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HYPOKALEMIA- INDUCED RHABDOMYOLYSIS – CASE REPORT AND LITERATURE REVIEW

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Abstract
Nowadays, rhabdomyolysis is a common cause of acute kidney injury and it is associated with severe, sometimes life-threatening hyperkalemia. We report the case of a patient with profuse diarrheic syndrome caused by Crohn's disease who developed hypokalemia-induced rhabdomyolysis and multifactorial anuric acute kidney injury. Prompt diagnosis and treatment of Crohn's disease, along with electrolyte replacement and dialysis were followed by full recovery of renal function and correction of hypokalemia. We also review literature data regarding the rare cases presenting with rhabdomyolysis secondary to hypokalemia.
Keywords: *hypokalemia, rhabdomyolysis, acute kidney injury, Crohn's disease.*

Rezumat
În prezent, rabdomioliza este o cauză frecventă de injurie acută a rinichiului şi se asociază de obicei cu hiperkaliemie severă, uneori ameninţătoare de viaţă. Prezentăm cazul unui pacient cu boală Crohn internat în secţia de nefrologie pentru injurie renală acută secundară rabdomiolizei produse de hipokaliemia severă. Diagnosticul şi tratamentul prompt al bolii Crohn împreună cu repleţia electrolitică şi dializa de urgenţă au permis recuperarea totală a funcţiei renale şi corecţia hipokaliemiei. Cauzele rare ale rabdomiolizei induse de hipokaliemie şi raportate în literatură sunt, de asemenea, trecute în revistă.
Cuvinte cheie: *hipokaliemie, rabdomioliză, injurie acută a rinichiului, boală Crohn.*

Introduction

A common feature of rhabdomyolysis is hyperkalemia secondary to increased potassium release from injured skeletal muscle[(1)]. Severe rhabdomyolysis may complicate with acute tubular necrosis due to release from the damaged skeletal muscle cells of myoglobin which produces renal vasoconstriction, obstruction of renal distal tubules with myoglobin casts and has also a direct toxic effect on proximal tubule epithelial cells[(1)]. Causes of rhabdomyolysis

may be classified as traumatic and non-traumatic. Among the latter, dyselectrolitemia is an increasingly recognized cause and hypokalemia is the most involved. We report the case of a patient with severe hypokalemia secondary to gastrointestinal losses in context of Crohn' disease who developed rhabdomyolysis and severe acute kidney injury needing emergency hemodialysis.

Case presentation

Reasons for hospitalization and history of illness

A 52-year-old male was being admitted to the nephrology for anuria, high levels of nitrogen waste products, watery stools, and altered general condition.

Anamnesis and history of illness were collected from the patient's wife. The patient had a 10-years history of gout, and a 4-years history of hypertension. His chronic medication regimen consisted of allopurinol 200 mg/day, candesartan 16 mg/day and indapamide 1.5 mg/day. He was a recognized alcoholic with an average quantity of 500-700 mL brandy or vodka ingested daily, but he did not consume at all alcohol in the last 2 weeks. His wife stated that he is compliant with the recommended low-sodium and low-purine diet and that he did not stop medication.

The onset of the sufferance was 2 weeks before hospital admission with diarrhea and abdominal pain for which he was treated with omeprazole 40mg/day, loperamide 8 mg/day and diet by the family doctor. There was no improvement of the diarrhea (over 10 watery stools daily at admission), and progressively the patient presented increasing generalized muscle weakness, parenthesias in upper arms and then both legs with difficulty to walk, muscle cramps in the both hands. Urine output also decreased, the patient being anuric at admission. As he progressively became confused and disorientated the family members brought him initially to an emergency neurology department and a cerebral CT-scan revealed diffuse cerebral and cerebellar atrophy, findings considered consistent with chronic alcoholism. Due to severe renal dysfunction revealed at laboratory screening in the neurology emergency room, the patient was urgently transferred to nephrology.

