Case Report

Periodic paralysis: An unusual presentation of drug-induced hyperkalemia

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ABSTRACT

Hyperkalemia is a life-threatening electrolyte abnormality. The most common cause of hyperkalemia includes renal disease and ingestion of medications. Drug-induced hyperkalemia may develop in patients with underlying renal impairment, disturbed cellular uptake of potassium load, excessive ingestion or infusion of potassium-containing substances. We report a case of "drug-induced severe hyperkalemia" presenting as periodic paralysis. A 67-year-old diabetic and hypertensive woman presented to emergency department with the complaint of intermittent episode of inability to walk for the past 5 days. Each episode lasted for 15-20 minutes and was associated with breathlessness and restlessness. There was no family history of periodic paralysis and drug history revealed that the patient was onolmesartan 20 mg per day (for past 2 years), perindopril 4 mg per day (for past 16 months), and torsemide 10 mg/day. On examination patient was found to be conscious, alert, and afebrile. Vitals were normal. Examination of cardiovascular and respiratory system did not reveal any significant finding. Blood report of the patient showed serum K+ level 8.6 mmol/l. All other investigations were within normal limits. A diagnosis of drug-induced hyperkalemia was made. Patient responded well to the symptomatic treatment. To the best of the author's knowledge, this is the first case report of drug-induced hyperkalemia presenting as periodic paralysis.

Key words: Drug-induced, electrolyte abnormality, hyperkalemia, periodic paralysis

INTRODUCTION

Hyperkalemia is a life-threatening electrolyte abnormality manifesting primarily as cardiovascular and neurological dysfunctions. Hyperkalemia is defined as serum potassium levels more than 5.5 mmol/l. It is further classified as mild (5.5-6.0 mmol/l), moderate (6.1-6.9 mmol/l) and severe (levels 7.0 mmol/l and above).[1]

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The most common cause of hyperkalemia includes renal disease and the ingestion of medications that disrupt potassium balance [Table 1].[2] Drug-induced hyperkalemia may either be due to increase K+ release from the cell, decreased activity of renin angiotensin axis or may be because of impaired renal potassium excretion.

Patients with hyperkalemia may experience a variety of dysrthymias including complete heart block, Mobitz type II second-degree atrioventricular block, ventricular tachycardia, ventricular fibrillation and asystole, muscle cramps, weakness, paralysis, paresthesias, tetany, and focal neurological deficit.[3,4]

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Table 1: Causes of hyperkalemia

Increased potassium intake	Potassium containing dietary supplements, intravenous potassium infusion
Increased potassium release from cells	Rhabdomyolysis, Blood transfusion, Low insulin levels, Acidosis, Hyperosmolarity, tumor lysis syndrome, Trauma (including noncrush trauma), Severe exercise
Ineffective urinary potassium excretion	Renal impairment, Volume depletion, Hypoaldosteronism
Medications	Angiotensin converting enzyme inhibitors (captopril, enalapril), Potassium-sparing diuretics (spironolactone, triamterene), Beta blockers (atenolol, metoprolol, propranolol), Non-steroidal anti-inflammatory drugs, Others (digoxin, sulfamethoxazole/ trimethoprim, cyclosporin, tacrolimus, trimethoprim, pentamidine, succinylcholine, heparin)

We report a rare case of severe drug-induced hyperkalemia presenting as periodic paralysis.

CASE REPORT

A 67-year-old woman presented to emergency department with complaints of episodes of inability to walk for the past 5 days, happening 4-5 times a day. Each episode lasted for 15-20 minutes and was associated with restlessness and breathlessness. Patient was apparently alright one month before, since then she started feeling generalized weakness on and off. However, for past 5 days symptoms were exaggerated and she started feeling sudden loss of power in both the lower limbs simultaneously and inability to walk. She could walk normally after the episode subsided. This episode was not associated with pain in the limbs. Patient was totally conscious during the entire episode. Her medical history was significant for diabetes and hypertension for the past 5 years. The patient's drug therapy consisted of insulin nova mixtard 30/70 (for the past 10 years), olmesartan 20 mg per day (for past 2 years), perindopril 4 mg per day (for past 16 months), and torsemide 10 mg per day (for past 6 months).

