Hyperkalemia-induced acute flaccid paralysis: a case report

Nefrologo in Corsia

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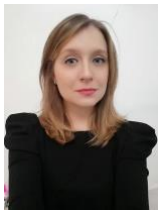
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ABSTRACT
Acute flaccid paralysis is a medical emergency that may be caused by primary neuro-muscular disorders, metabolic alterations, and iatrogenic effects. Severe hyperkalemia is also a potential cause, especially in elderly patients with impaired renal function. Early diagnosis is essential for appropriate management. Here, we report the case of a 78-year-old woman with hypertension and diabetes presenting to the emergency department because of pronounced asthenia, rapidly evolving in quadriparesis. Laboratory examinations showed severe hyperkalemia of 9.9 mmol/L, metabolic acidosis, kidney failure (creatinine 1.6 mg/dl), and hyperglycemia (501 mg/dl). The electrocardiography showed absent P-wave, widening QRS, and tall T-waves. The patient was immediately treated with medical therapy and a hemodialysis session, presenting a rapid resolution of electrocardiographic and neurological abnormalities. This case offers the opportunity to discuss the pathogenesis, the clinical presentation, and the management of hyperkalemia-induced acute flaccid paralysis.

KEYWORDS: hyperkalemia, acute flaccid paralysis, hemodialysis, diabetes

Introduction

Hyperkalemia is associated with poor outcomes and a high mortality rate among the general population, and among patients with cardiac and renal disease [1,2]. Hyperkalemia-related clinical complications and deaths are determined mainly by the cardiac electrophysiological effects of elevated potassium levels [3]. Indeed, hyperkalemia may result in ventricular arrhythmias and sudden death. Moreover, hyperkalemia may also cause other physiologic perturbations, such as muscle weakness and paralysis, paraesthesia, and metabolic acidosis.

Here, we report a case of severe hyperkalemia presenting with dramatic neurological manifestations in the form of acute flaccid paralysis (AFP).

Case report

A 78-year-old woman presented at the Emergency Department (ED) because of severe asthenia and acute onset quadriparesis. She was conscious and referred that a growing weakness during the last four days had evolved in the inability to move the four limbs. She had not noticed any decrease in urine output. According to her history, the patient had diabetes and hypertension, she was taking metformin, sitagliptin, and amiloride/hydrochloride. Physical examination showed elevated blood pressure 170/90 mmHg, normal body temperature, and oxygen saturation. Neurological evaluation revealed flaccid quadriparesis with hypotonia in all four limbs (but especially the lower limbs) without pain. Swallowing and breathing were not impaired. Laboratory examinations showed severe hyperkalemia 9.9 mmol/l, metabolic acidosis (pH 7.29, HCO_3– 16 mmol/l, pCO2 32 mmHg), a mild renal impairment (creatinine 1.6 mg/dl) and high glucose serum levels (501 mg/dl). She presented normal values of transaminase, creatine kinase (79 UI/L), bilirubin, hemoglobin and complete blood count. Electrocardiography showed tall T waves, loss of the P wave, and widening of the QRS interval (Fig. 1). Medical therapies with calcium gluconate (10% solution, 10 ml), i.v. regular insulin (50 U in 50 ml 0.9% saline at 0.1 ml/kg/hour), i.v. bicarbonate (8.4% solution, 100 ml), furosemide (50 mg), and beta-2 agonist nebulization (salbutamol 10 mg) were immediately initiated. About one hour after admission, serum potassium had decreased to 8.5 mmol/L. At the same time, because of potentially life-threatening complications, a hemodialysis (HD) session was started. At the beginning of HD, the patient presented an initial recovery of limb mobility (see Video 1). At the end of a 5-hour HD session, serum potassium lowered to 5 mmol/L, accompanied by a normalization of arterial blood gas (ABG) and reduced glucose levels. Moreover, electrocardiographic abnormalities resolved (Figure 2), while the patient presented a significant improvement in limb mobility (see Video 2).

