

EXERCISE INDUCED PARALYSIS IN TWO YOUNG GHANAIAN MEN

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Summary

We present two cases of young Ghanaian males who presented to the Korle Bu Teaching Hospital between August and September 2013 with a history of exercise induced quadriplegia and diagnosed to have hypokalaemic periodic paralysis. Both patients had had recurrent paralysis for years without a diagnosis.

The condition is part of a heterogeneous group of channelopathies that affect sodium, potassium, and calcium channels in membrane cells. It has autosomal dominant inheritance with male preponderance, common in Caucasians and Asians and rare in blacks

Key Words: *hypokalaemia, periodic paralysis, quadriplegia*

Introduction

Hypokalaemic paralysis is a form of metabolic myopathy, which represents a heterogeneous group of disorders associated with hypokalaemia, acute flaccid paralysis which may be potentially fatal when the weakness involves the respiratory muscles or there is life-threatening cardiac arrhythmia. The first known description of periodic paralysis was given by Musgrave in 1727¹. Since then, hypokalaemic paralysis has been reported from different parts of the world predominantly in South East Asia². Hypokalaemic periodic paralysis (HPP) can be a primary disorder, which may be familial with autosomal-dominant inheritance or sporadic, or it may be secondary with causes like renal tubular acidosis (RTA), thyrotoxic periodic paralysis (TPP), primary hyperaldosteronism, Gitelman syndrome, barium poisoning, and diarrhoea³. Familial periodic paralysis (FPP) is the commonest cause of HPP in Caucasians, and TPP is the leading cause in Asian population^{4,5}. Although the clinical manifestation may be similar in both types, the severity and the long-term management may be different and, therefore, it is imperative for physicians to find out the cause of hypokalaemic paralysis. Failure to make a distinction between these two types may result in mismanagement, which can be fatal.

Case Reports

Case 1

A 26 year old male university student was referred to emergency department in July 2013 with a history of inability to move all his four limbs upon waking up early in the morning 2 days prior to presentation. It began in

the evening as ascending weakness of both lower limbs 3 hours after a basketball game. By the following morning he could not get out of bed. This was his fourth experience of such a presentation; the previous presentations were in 2003, 2006, and 2009 which he recovered spontaneously without a deficit within 48-72 hours. There was no history of diarrhoea or vomiting with the current or previous episodes of weakness.

He had received empirical treatment comprising antibiotics and steroids with a diagnosis of recurrent Guillaine Barre syndrome. He had neither family history of a similar illness nor a chronic medical condition. Central nervous system (CNS) examination revealed decreased muscle tone including loss of neck control but normal muscle bulk and muscle power of MRC grade 2/5. Deep Tendon Reflexes were reduced in all areas with a normal sensory examination and he had no evidence of respiratory distress or abnormal cardiac rhythm. Serum electrolytes showed potassium of 1.8 mmol/L

Case 2

A 21 year old senior high school graduate presented with 3 days history of progressive muscle weakness which had worsened to quadriplegia on day of presentation. He had had several episodes of such weakness over the years which frequently occurred after vigorous exertion, the current presentation having occurred after sexual intercourse. He would regain full muscle strength spontaneously, within 6 hours without going to the hospital. In the current situation, the weakness had persisted beyond the usual 6 hours necessitating him to seek medical attention. He had no family history of a similar illness, no chronic medical condition and had had neither diarrhoea nor vomiting with the current or previous episodes. On physical examination he was not in respiratory distress and did not have any abnormal cardiac rhythm. Central Nervous System Examination revealed a normal muscle bulk, decreased tone, and muscle power of MRC grade 2/5. The rest of the examination was unremarkable.

Serum electrolytes showed potassium of 1.9mmol/l

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Case 1 Electrolyte chart:

	Day 1	Day 3	OPD (2wks)
Na ⁺	137mmol/l	137mmol/l	134mmol/l
K ⁺	1.8mmol/l	4.5mmol/l	4.0mmol/l
Cl ⁻	98mmol/l	103mmol/l	100mmol/l
Bicarbonate	26mmol/l	29mmol/l	26mmol/l
Urea	7.5mmol/l	4.7mmol/l	4.0mmol/l
Creatinine	98umol/	88umol/l	74umol/l

Case 2 Electrolyte chart:

