CASE SERIES

THYROTOXIC PERIODIC PARALYSIS

Miqdad Haider, Aijaz Zeeshan Khan Chachar, Atif Munir
Department of Medicine, Fatima Memorial Hospital, Lahore-Pakistan

Thyrotoxic periodic paralysis is an uncommon disorder characterized by hypokalaemia, thyrotoxicosis and paralysis, most commonly seen in South Asian males. Aim of our case series is to highlight the significance of this reversible cause of patients presenting with neuromuscular paralysis. We present case series of 1 Asian and three Caucasian patients with thyrotoxic periodic paralysis who came with neuromuscular weakness secondary to thyrotoxicosis. All made a swift and uneventful recovery with no recurrence. Thyrotoxic periodic paralysis (TPP) is an infrequent condition having recurrent episodes of muscle weakness as main feature. Hypokalaemia is a common finding seen in these patients. Resolution of the attacks is achieved with correction of hypokalaemia and hyperthyroidism.

Keywords: Hyperthyroidism; Thyrotoxic periodic paralysis; Hypokalaemia; Paraparesis

Citation: Haider M, Chachar AZK, Munir A. Thyrotoxic periodic paralysis. J Ayub Med Coll Abbottabad 2019;31(4):619–21.

INTRODUCTION

Thyrotoxic periodic paralysis is an acquired condition, more common in males of Asian origin.[1] The pathogenesis of thyrotoxic periodic paralysis is not established however it is considered that there is a role of increased Na^+–K^+ATPase action provoked by thyroid hormone, hyperadrenergic activity and hyperinsulinemia.[2] Paralysis usually occurs when the patient is at rest, like in bed at night. The possible precipitants include heavy exercise, carbohydrate rich meals.[3] We report four cases of this rare condition who presented to us with recurrent episodes of paralysis.

CASE 1

A 24-year-old Asian man was received at the hospital for workup and treatment of recurrent muscular weakness. On history it was noted that the patient had a total of 8–10 episodes of painless lower limbs weakness over 4 months, which started during sleep in early morning with different recovery time in each episode (within 10–60 minutes). There were episodes of flaccid muscle weakness with variable intensity, i.e., from mild proximal leg weakness to quadriparesis, mainly involving only lower limbs. Conscious level during, after and before the attacks was conserved. Patient had been having positional tremors, decreased sleep, intolerance to hot weather, slight weight loss and palpitations for the last 6 months. There was no history of any other neuromuscular symptoms or any other prevailing illness. There was no family history of a similar presentation although his mother was a diagnosed case of hyperthyroidism.

At presentation, he was a well looking, alert and conscious gentleman, afebrile, blood pressure of 130/90 mmHg and regular pulse of 110 beats/minutes. On examination of the limbs there was minor bilateral proximal weakness of the lower limbs (power 4/5). Cranial nerves, sensations and reflexes were intact.

Hypokalaemia (2.1 mmol/L, 3.0) was documented in previous episodes and treated with intravenous potassium chloride. In between hypokalaemic episodes, he presented to our hospital where his laboratory studies revealed normal Ck levels, renal and liver function tests, serum sodium (Na) 141 mmol/L (135–150), magnesium (Mg) 2.1 mg/dL (1.7–2.5) potassium (K) 4.5 mmol/L (3.5–5.0), calcium(Ca-i) 1.21 mmol/L (1.15–1.32). Thyroid stimulating hormone (TSH) level was 0.0005 µIU/mL (0.35–4.94), free T4 2.18 ng/dL (0.70–1.48), and free T3 10.03 pg/dL (1.71–3.71). Thyroid scan showed diffuse goitre (Total thyroid uptake: 5.9%) Electrocardiogram was unremarkable.

The patient, after the workup, was diagnosed to have Graves' thyrotoxicosis related thyrotoxic periodic hypokalaemic paralysis. To prevent further episodes of paralysis and for the hyperthyroidism of the patient, treatment with propranolol and carbimazole was initiated and regular follow up in Endocrine OPD advised.