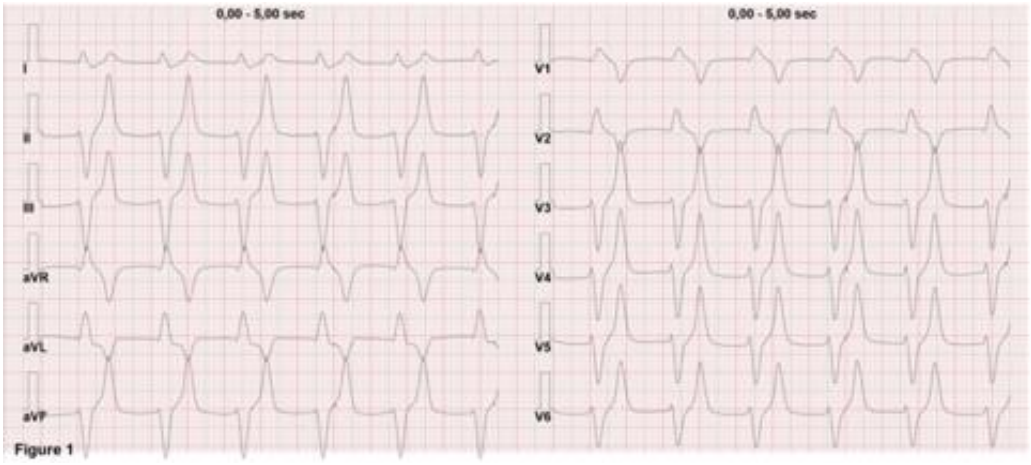


Figure 1: Electrocardiography at admission to ED showed tall T waves, loss of the P wave and widening of the QRS complexes (K+ 9.9 mmol/L)

