

Articolo Originale - Original Article

Hypokalemia-induced severe rhabdomyolysis in a patient with short bowel syndrome: A case report

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ABSTRACT: *A 41-year-old female with Crohn's disease, who had undergone multiple previous surgery and had short bowel syndrome, was admitted to our department due to the onset of rhabdomyolysis caused by severe potassium depletion. Despite her critical clinical condition on admission, intense fluid and electrolyte support arrested the process of muscle necrosis and the patient recovered completely. (RINPE 2004; 22: 73-7)*

KEY WORDS: *Rhabdomyolysis, Hypokalemia, Short bowel syndrome*

PAROLE CHIAVE: *Rabdomiolisi, Ipopotassiemia, Sindrome dell'intestino corto*

CASE REPORT

We report the case of a 41-year-old female with a 10-year history of Crohn's disease. During this period, complications of the underlying disease (intestinal occlusion, perforation and enterocutaneous fistula formation) had led the patient to require three intestinal resections, with the overall excision of the last 100 cm of the ileum and caecum and an anastomosis between the ileum and was dependent on non-steroidal anti-inflammatory drugs and opioid analgesics because of her continuing abdominal pain. One year prior to the current admission she had undergone excision of the duodenum and the head of pancreas because of a bleeding ulcer in the 2nd part of the duodenum: a gastro-jejunal anastomosis had been created. The clinical data from the period immediately after this operation indicated that the patient had severe protein and caloric malnutrition, with a body weight of 30 kg and a body mass index (BMI) of 11.7.

The patient was admitted to our ward with a 3-day history of generalized and worsening muscle pain (treated with buprenorphine i.m., up to 1.5 mg per day), associated with progressive muscle weakness in the limbs, particularly proximally, and in the neck. The patient reported that these symptoms had started some time after a worsening of the chronic diarrhea from which she suffered.

The patient appeared cachectic (weight 35 kg, height 160 cm, BMI 13.7) and distressed. Her muscula-

ture appeared globally atrophic, mainly evident in the proximal musculature, with marked asthenia in the four limbs, almost to the point of paralysis. The main muscle groups were painful at rest; this pain increased with palpation, and active and passive movements. The biceps reflex was present, the patellar reflex was hard to elicit and the ankle reflex was absent. Sensitivity to touch, pain and vibration was apparently normal. The patient seemed to have a compensated cardiocirculation: she was eupnoic, had no signs of pulmonary or systemic edema, a blood pressure of 120/80 mmHg, and a regular heart rate of 72 bpm. The ECG trace showed sinus rhythm and non-specific repolarization changes.

The initial examinations revealed very high enzyme concentrations of muscular necrosis (myoglobin 9440 ng/mL, CPK 8490 U/L, aldolase 69 U/L, LDH 880 U/L). There were profound serum electrolyte disturbances (potassium 1.2 mEq/L, magnesium 0.55 mg/dL, calcium 6.9 mg/dL). Creatinine was 2.5 mg/dL, and blood urea concentration was normal. The transaminases, alkaline phosphatase and γ -GT were all slightly raised, while bilirubin, serum protein electrophoresis and coagulation indices were normal. Blood glucose concentration was 92 mg/dL, and there was no evidence of pseudo-diabetic glycosuria. The blood count did not show anemia, but a predominantly neutrophilic (88.8%) leucocytosis was present (15,600/mm³). The erythrocyte sedimentation rate was normal.

The urine was straw-colored and dilute (specific gravity 1.003 g/L), with a very high myoglobin content and a pH of 6.5. Potassium excretion was particularly reduced (5 mEq/L). Blood-gas analysis results were compatible with a compensated metabolic acidosis (pH 7.38, pO₂ 114, pCO₂ 23, HCO₃⁻ 14.1, base excess -8.2).

In addition to the extremely low BMI, the main serum nutritional indices had the following values: pre-albumin 16.3 mg/dL, albumin 6 g/dL, transferrin 88.8 mg/dL, lymphocytes 858/mm³, total cholesterol 89 mg/dl, and triglycerides 60 mg/dL. However, the patient had gained 5 kg in body weight in the preceding 15 months (+16.7%).

The history excluded the abuse of salicylates, diuretics or laxatives, or the intake of cholesterol lowering drugs or fungi (for suspected *Tricholoma equestre* intoxication). However, it was found that electrolyte tests a month previously (well before the worsening diarrhea) had shown a K⁺ concentration of 2.2 mEq/L, for which no corrective action had been taken. Therefore, it was concluded that the ongoing rhabdomyolysis was the consequence of severe, prolonged hypokalemia.