	Day 1	Day 3	OPD (2 wks)
Na ⁺	142mmol/l	142mmol/l	137mmo/l
K ⁺	1.9mmol/l	4.3mmol/l	4.5mmol/l
Cl ⁻	106mmol/l	103mmol/l	96mmol/l
Urea	5.2mmol/l	3.8mmol/l	3.1mmol/l
Creatinine	63umol/l	66umol/l	60umol/l

Both patients were diagnosed to have hypokalaemic periodic paralysis based on the typical history and the low serum potassium on admission to the emergency room without objective clinical loss of potassium. Case I received parenteral potassium chloride because of the clinical severity (Loss of neck control) and case 2 received oral potassium supplementation. Both cases were walking by the 3rd day of admission regardless of the different approaches to treatment. The repeated serum electrolytes were also normalized. Other laboratory results including FBC, urine analysis, ECG, chest X ray, Liver and thyroid function tests were normal.

Thyroid function tests for the two patients are below:

Case 1 Thyroid Function tests

Parameter	Results	Reference Range
S-TSH (Thyrotropin)	1.12 uIU/mL	0.34-5.6
S-FT3 (Direct)	7.2 pmol/L	3.7-10.4
S-FT4 (Thyroxine)	8.6 pmol/L	7.5-21.1

Case 2 Thyroid Function tests

Parameter	Results	Reference Range
S-TSH (Thyrotropin)	1.08 uIU/mL	0.34-5.6
S-FT3 (Direct)	5.3 pmol/L	3.7-10.4
S-FT4 (Thyroxine)	8.4 pmol/L	7.5-21.1

Discussion

Acute hypokalaemic paralysis, a clinical syndrome characterized by acute systemic weakness and low serum potassium, is a rare but treatable cause of acute weakness. Therefore, it is imperative for physicians, particularly those working in acute care settings, to be aware of this condition and to take prompt action when encountered. If recognized and treated appropriately,

patients recover without any clinical sequelae³. There have been no reported cases of this condition in Ghana in the recent past and this may be due to the rarity of the condition or misdiagnosing it for other causes of acute flaccid paralysis. The patient in case 1 for instance, was not diagnosed for 10 years despite several hospital admissions for acute paralytic attacks. Most cases of hypokalaemic paralysis are due to familial or primary hypokalaemic periodic paralysis; sporadic cases are associated with numerous other conditions including barium poisoning, hyperthyroidism, renal disorders, certain endocrinopathies and gastrointestinal potassium losses. The age of onset, race, family history, medications, and underlying disease states can help in identifying the cause of hypokalaemic paralysis^{3,6,7}. None of our patients had a known family history of periodic paralysis and neither of them had any form of thyroid disease. Clinical symptoms of hyperthyroidism have been found to be mostly subtle in patients with hypokalaemic periodic paralysis despite obvious biochemical derangement³. In addition they had no renal or gastrointestinal disease.

Because our patients had no concurrent illness and had had no procedures, they were unlikely to have the familial forms of hypokalaemic paralysis. Familial hypokalaemic periodic paralysis is however an autosomal dominant condition with symptoms usually beginning before the age of 25 years with a male preponderance⁸. Our patients were both males, 26 and 21 years of age and had no family history. It is likely that they may have the primary (sporadic) form of hypokalaemic periodic paralysis. This could not be affirmed because of our inability to do genetic testing in our setting for ultimate defective ion channel. Attacks may be precipitated by a carbohydrate-rich meal (secondary to insulin secretion) or physical exertion associated with increased muscle consumption of glucose and intracellular potassium influx^{2,7,9}. Of the several precipitating factors, increased physical activity has been observed to be the most common trigger factor^{2,10}. Because of the precipitation of weakness by a high carbohydrate meal, increased plasma glucose may be a presentation finding which may result in the inadvertent use of insulin in such patients. It is therefore worth emphasizing that, patients presenting with flaccid paralysis or extreme weakness in the setting of a high blood sugar need to have their potassium levels evaluated and corrected before administering insulin, especially if the patient is not known to have diabetes mellitus or with a family history of periodic paralysis. If this precaution is not taken, the high blood sugar in the presence of increased insulin level will worsen the hypokalaemia by driving the little potassium left into the intracellular space leading to cardiac conduction abnormalities.