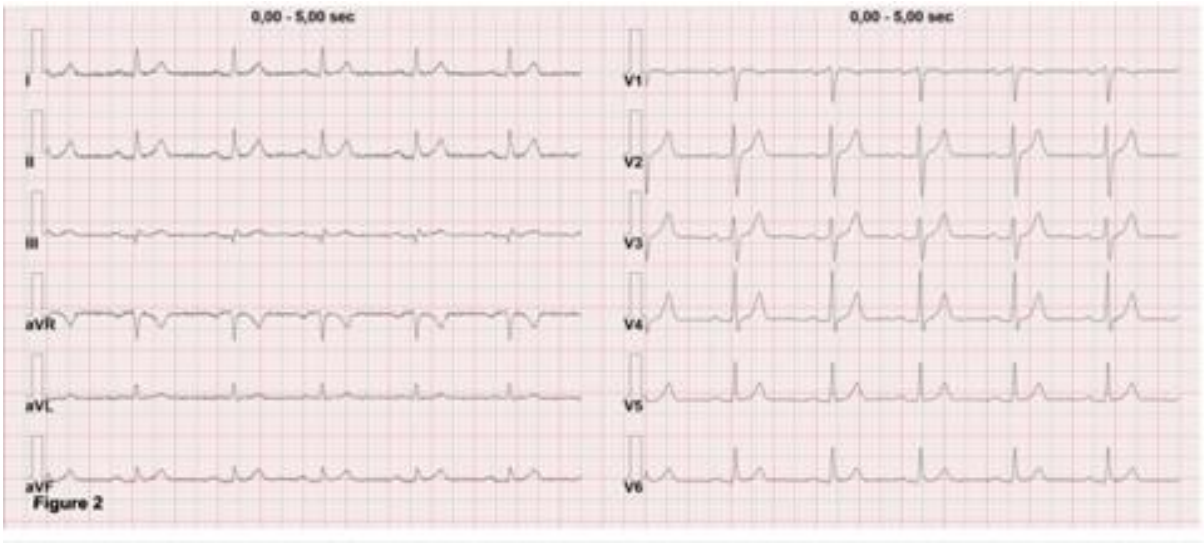
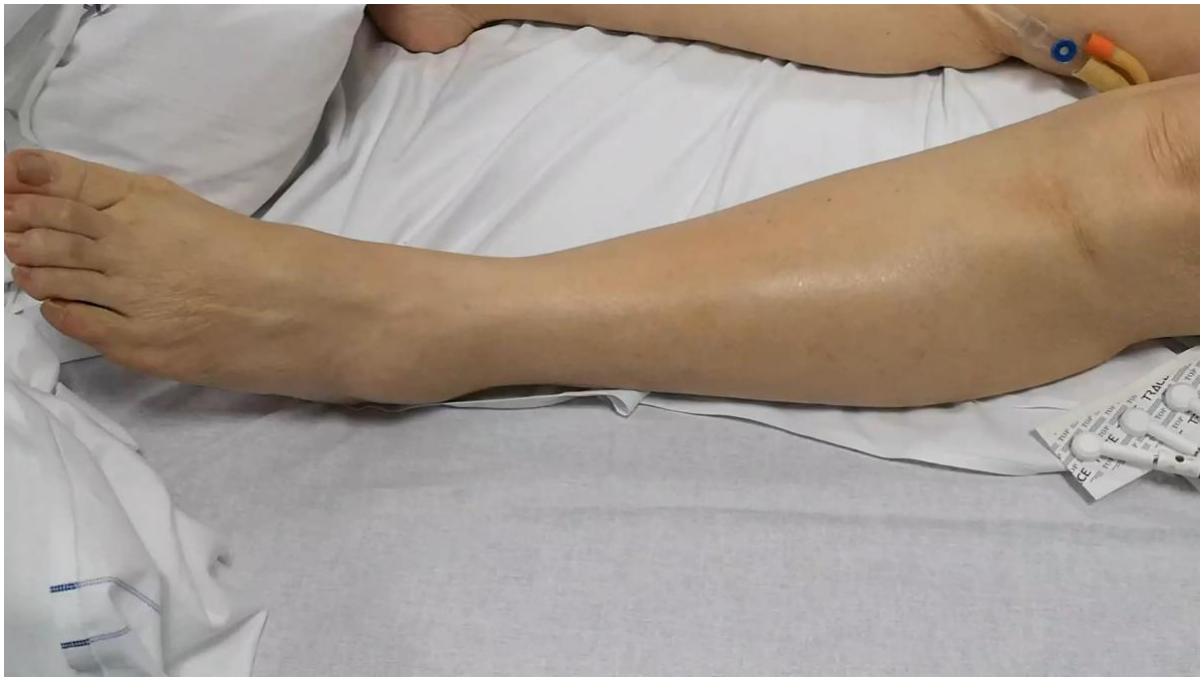
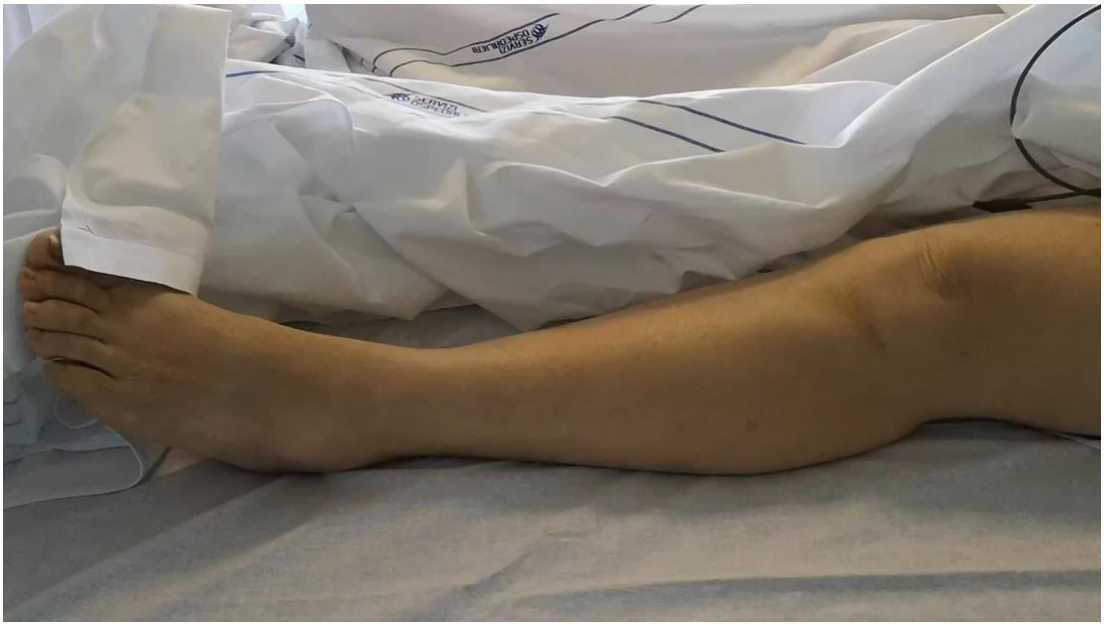