The patient was treated with massive fluid and electrolyte support to replace the K⁺ and Mg⁺⁺ and maintain good diuresis (daily infusion of 4,500 cc of physiological saline with added potassium (160 mEq per day) and magnesium sulfate (80 mEq per day). Strong diuretics were not administered in order not to aggravate the hypokalemia. Bicarbonate infusion (to alkalinize the urine and prevent intratubular myoglobin precipitation) was limited to 40 mEq per day. The patient was also severely hypocalcemic (clinically manifested by localized tetany of the forearm following venous stasis while a blood sample was taken), and she was treated with 4 g per day calcium gluconate supplementation.

No specific parenteral nutritional supplementation was prescribed. The patient was given a hypolipidemic diet, combined with orally administered pancreatic enzymes and loperamide hydrochloride (2 mg twice daily), obtaining a reduced faecal discharge.

On day 2 of her admission the electrocardiographic picture worsened (bradycardia at 44 bpm with atrio-ventricular dissociation and frequent bigeminal ventricular extrasystoles; prolonged QT interval, marked changes of the ST segment and T waves; evident U waves) and cardiac electrical activity was monitored. Despite the infusion therapy, described above, only on the 8th day did the patient achieve a plasma potassium concentration of 3.3 mEq/L (after a total K⁺ infusion of 1,120 mEq), which was accompanied by electrocardiographic normalization, paralleled by a dramatic reduction in muscle enzymes (Tab. I, Fig. 1), the normalization of the renal function indices and the gradual disappearance of pain

and functional impairment. In the meantime, stool studies had not demonstrated the presence of protozoa, helminths, bacteria or pathogenic toxins; however, they had shown findings compatible with the malabsorption of carbohydrates and lipids.

DISCUSSION

The causes of hypokalemia

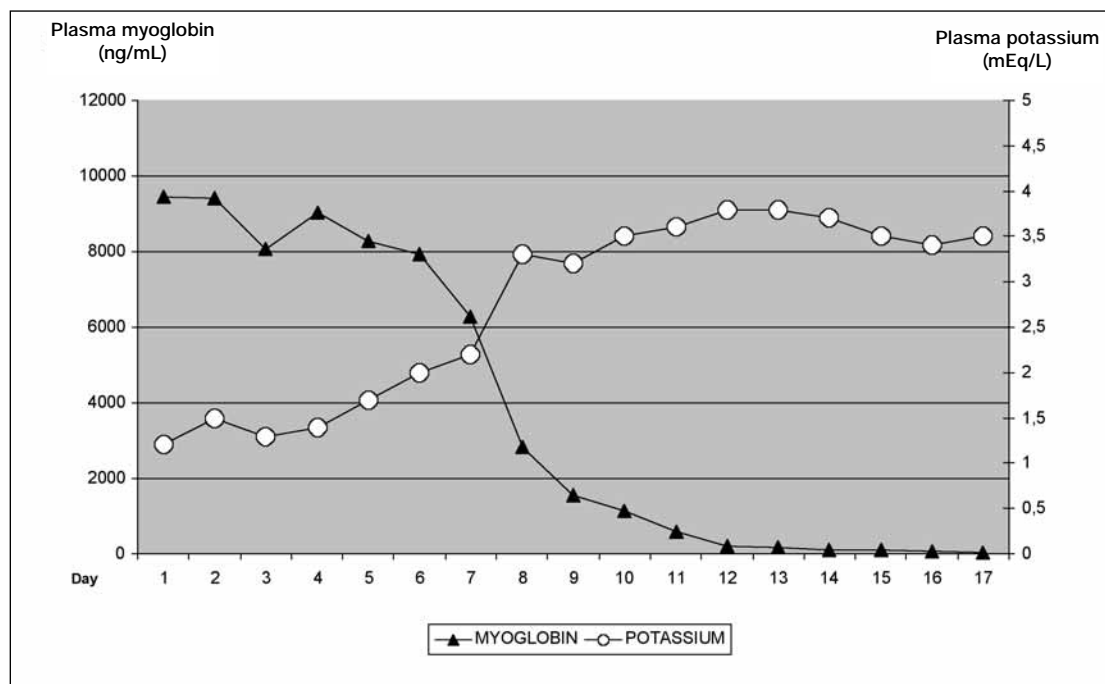
Assuming that our patient was eating a normal diet each day, i.e. containing approximately 80 mEq per day of potassium (1), the main cause of the rhabdomyolysis was chronic hypokalemia due to chronic diarrhea and malabsorption. It should be remembered that the daily faecal excretion of K⁺ is only 9 mEq/die in healthy adults, while the faecal concentration in our patient was 83÷95 mEq/L, which is drastically higher than the level in the plasma (2). When diarrhea develops, the concentration of faecal K⁺ decreases, but nevertheless, the total daily elimination becomes much higher than usual, up to the point of there being a massive loss (3).