On examination she was found to be alert and fully oriented. Vital signs revealed a regular pulse rate of 93 beats per minute, blood pressure of 130/80 mmHg, temperature of 36.8°C, a respiratory rate of 14/min and oxygen saturation of 100% on room air by pulse oxymetry. Cardiac auscultation revealed normal heart sounds, respiratory examination revealed bilateral vesicular breath sounds with bilateral basal crepitations. Complete neurological examination did not reveal significant finding.

Investigations

The results of laboratory examination were as follows: 10.6 g%, Total Leukocyte Count: 10,500, Differential Leukocyte Count: N70 L26 M3 E1 B0, ESR: 12 mm/hr, Random blood sugar: 98 mg/dl, Urea: 24 mg/dl, Creatinine: 1.2 mg/dl, Total Cholesterol: 198 mg/dl, Triglyceride: 112 mg/dl, HDL: 38 mg/dl, LDL: 138 mg/dl, Serum sodium: 134 mEq/L, Serum potassium: 8.6 mEq/L, Total calcium: 11 mg/dl, Ionized calcium: 1.30 mEq/L, Serum Magnesium: 2.5 mg/dl, Serum chloride: 104 mmol/L, Serum Bicarbonate: 24 mmol/l. ECG showed normal sinus rhythm, normal axis, and tall T waves. CT scan and EMG were not done.

Differential diagnosis

Diabetic neuropathy, Gullian Barre Syndrome, metabolic cause of periodic paralysis.

The diagnosis of drug-induced hyperkalemia presenting as periodic paralysis was suggested by very high serum potassium concentration during the attack and also persistent hyperkalemia between attacks.

Treatment

Patient was immediately admitted and the treatment for hyperkalemia was instituted. Drugs causing potassium retention were immediately stopped. Medical measures were started to lower down the level of serum K+ which included K+ bind sachet (calcium polystyrene sulfonate) thrice daily. Lactulose syrup and magnesium sulfate was given to avoid constipation. Her K+ started decreasing progressively and within 24 h K+ got reduced from 8.4 mEq/L to 6.8 mEq/L. In the next 24 h serum K+ further lowered from 6.8 to 5.4 mEq/L.

There was progressive fall of blood pressure during the course of the treatment and patient was overall drowsy and disoriented. Measures were taken to maintain her blood pressure.

Outcome

Patient responded well to the treatment and was discharged in a stable state with serum K+ level of 5.1 mEq/L, and blood pressure of 120/80 mmHg on 5th day of admission.

The patient has been followed-up on an outpatient basis, her serum potassium has been stable with no further episodes of periodic paralysis.

DISCUSSION

In normal subjects capacity to maintain K+ homeostasis is highly effective as renal handling of K+ avoids the development of hyperkalemia.[5-8] Thus practically in all the cases of hyperkalemia a predisposing cause is present. In the present case the patient was an elderly diabetic female on drug therapy which is known to increase the serum potassium level. It is known that diabetic patients are more prone to serum potassium abnormalities, because blood glucose

affects the shifting of potassium in and out of the cells.[9] These predisposing conditions interfered with the potassium homeostasis resulting in hyperkalemia.

Compared to cardiac presentation, neurological presentation is a rather rare occurrence in hyperkalemia. This may be due to the fact that cardiac manifestation usually begins before muscle weakness and corrective action is taken before K+ reaches to a level at which neurological manifestation begins to appear.[10] It has also been documented that increase serum calcium concentration minimizes the effect of hyperkalemia on the heart.[11-13] In the present case the total serum calcium level was also found to be raised (11 mg/dl). This increased calcium level might have played its role in protection of the heart in this case.