Clinical exam and laboratory work-up

Upon admission in nephrology the patient was disoriented, confused, with generalized muscle hypotonia and impossibility to walk. He had delayed deep tendon reflexes, but no other neurological findings. He was in a severe state of dehydration with reduced skin turgor, hypotension (80/65mmHg), cold extremities, tachycardia 130/min, tachypneea 32/min, and uremic halitosis. He

Analysis	Results at admission	Normal range
Hemogram		
Hemoglobin (g/dL)	16.7	11.7 – 15
WBC (/µL)	3580	4.00 – 11.00
Leukocites (/µL)	2200	2.00 – 8.00
Platelets (/µL)	48,000	150.00 – 450.00
Erythrocyte sedimentation rate (mm/1h)	64	2.00 – 30.00
C reactive protein (mg%)	61.65	≤ 5
Fibrinogen (mg%)	827	200.00 – 400.00
Urea (mg/dL)	286	12.6 – 43.00
Creatinine (mg/dL)	12.6	0.70 – 1.20
Uric acid (mg/dL)	5.9	2.4 – 5.7
Acid base – venous blood		
pH	7.15	7.34 – 7.36
Bicarbonate (mmol/L)	9	22.00 – 26.00
pCO2 (mmHg)	48	44.00 – 46.00
Anion gap (mmol/L)	28.9	8.00 – 16.00
Sodium (mEq/L)	118	136.00 – 146.00
Potassium (mEq/L)	1.8	3.50 – 5.10
Magnesium (mg/dL)	0.96	
Total serum calcium (mg/dL)		8.60 – 10.20
Ionized calcium (mg/dL)	2.6	3.80 – 5.60
Creatin kinase total (IU/L)	5252	26.00 – 192.00
Creatin kinase – MB fraction (IU/L)	36.1	≤ 25
Glutamic-oxaloacetic transaminase (IU/L)	255.90	00.00 – 40.00
Glutamate-pyruvate transaminase (IU/L)	83.50	00.00 – 41.00
Gamma glutamyl transferase (IU/L)	422	8.00 – 61.00
Lactat dehydrogenase (IU/L)	363	135.00 – 225.00
Serum protein electrophoresis:		
Total proteins (g/dL)	8.95	6.40 – 8.30
Globulins (%)	16.60	11.10 – 18.80
Alpha1 globulin (%)	8.7	2.90 – 4.90
Alpha2 globulin (%)	12.1	7.10 – 11.80
Beta1 globulin	5.9	4.70 – 7.20
Beta2 globulin	7.9	3.20 – 6.50
Albumin (%)	48.8	55.80 – 66.10
Album/globulin ratio	0.95	
Total cholesterol (mg/dL)	227.3	120 - 200
Triglycerides (mg/dL)	360.6	< 75

Table 1. *Abnormal blood tests at admission*

was anuric, had no edema, no cardiac murmurs or pulmonary crackles. Upon abdominal palpation he presented severe pain, but an abdominal x-ray and a surgeon consult at the ER ruled out a surgical acute abdomen. His body mass index was 17 kg/m^2, the patient's wife declaring that he did not eat properly in the last 2 weeks and he lost about 10 kg in this period.

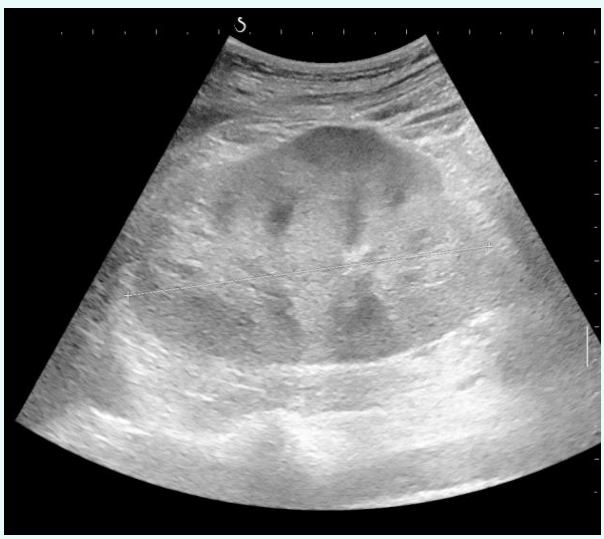

Figure 1. *Left kidney on ultrasound*

A full laboratory work-up was performed. Abnormal findings are presented in table 1. We found normal values of blood glucose, alkaline phosphatase, troponin, bilirubin, serum amylase. No urine sample could be collected for analysis because the patient was anuric for about 15 days (2 days before admission and 13 days during hospitalization). Clostridium difficile GDH rapid testing was negative.

