3 and had bilateral extensor plantar reflexes. Laboratory findings including full blood count, serum electrolytes, urea, glucose, liver function tests, arterial blood gases and chest radiography, computed tomography (CT) and magnetic resonance imaging (MRI) of the brain were normal (Figures 1 and 2). He had another tonic clonic seizure in the emergency room. Then he received intravenous injection of 10 mg diazepam and infusion of 1250 mg phenytoin was started for controlling convulsions followed by IV phenytoin 125 mg every 8 hours. Levetirasetam oral dosage was also given 500 mg twice a day. Approximately 4 hours after admission, a repeat creatine phosphokinase (CK) value of 1136 U/l (normal, 0-171) and lactate dehydrogenase (LDH) 292 U/l (normal, 0-248) were recorded. On the second day of his hospitalization IV phenytoin was reduced to dosage of 125 mg twice a day. His CK levels and liver function tests and serum myoglobin levels were significantly elevated. Laboratory tests included: CK: 15655 U/l, LDH: 405 U/l, aspartate aminotransferase (AST) 135 (normal, 0-35 U/l), alanine aminotransferase (ALT) 74 (normal, 0-45 U/l),

myoglobin 1493 ug/l (normal, 0-72 ug/l) with normal level of CK in cardiac muscle (CKMB) and troponin. Laboratory on the third day included: CK: 22112 U/l, myoglobin 1584 ug/l, LDH 410 U/l, AST 169 U/l, ALT 70 U/l. He experienced pain in the lower extremities. A diagnosis of phenytoin-induced rhabdomyolysis was made and phenytoin treatment stopped and his levetirasetam dosage is increased to 750 mg twice a day. The Naranjo probability scale indicated a probable relationship between rhabdomyolysis and phenytoin therapy. Bolus of 0.9% saline followed by an infusion of 0.45% normal saline at 150-200 ml/hour was given and subsequently serial measurements of CK showed a decrease. He did not experience renal failure. The total dose of phenytoin he administered was 1875 mg. All laboratory parameters were within normal limits by the tenth day. He improved rapidly and completely recovered. He was discharged on levetirasetam and remained seizure-free during follow-up.

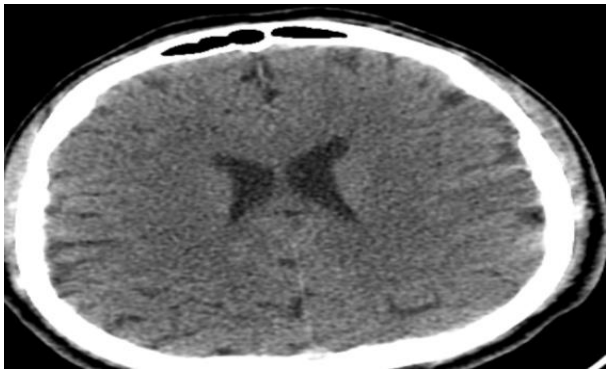

Figure 1: Axial brain CT scan of the patient.

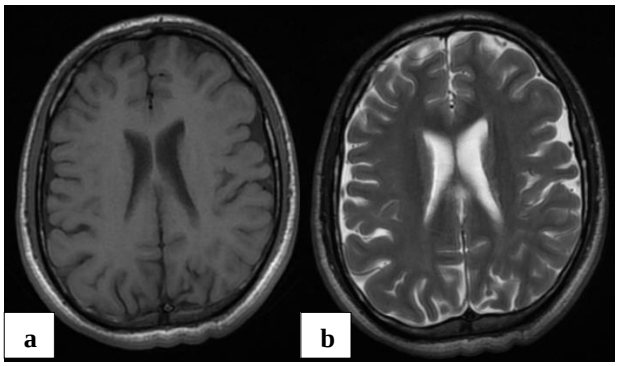

Figure 2: Axial brain T1 (a) and T2 (b) MR imagings of the patient.

DISCUSSION

There are few case reports of rhabdomyolysis that have been associated with phenytoin in the literature.[4,5] Most of them coexist with phenytoin hypersensitivity syndrome which is characterized by fever, lymphadenopathy, rash and eosinophilia.[6,7]

In our case, phenytoin hypersensitivity syndrome was not observed. The cases of phenytoin-induced rhabdomyolysis without any features of hypersensitivity have been reported recently.[8,9] The most significant feature that distinguishes our case from others is that our patient developed acute rhabdomyolysis and our patient had isolated rhabdomyolysis without hypersensitivity syndrome or another disease.

CONCLUSION

This case highlights the rare complication of phenytoin. Early recognition and appropriate management may help to prevent mortality and morbidity in the patients.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Çokal BG, Guler SK, Guneş N. Phenytoin-induced rhabdomyolysis. Int J Res Med Sci 2022;10:277-8.