Muscle weakness associated with hyperkalemia appears to result from changes in neuromuscular conduction. Hyperkalemia results in persistent depolarization and thus inactivation of Na+ channel in the membrane, thereby producing a net decrease in the membrane excitability that may be manifested clinically by muscle weakness and paralysis.[14] Panichpisal *et al*., reported hyperkalemia to be a rare cause of acute flaccid paralysis. The authors presented a case of a 52-year-old man with end-stage renal disease with ascending quadriplegia and dyspnea, His investigations detected life-threatening hyperkalemia (9.0 mEq/L). The patient was consuming large amounts of high potassium foods and was taking ibuprofen.[15]

Periodic paralysis is a condition which is manifested by episodes of short lived, hyporeflexic skeletal muscle weakness with or without myotonia and without any sensory deficit or loss of consciousness.[16] There are number of etiological factors which are responsible for periodic paralysis. Periodic paralysis can be classified into primary (familial) and secondary periodic paralysis [Table 2].

Periodic paralysis itself is a relatively rare disease in clinical practice. SN Arya reported only 39 cases of periodic paralysis during his observation between 1972 and 2001.[16]

Deranged K+ manifesting as periodic paralysis has been described in number of circumstances, but majority of time it is hypokalemia which is triggering periodic paralysis, hyperkalemia presenting as periodic paralysis is rather a rare occurence. Arya noticed that "primary" periodic paralysis was mainly of hypokalemic variety and "secondary" periodic paralysis was mainly of hyperkalemic variety.[16] In his analysis he found that the basic causes of hyperkalemia in secondary periodic paralysis were acute tubular necrosis, acute oliguric renal failure and chronic renal failure. He did not report any patient with drug-induced hyperkalemia manifesting as periodic paralysis.

Table 2: Classification of periodic paralysis

Familial periodic paralysis: Hyperkalemic/hypokalemic	
Thyrotoxic periodic paralysis	
Andersen-Tawil syndrome	
Secondary hyperkalemic periodic paralysis	Secondary hypokalemic periodic paralysis
Hypoaldosteronism	Cushing's disease/syndrome
Hyporeninaemia	Hyperinsulinemia
Chronic renal failure	Thiazide or loop diuretic induced
Addison's disease	Distal tubular acidosis
High dose of angiotensin-converting inhibitor	Potassium losing nephropathy
Potassium sparing diuretics (spironolactone, triametrene, amiloride)	Drug/Toxins: Gentamicin, carbenicillin, amphotericin B, degraded tetracycline, carbenoxolone, barium poisoning, toluene exposure, vitamin B12, alcohol
	Hyperaldosteronism (primary or secondary)
	Severe diarrhea and vomiting
	Ileostomy
	Uterosigmoidostomy

Khuller *et al*., in 1994 reported a rare case of hyperkalemic periodic paralysis in chronic renal failure patient.[17] Kane MP and Busch RS reported an uncommon case of iodine-induced (Jod-Basedow) hyperthyroidism leading to thyrotoxic periodic paralysis in a 64-year-old white male, his laboratory test results included a potassium level of 3.0 mEq/L.[18]

Tengan CH *et al*.,[19] evaluated 20 patients of periodic paralysis, majority of them were having hypokalemic periodic paralysis and only four patients had hyperkalemic periodic paralysis.

CONCLUSION

To the best of our knowledge, this is the first ever case reported for "drug-induced hyperkalemia" presenting as Periodic Paralysis. Physicians should have high index of suspicion in a patient presenting with periodic paralysis. Eliciting good clinical and drug history is very important in such presentations as there are number of drugs which can induce derangement of potassium level which can be manifested as periodic paralysis. Geriatric patients with comorbid conditions like diabetes as well as renal disease are specially prone to develop hyperkalemia if they are put on medications which are known to produce hyperkalemia. This case report certainly will widen the vision of clinician to consider "hyperkalemia" as a cause of periodic paralysis, simultaneously highlighting the importance of doing a simple investigation like serum electrolyte for

patients presenting with such features so that the precious time is not lost in diagnosing such cases.

Learning point

- Drug-induced hyperkalemia though rare is not inevitable
- It should always be considered as a cause of periodic paralysis specially if patient's medical history denotes the consumption of drugs which are known to cause potassium retention
- Serum electrolyte is a simple and rapid investigation. Assessment of serum electrolyte should be done at appropriate intervals for the patients who are being treated with potassium-altering medications. This may avoid unnecessary delay in diagnosis and can avoid unfateful complications.

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