Figure 2: Electrocardiography at the end of 5-hour HD treatment showed a resolution of hyperkalemia-related abnormalities, expect for residual tall T waves (K+ 5.0 mmol/L)



Video 1: Difficulties in moving the lower limbs at the beginning of hemodialysis (K^+ 8.5 mmol/L). At admission to ED (K^+ 9.9 mmol/L) the patient presented quadriparesis. Video's link https://giornaleitalianodinefrologia.it/2021/03/paralisi-flaccida-acuta-da-iperkaliemia-patogenesi-e-gestione-clinica/



Video 2: Partial recovery of lower limb mobility at the end of 5-hour HD treatment (K^+ 5.0 mmol/L). The day after, the patient could move the four limbs normally. Video's link https://giornaleitalianodinefrologia.it/2021/03/paralisi-flaccida-acuta-da-iperkaliemia-patogenesi-e-gestione-clinica/

Discussion

Hyperkalemia, defined as a serum potassium level greater than 5.0 mmol/L, is a common disorder. It has been estimated that 1-3 per 100 persons per year in the general population, and 10% of hospitalized patients may present a hyperkalemia episode [4]. Moreover, its incidence may be significantly high in the presence of conditions such as diabetes, chronic heart failure and chronic kidney disease (CKD) [5]. Hyperkalemia is particularly common in HD patients: a recent study reported an incidence of 74% anytime over a 2-year follow-up period [6].

Hyperkalemia may be caused by several conditions [7]. It can be a consequence of increased potassium (K^+) body content, due to excessive K^+ intake or reduced renal excretion. The ability of the kidney to excrete K^+ may be compromised by both acute and chronic kidney damage. Moreover, hyperkalemia can result from a decreased mineralocorticoid activity (e.g. hypoaldosteronism), which reduces the capacity of K^+ excretion in the distal nephron. In turn, impairment of mineralocorticoid activity may be caused by diabetes, adrenal disease, tubular defects, numerous drugs (e.g., nonsteroidal anti-inflammatory drugs, beta-blockers, renin-angiotensin-aldosterone system inhibitors, mineralocorticoid receptor blockers, calcineurin-inhibitors, etc.), and old age.

Alterations in K^+ distribution across cell compartments, the so-called internal K^+ balance, can also lead to hyperkalemia. These conditions comprise the net release of potassium in case of cell damage, as it occurs after a trauma, rhabdomyolysis, or haemolysis. Moreover, an altered distribution of K^+ in the intracellular and extracellular spaces can also be due to metabolic acidosis, insulin deficiency, or dysfunctions of the autonomic nervous system, that in physiological conditions regulate K^+ transcellular shift [8].

In the case we are presenting, laboratory examinations excluded potassium release from cell lysis. To investigate the potential causes of the hyperkalemia, a full medical history was collected. The patient did not refer previous episodes of hyperkalemia, while she admitted eating large amounts

of high-potassium foods and juices and taking daily ibuprofen during the last ten days. Moreover, she confirmed the assumption of amiloride, a drug known to exert a potassium-sparing effect through the inhibition of sodium reabsorption in the collecting tubule.

In the days following hospital admission, potassium levels stabilized about 4 mmol/L, even after the suspension of potassium-lowering therapies, while clinical conditions definitively improved, and the patient recovered normal mobility. Laboratory examinations showed serum creatinine of 1.3 mg/dl and glucose levels of 150 mg/dl, while ABG remained normal. At that time, we measured serum cortisol, renin, and aldosterone levels and markers of urinary acidification, such as urine pH (6.5) and urinary anion gap (39 mmol/l). All the examinations resulted within the normal range, so the diagnoses of chronic hyporeninemic hypoaldosteronism and renal tubular acidosis were ruled out. We finally made a diagnosis of hyperkalemia provoked by multiple factors modifying both internal and external potassium balance, such as chronic kidney disease, excessive potassium intake, decompensated diabetes, and medications (namely, potassium-sparing and nonsteroidal anti-inflammatory drugs).