Imaging tests performed at admission showed normal pulmonary radiography and ultrasound with increased-sized kidneys with pale cortex, but no hydronephrosis (figure 1); no other abdominal abnormal findings were found. Very interesting, no ECG abnormal findings were noted.

Treatment and evolution during hospitalization

Candesartan and indapamide were stopped. Parenteral intensive treatment with fluids and electrolyte solutions was performed for the first 36 hours, but no recovery of renal function was obtained. Therefore hemodialysis was initiated on temporary central vein catheter.

The patient underwent a lower gastrointestinal endoscopy, which showed an edema, hyperemia and multiple ulcerations at the ileocecal valve and in the last 5 cm of ileum; biopsy samples were taken. No mucosal involvement of the colon was revealed, but an upper gastrointestinal endoscopy performed a few days later showed similar lesions in the mucosa of esophagus and stomach. Due to the high suspicion of Crohn's disease, parenteral corticosteroid therapy associated with oral mesalazine and metronidazole, and subcutaneously low molecular weight

heparin were initiated. The evolution was spectacular: diarrhea and abdominal pain disappeared; resumption of diuresis occured about 13 days after admission and renal function recovered rapidly requiring with hemodialysis cessation. At the time of discharge from the hospital, the patients had normal electrolyte values and also normal nitrogen waste products. One month after discharge, pathologist confirmed Crohn's disease.

Discussion and literature review

We present a patient who was admitted for acute kidney injury (acute tubular necrosis) produced by both ischemic (severe hypovolemia, hypotension, renal hemodynamic alterations due to sartan use) and nephrotoxic factors (rhabdomyolysis). What is particular interesting in this patient is concomitant presence of hypokalemia and rhabdomyolysis, especially when an anuric and severe acute kidney injury is present.

It is obviously that the severely reduced serum potassium was mainly due to watery profuse diarrhea, but other factors may have contributed, like chronic alcohol abuse, alcohol sudden withdrawal[2], treatment with thiazide diuretic[3], reduced appetite. We found no factors responsible for rhabdomyolysis; medication used in chronic regimen or recently for diarrhea is not associated with this side-effect. Therefore we concluded that the severe hypokalemia was responsible for rhabdomyolysis, especially in the context of severe dehydration.

Hypokalemia-induced rhabdomyolysis is rarely present in clinical practice because, usually, rhabdomyolysis is associated with severe, potentially life-threatening hyperkalemia[1]. The mechanism by which hypokalemia causes rhabdomyolysis is related to the role of potassium in the regulation of blood pressure in peripheral capillaries[4]; severe hypokalemia causes muscle ischemia by inducing capillary contraction and decreasing muscle blood supply[4]. Rhabdomyolysis induced by potassium depletion usually occurs at very low serum levels of potassium (as happened in the patient presented), and the association of severe hypovolemia increases the risk of this effect.

In the case of our patient, hypokalemia and hypovolemia occurred secondary to the profuse diarrhea of Crohn's disease and induced rahbdomyolysis and severe anuric acute kidne injury. We found another case reported in the literature presenting with hypokalemia-induced rhabdomyolysis in a patient with Crohn disease[5], but not acute kidney injury was present. Most frequent cases reported in the literature are after liquorice abuse and they present, beside rhabdomyolysis, several other abnormalities like Gitelman syndrome, hypokalemic paraparesis or nephrogenic diabetes insipidus[6-9], but also no acute kidney injury was present or there was noted mild azotemia.

Other more rare cases of rhabdomyolysis secondary to hypokalemia have been reported in primary hyperaldosteronism[10-12], uncontrollable vomiting[13], distal tubular acidosis[14], high doses of diuretic[15] or very rare genetic diseases like familial hypokalemic periodic paralysis[16].

Conclusions

This case highlights the need to monitor rhabdomyolysis markers in patients at high risk of dyselectrolyemia. Nowadays there is an increasing number of cases with rhabdomyolysis secondary to side effects of

various drugs or predisposing conditions and the underlying mechanism is one or more electrolyte disorders.

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