The diagnosis of hypokalaemic paralysis is based on a combination of history, physical examination, laboratory and ancillary studies. Laboratory investigations to be done include serum levels of

sodium, potassium, calcium, magnesium, urea and creatinine, serum Creatinine Phosphokinase (CPK), thyroid function tests, urine pH, arterial blood gas analysis, and 12 lead electrocardiogram (ECG). Laboratory studies should be consistent with low serum potassium levels. The ECG may show U waves, prolonged QT interval or even ventricular arrhythmia. Transtubular potassium concentration gradient and potassium-creatinine ratio during paralytic attack is very important to distinguish potassium loss from a renal disease. For example a urinary potassium concentration >20 mmol/L, or a urinary potassium/creatinine ratio of >2.5 indicates urinary loss of potassium. Also, a transtubular potassium concentration gradient (TTKG) >3.0 suggests hypokalaemia of renal origin¹¹

The weakness in hypokalaemic paralysis can range from mild isolated transient involvement of specific muscle groups to diffuse generalized weakness leading to quadriplegia. Our patients presented with quadriplegia and serum potassium level below 2.0 mmol/l. Both patients usually got the attacks after a rest following physical exertion and never during the activity. The first case never thought the physical activities had a connection with his attacks unlike the second patient who noticed the relationship between activity and his attacks.

Acute cases can last from hours to several days and can be a onetime event or recurrent periodic episodes¹. The patient in case 1 had his attacks usually lasting more than 24 hours and this resulted in 3 different occasions of hospitalization. The second case usually had his attacks lasting in less than a day but usually frequent. The longest period of attack resulted in the presentation in this report

Thyrotoxic periodic paralysis (TPP) is another differential when evaluating hypokalaemic paralysis^{3,12}. TPP is common in the Asian sub-continent, age of onset of symptoms and inheritance pattern are similar to the familial type¹².

In a large study from Taiwan, which included 97 patients, 68% patients had demonstrable secondary causes of which thyrotoxicosis was the most frequent (40.2%) cause².

There are various theories regarding the mechanism of the hypokalaemia in an elevated thyroid state, including the direct effect of high circulating hormone titers on Na⁺-K⁺-ATPase pump, which lead to increased cellular potassium uptake and hypokalaemia. The exact mechanism however remains unclear. It is therefore imperative to do serum free T4, T3, and TSH levels to exclude TPP in patients presenting with hypokalaemic paralysis. This was done in our patients however they had normal thyroid function.

Potassium supplementation is warranted in acute cases of hypokalaemic paralysis. Oral replacement with potassium chloride is usually preferred over intravenous supplementation^{12,13}. Intravenous potassium should be used in cases with cardiac arrhythmia or respiratory compromise secondary to pharyngeal weakness or

involvement of respiratory muscles^{1,13}. A recommended initial dose of 0.5 to 1 mmol/kg would raise serum potassium concentrations by 1 to 1.5 mmol/L¹. Because the hypokalaemia and subsequent changes in potassium concentration induced by treatment may result in cardiac arrhythmias, it is important to monitor the electrocardiogram (ECG) before, during, and after treatment and to have repeated assessment of blood potassium concentration⁴.

Prophylactic management with carbonic anhydrase inhibitors (CAIs) such as acetazolamide can be considered in cases with frequent, recurrent attacks^{11,13,14}. In patients with limited response to CAIs, potassium-sparing diuretics such as triamterene and spironolactone can be considered⁵. The efficacy of topiramate, an anticonvulsant with CAI-like activity, has been described in a case report¹ and it is not well characterised

It will be noticed that we treated our initial case with parenteral potassium chloride on day one due to the profound weakness that was threatening respiratory function. The second patient had oral potassium supplementation.

Patients with history of hypokalaemic paralysis need special care when they are being worked up for surgical procedures to prevent secondary complications such as Pre- or postoperative paralysis¹⁵. The following are recommended:

- Close control of serum potassium concentration
- Low carbohydrate intake
- Avoidance of large glucose and salt loads
- Maintenance of body temperature and acid-base balance
- Careful use of neuromuscular blocking agents with continuous monitoring of neuromuscular function

Conclusion

Hypokalaemic paralysis is a serious but reversible condition if recognized in time and treated promptly. It is supposed to be uncommon in sub-Saharan Africa but we have presented here two cases of such with rather interesting presentation very common to most emergency room settings. Even though we had limitations in doing genetic testing, hypokalaemic paralysis remains a clinical diagnosis and we propose Hypokalaemic paralysis should be considered as a differential diagnosis in patients presenting with acute flaccid paralysis in the absence of an acute illness in emergency rooms in Ghana. Emergent management should include adequate and timely potassium replacement, diagnostic evaluation, and close monitoring.

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