Clinical presentations of hyperkalemia may vary on an individual basis and depend on the severity and rapidity of the onset. So, while many patients are asymptomatic, hyperkalemia may cause severe complications in others, mainly determined by the cardiac electrophysiological effects of elevated K^+ levels, which may result in ventricular arrhythmias and sudden death. Besides its cardiac effects, hyperkalemia is also related to other physiologic perturbations, such as muscle weakness progressing to flaccid paralysis, paresthesia, alterations of gastrointestinal motility and metabolic acidosis [9].

A full description of the pathogenesis and clinical manifestations of all these conditions is beyond the scope of this report and can be found in well-detailed and comprehensive reviews [7, 10]. However, it should be noted that, although hyperkalemia-related muscle weakness is commonly reported, quadriparesis presenting as AFP has been rarely described. Clinically, it mostly presents as an ascending paralysis with areflexia, with normal sensory function cranial nerves, without the involvement of respiratory muscles [11]. Hyperkalemia-induced paralysis is the consequence of the electrophysiological effects of potassium on muscle fibers and nerves. Indeed, hyperkalemia reduces membrane potential, by diminishing the K^+ intracellular/K^+ extracellular ratio and causing a partial depolarization of the cell membrane, resulting in an initial increase of conduction velocity. Then, if persistent and profound, as in our case, hyperkalemia decreases the membrane excitability, also through the inactivation of the voltage-gated sodium channels, making the muscle cell and the axons refractory to excitation, thus leading to muscle paralysis [12]. These pathophysiological mechanisms are coherent with electrodiagnostic findings, which show a slowing down of nerve conduction speed, a reduction in amplitudes and conduction blocks [13].

In our case, in parallel with hyperkalemia-related neuromuscular dysfunctions, cardiac alterations were also present. The reasons why neuromuscular manifestations are predominant in some patients are not yet clear. In the reported cases of hyperkalemia-induced AFP, several causes of elevated potassium levels have been described, including renal failure, Addison disease, renal tubular acidosis, and use of K^+-sparing diuretics [14]. However, besides these secondary causes, primary forms of this condition have also been described. Hyperkalemic periodic paralysis (HPP) refers to an autosomal dominant hereditary disease caused by mutations in the gene encoding a protein (SCN4A) of the sodium channel gene of skeletal muscle. HPP is characterized by episodes of hyperkalemic paralysis that usually begin in the first decade of life and are often precipitated by exposure to cold, by fasting, or by resting after exercise [15]. Notably, in this case hyperkalemia is not responsible for muscle paralysis but it is a consequence of the release of potassium from the muscle during the paralysis episodes. When evaluating a patient with AFP, other differential

diagnoses include Guillain-Barré syndrome, acute myelopathy, myasthenic crisis, and botulism [16].

In these cases, unlike in hyperkalemia-related paralysis, cranial nerve, ocular and respiratory muscle are commonly involved.

The therapeutic goal in treating patients suspected of hyperkalemia-induced paralysis is to achieve the rapid reduction of potassium levels. Indeed, in all the reported cases, the quadriparesis disappeared after the resolution of the hyperkalemia, regardless of the treatment [11,14]. In our specific case, anti-hyperkalemic medical therapy, administered immediately after admission to the ED, and HD were able to significantly reduce serum potassium levels, leading to the resolution of all neurological symptoms.

Conclusions

We want to raise awareness that hyperkalemia-induced acute flaccid paralysis may represent a life-threatening condition. Early diagnosis is essential for appropriate management (Table 1).

Hyperkalemia is a common condition in the clinical practice, especially among high-risk populations, such as patients with kidney disease
Neuromuscular manifestations, including acute flaccid paralysis, may constitute the dominant clinical presentation in patients with hyperkalemia
Hyperkalemia should be included in the diagnostic workup of patients presenting acute flaccid paralysis
Prompt recognition of hyperkalemia and its causes is necessary to effectively treat hyperkalemia-related neuromuscular complications

Table 1: Hyperkalemia-related acute flaccid paralysis: key points for clinical practice

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