Diarrhea increases the concentration of unabsorbed or secreted anions (mostly chlorides) within the intestinal lumen, creating an electrochemical gradient unfavorable to potassium absorption. Since potassium absorption occurs passively at a rate directly proportional to its concentration, an increase in intraluminal fluid (as occurs in diarrhea) dilutes the K⁺ and hampers its absorp-

TABLE I - DAILY VALUES OF PLASMA POTASSIUM AND MYOGLOBIN CONCENTRATIONS

Day	Plasma myoglobin (ng/mL)	Plasma potassium (mEq/L)
1	9440	1.2
2	9400	1.5
3	8060	1.3
4	9020	1.4
5	8270	1.7
6	7940	2
7	6280	2.2
8	2820	3.3
9	1545	3.2
10	1150	3.5
11	600	3.6
12	210	3.8
13	170	3.8
14	110	3.7
15	99	3.5
16	70	3.4
17	36	3.5

Fig. 1 - Comparison of the trends in plasma potassium and myoglobin concentrations.



tion. Other mechanisms, such as the adsorbent effect of unassimilated fatty acids and increased transit velocity, probably have some, but less influence.

What role did the intestinal resections play? The literature lacks detailed analysis of the relationship between loss of mucosal surface area and potassium malabsorption (2). However, we should remember that the small intestine of a healthy person is responsible for the absorption of 85% of dietary potassium (4). Studies carried out on patients with short bowel syndrome showed that the main absorption sites are the duodenum and jejunum (5). The colon contributes very little to potassium homeostasis since it absorbs or secretes only about 4 mEq of potassium each day (2).

Therefore, we can hypothesize that the excision of the duodenum and the head of the pancreas, which our patient had undergone 1 year previously, had laid the foundation for a precarious compensation of digestion and absorption. The impaired lipid digestion and the steatorrhea meant that the residual intestine (jejunum, first part of the ileum and almost all the colon, even assuming these to be free from Crohn's disease), were, for many months, unable to absorb dietary potassium adequately, without the renal mechanism of potassium sparing being able to balance the chronic intestinal loss. The exacerbation of the diarrhea, which occurred in the final days, broke the fragile compensation that had been created, unmasking the full severity of the hypokalemia.

From hypokalemia to rhabdomyolysis

Our patient's neuromuscular symptoms can be attributed to the very low potassium concentration associated with muscle damage. Aggravating factors were chronic protein malnutrition and abnormal plasma Ca^{++} and Mg^{++} concentrations. On the other hand, it is possible that the signs and symptoms were mitigated by the fact that the hypokalemia developed slowly over a period of weeks (6). Patients with hypokalemia are usually asymptomatic if the deficit is mild (plasma potassium 3.0-3.5 mEq/L). With more severe hypokalemia, non-specific symptoms such as generalized weakness, lassitude and constipation are more common. When serum potassium reduces to <2.5 mEq/L, muscle necrosis can occur, and at serum concentrations <2.0 mEq/L, an ascending paralysis can develop, with eventual respiratory function impairment. In hypokalemic patients, the muscle loses its ability to adapt to work because of changes in the microcirculation. The result is regional ischemia, changes in glycogen metabolism and muscle breakdown (7-9). It is possible that the severity of our patient's hypokalemia was in some way mitigated by the release of potassium contained in the lysed muscle cells.

Striated muscle cell stress was aggravated by the concomitant low blood magnesium concentration. The lack of intracellular Mg^{++} blocks the transmembrane $\text{Ca}^{++}/\text{Mg}^{++}$ pumps; therefore, preventing intracellular cal-

cium extrusion and leading to the onset of spontaneous contractions, depletion in ATP reserves and rhabdomyolysis (9).

The ECG abnormalities observed (prominent U wave, flattening and inversion of the T wave, prolonged QT interval) are present in half of the patients with $K^+ < 2.5$ mEq/L. However, hypokalemia alone does not increase the probability of the onset of cardiac arrhythmias, at least not in patients who do not have ischemic disease, heart failure or left ventricular hypertrophy (6). The atrio-ventricular dissociation that occurred in our patient should, once again, be attributed to the effects of the concomitant substantial reductions in Ca^{++} and Mg^{++} concentrations, predisposing to the onset of ventricular arrhythmias (10).

