Case Report

Hypokalemia and rhabdomyolysis

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ABSTRACT

The adverse drug event manager of the Capital Region of Denmark received a report of a 65-year-old male with type II diabetes and long-lasting treatment with indapamide. In addition, he had a history of a high consumption of licorice. For 2 weeks, the patient suffered from myalgia, which the general practitioner suspected to be polymyalgia rheumatica and referred him to the hospital. Initial blood samples revealed a reduced potassium concentration of 1.5 mmol/L (reference value: 6.6-4.6 mmol/L) and an elevated creatine kinase of 18,400 IU/L (reference value: 40-280 IU/L). We believe that the patient developed rhabdomyolysis due to severe hypokalemia, possibly induced by a pharmacodynamic interaction between licorice and indapamide.

Key words: Hypokalemia, indapamide, licorice, rhabdomyolysis, side-effects

INTRODUCTION

Rhabdomyolysis is a relatively rare but potentially lethal condition. Almost half of the patients with rhabdomyolysis develop acute renal failure and, in a large survey, the short-term mortality was 3.4%.[1] The etiology of rhabdomyolysis is multifactorial, but the most common risk factors are medical and illicit drugs, alcohol, muscle trauma and diseases.[1] In this paper, we describe a highly unusual cause of rhabdomyolysis.

CASE REPORT

This case was reported to the adverse drug event manager of the Capital Region of Denmark.; A 65-year-old man with type II diabetes, mild hypertension and a previous history of gout was admitted to the Bispebjerg Hospital, University of Copenhagen, Denmark. The patient's daily prescriptions were indapamide 1.5 mg, allopurinol 300 mg, metformin 2000 mg and simvastatin 40 mg.

Fourteen days prior to hospitalization, he experienced muscle fatigue and soreness in the lower extremities. The symptoms gradually progressed to the upper limbs and neck. The general practitioner suspected polymyalgia rheumatica. On arrival, his blood pressure was 153/88 mm Hg, his pulse was 87 bpm and his temperature was 37°C. The blood samples revealed rhabdomyolysis, severe hypokalemia and normal renal function [Table 1]. Furthermore, the anamnesis uncovered a newly acquired habit of a relatively high consumption of licorice (approximately 100 g/day). There were no signs or history of trauma, diarrhea, polydipsia, infection, intoxication or alcohol intake.

Simvastatin and indapamide were discontinued. Treatment with IV fluids, including potassium substitution, returned the patient's potassium level to normal within 2 days and creatine kinase gradually decreased [Figure 1]. The patient was discharged after 9 days of hospitalization with no signs of kidney injury and an estimated glomerular filtration rate above 90 mL/min.

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Table 1: Blood samples at admission

	Plasma concentration	Reference
Creatine kinase	18400 IU/L	40-280 IU/L
HCO_3-	38.9 mmol/L	22-27 mmol/L
pH	7.56 mmol/L	7.37-7.45 mmol/L
pCO_2	5.9 kPa	4.6-6.0 kPa
Creatinine	101 µmol/L	60-105 µmol/L
Potassium	1.5 mmol/L	3.5-4.6 mmol/L
Sodium	138 mmol/L	137-144 mmol/L
Glucose	6.7 mmol/L	4.2-7.2 mmol/L
Aspartate aminotransferase	543 IU/L	15-45 IU/L
Alkaline phosphatase	74 IU/L	35-105 IU/L
Albumin	47 g/L	36-45 g/L
INR	1.1	<1.2
Leukocytes	15.8×10^9/L	$3.5\text{-}8.8\times10^9$/L
Thrombocytes	411×10^9/L	$145\text{-}390\times10^9$/L
C-reactive protein	19 mg/L	<10 mg/L

INR: International normalized ratio

DISCUSSION

The patient presented in this case report was on daily treatment with simvastatin, which has been associated with rhabdomyolysis. We cannot rule out this causal relationship; however, this usually implies hyperkalemia instead of hypokalemia.

Severe potassium deficiency could also explain the symptomatology and pathogenesis. Forty years ago, Knochel and Schlein showed that muscle blood flow was severely impaired in potassium-depleted dogs.[2] Thus, one possible explanation of the association between hypokalemia and rhabdomyolysis could be ischemia.

The most probable cause of hypokalemia is indapamide. Indapamide inhibits the Na+/Cl- cotransporter in the distal convoluted tubule, and its primary side-effects are electrolyte disturbances and alkalosis, to a large extent mediated through the aldosterone system. The proposed mechanism is an increased conductance of the epithelial sodium channel and enhanced activity of the renal outer medullary potassium channel and H/K ATPase.[3,4]

Licorice consumption may also have contributed to the pathogenesis. The main component of licorice is glycyrrhizin

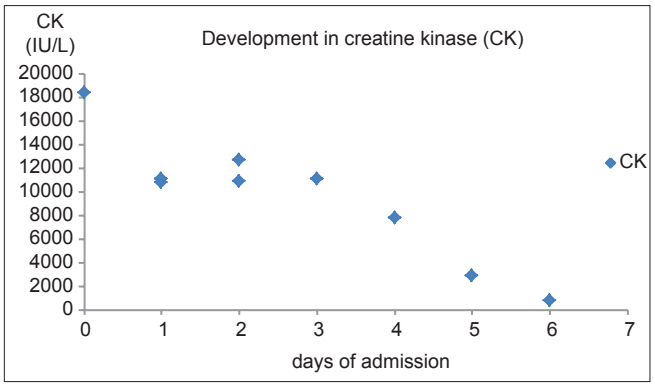

Figure 1: The development in creatine kinase during admission. The patient was treated intensively with IV-fluid and had a daily diuresis of 3 to 5 L

and its metabolites strongly inhibit the 11-β-hydroxysteroid dehydrogenase, which transforms cortisol to cortisone and 5-β-reductase, which is involved in the metabolism of aldosterone. The main effect is symptoms of hyperaldosteronism: Hypertension, hypokalemia and alkalosis.[5]

This case report is an example of the multifactorial etiology of rhabdomyolysis. We conclude that this patient developed rhabdomyolysis due to severe hypokalemia, possibly induced by a pharmacodynamic interaction between licorice and indapamide.

REFERENCES

1. Melli G, Chaudhry V, Cornblath DR. Rhabdomyolysis: An evaluation of 475 hospitalized patients. Medicine (Baltimore) 2005;84:377-85.
2. Knochel JP, Schlein EM. On the mechanism of rhabdomyolysis in potassium depletion. J Clin Invest 1972;51:1750-8.
3. Palmer BF, Naderi AS. Metabolic complications associated with use of thiazide diuretics. J Am Soc Hypertens 2007;1:381-92.
4. Tamargo J, Segura J, Ruilope LM. Diuretics in the treatment of hypertension. Part 1: Thiazide and thiazide-like diuretics. Expert Opin Pharmacother 2014;15:527-47.
5. Omar HR, Komarova I, El-Ghonemi M, Fathy A, Rashad R, Abdelmalak HD, *et al*. Licorice abuse: Time to send a warning message. Ther Adv Endocrinol Metab 2012;3:125-38.

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