Comments on the aims of treatment

In the absence of alterations in the acid-base balance, plasma potassium concentrations mirror the changes in the total body potassium content: the plasma potassium reduces by approximately 1 mEq/L for every 200÷400 mEq of total body potassium lost (Tab. II), if the blood pH is in the normal range. If this is not the case, every change in pH value causes a proportional and inverse change in the plasma potassium concentration according to the following formula:

$$[K^+]_{\text{corrected}} = [K^+]_{\text{observed}} - [(7.4 - \text{pH}_{\text{observed}}) \times 6].$$

Recalculating our patient's potassium status according to this formula, we found that her initial plasma potassium concentration was 1.08 mEq/L, worse than that apparent from the simple laboratory result, and an expression of massive and prolonged depletion in the total body pool. This was confirmed by the fact that she slowly achieved a plasma potassium concentration of 3.3 mEq/L after as much as 1,120 mEq of K^+ had been infused, although in the first 3 days the massive intravenous supplementation did not cause appreciable increases. The restoration of lost potassium is, a inevitably slow process, both because the greater part of the potassium administered is rapidly taken up into the cells, and because the renal excretion swiftly increases.

At this point, it is worth remembering the importance of correcting a low magnesium concentration if this is also present along with hypokalemia, as in our patient. A low magnesium concentration interferes with potassium reabsorption in the renal tubules, hampering the achievement of normal plas-

ma potassium concentrations.

Regarding the treatment of rhabdomyolysis, we should consider that the renal damage is caused by intratubular precipitation of myoglobin and uric acid, as well as renal ischemia (mediated by vasoconstricting agents released by the damaged muscles). This renal damage predisposes to hypovolemia (which causes renal arteriolar vasoconstriction), metabolic acidosis and urinary acidity (9). Our patient responded well to intense fluid replacement, quickly regaining normal values of creatinine and maintained satisfactory diuresis. Therefore, it was unnecessary to use loop diuretics, which would have been inadvisable since these agents increase urinary potassium excretion and urinary acidity.

The compensated metabolic acidosis was probably caused by intestinal HCO_3^- loss and early renal failure. Intravenous bicarbonate administration (recommended in cases of rhabdomyolysis to alkalinize the urine and prevent intratubular myoglobin precipitation) was carried out with extreme care given our concerns that a rising pH, a direct effect of bicarbonate, would worsen the hypokalemia by inducing a rapid potassium influx into the cells.

The patient's hypocalcemia could not be ascribed to intestinal malabsorption, but rather to the process of muscle tissue destruction, which causes calcium precipitation in the damaged tissues. The patient's plasma calcium levels were, infact, within normal limits only 1 month before admission. It is possible that renal failure further lowered the plasma Ca^{++} concentration.

The literature suggests not treating hypocalcemia during rhabdomyolysis. However, our decision to provide a moderate supplementation intravenously did gradually correct the plasma Ca^{++} concentration, preventing the onset of new tetanic crises without causing "rebound" hypercalcemia.

TABLE II - TOTAL BODY DEFICIT OF POTASSIUM DURING HYPOKALEMIA

Serum potassium (mEq/L)	Potassium deficit	
	mEq	Total body potassium (%)
3.0	175	5
2.5	350	10
2.0	470	15
1.5	700	20
1.0	875	25

Deficit estimated for a 70 kg adult with a total body potassium content of 50 mEq/kg, with a blood pH=7.4 (adapted from Marino PL, "Terapia Intensiva". Milano: Masson 1999; 651).

CONCLUSIONS

Short bowel syndrome is a condition predisposing to severe malabsorptive states. Hypokalemic rhabdomyolysis can be a dramatic consequence, although fortunately extremely rare: we have found only two other reported cases (11, 12). Given the severity of the clinical picture and the possible multisystem complications, patients with short bowel syndrome should undergo frequent checks of their plasma electrolyte levels. Therefore, follow-ups by the gastroenterology team in our center were arranged with the patient and her family when the patient was discharged. She will have periodic evaluations of her electrolyte balance and nutritional status. Furthermore, she was carefully informed that diarrhea, of any cause, can produce severe, even fatal, fluid and electrolyte disturbances and that these disturbances must be identified quickly and could necessitate intensive treatment.

RIASSUNTO

Una donna di 41 anni, affetta da morbo di Crohn plurioperato e sindrome dell'intestino corto, è stata ricoverata presso la nostra Unità Operativa per l'insorgenza di una rhabdomyolisi provocata da una grave deplezione potassica. Nonostante il grave quadro clinico all'ingresso, l'intensa supplementazione idrica ed elettrolitica cui è stata sottoposta ha consentito di arrestare il processo di necrosi muscolare, portando la paziente a un completo recupero.

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