CASE 2

A 37-year-old Caucasian man came to casualty department with sudden onset progressive lower limb weakness following an alcohol- and carbohydrate-heavy meal the night before. There was no history of viral illness in the recent past. He did not report any visual disturbances. He was on no medication and had no significant family history. Pulse rate was 110/min and blood pressure 167/92 mmHg. There was generalised muscle weakness, more pronounced in his legs, with hypotonia and hyporeflexia. Plantar responses were down-going and no sensory deficits

were apparent and there was no hypoxia or respiratory distress.

ECG confirmed sinus tachycardia with U waves in V2-V3, consistent with the degree of hypokalaemia (serum potassium 2.4 mmol/L). This was corrected with intravenous potassium chloride (KCl), 40 mmol over 4 hours, followed by oral supplements. Neuromuscular weakness resolved completely once the serum potassium (K) had normalised. Further assessment revealed that he had a 2-year history of intermittent palpitations, heat intolerance and tremors but no weight loss or increased appetite. He had a mild tremor but no signs of thyroid eye disease. He also had a small diffuse goitre. His thyroid function test revealed evidence of hyperthyroidism with TSH of <0.05 mIU/L (0.3–4.7), total T4: 198 nmol/L (70–140), raised Antithyroid peroxidase antibodies at 489 kU/L (0–60) and TBII at 48 (0–10).

The diagnosis of hypokalaemic thyrotoxic periodic paralysis (TPP) was made and he was started on propylthiouracil (PTU) (he was intolerant of carbimazole) and beta-blockers. His potassium supplements were tailed off once he was rendered euthyroid. Review of his old case notes from a neighbouring hospital subsequently revealed that he had become thyrotoxic with TSH of <0.05 mU/L (0.3-4.1), Free T4 of 21 pmol/L (9–19), and Free T3 of 3.1 nmol/L (0.9–2.2) 10 years previously following an iodide load for intravenous contrast-urogram. His symptoms at the time were limited to sweating and heat intolerance, with no muscle weakness and he had responded fully to carbimazole dose-titration therapy for eight months.

Three months later, he elected to have definite therapy with radioactive iodine (^{131}I). He was advised to stop his PTU for the three days before and after ^{131}I treatment. Despite beta-blockade and oral potassium supplements and a potassium-rich diet taken on his own initiative, he was readmitted with a further hypokalaemic paralytic episode on the day following ^{131}I administration. This episode was successfully managed with intravenous potassium and by restarting PTU. He eventually became hypothyroidism over a period of months and has since remained well and symptom free on Thyroxine replacement.

CASE 3

A 37-year Caucasian man who presented to casualty department in the morning with sudden weakness of his limbs more prominent in the lower limbs. He was unable to move his legs or walk, despite having played a full round of golf the day before. On examination he had tachycardia of 116/min and normal blood pressure. He had marked muscle weakness most prominent in proximal muscle groups of both legs with hypotonia and hyporeflexia. There was no sensory deficit. His serum potassium was low at 2.5 mmol/l and this was corrected by intravenous followed by oral potassium supplement with improvement of his symptoms. Further enquiry revealed a 6-month history of poor sleep, weight loss, tremors, and increased bowel frequency as well as family history of hyperthyroidism. He had a small diffuse goitre and mild left-sided proptosis. Thyroid function showed evidence of hyperthyroidism with TSH: < 0.03 mIU/L (0.3–4.7) and Free T3: >30 pmol/L (3.5–5.5). He had positive thyroid antibodies. He was initially treated with Carbimazole and and beta-blockers as a prelude to definitive treatment with ^{131}I, following which he was rendered hypothyroid, ultimately remaining well and symptom free on Thyroxine.

CASE 4

An 88-year-old Caucasian female with a background of stable angina and chronic back pain presented with a several months history of tiredness, anorexia, dysphagia, and weight loss. Her mobility had deteriorated over the same period and she was having recurrent episodes of limb weakness and falls. She was on NSAID for back pain and treatment for angina which included; Diltiazem, Isosorbide Mononitrate, and Aspirin. On examination she was mildly dehydrated but had normal pulse and blood pressure. There were few bruises on her face and limbs due to a recent fall. She was unable to mobilize due to generalised weakness of both legs. Blood results revealed mild normochromic anaemia with haemoglobin (Hb) of 11.0 g/dL and low plasma potassium of 2.7 mmol/L. In view of her symptoms and the anaemia, she underwent gastroscopy which showed normal stomach and duodenum but there was some distortion of the oro-pharyngeal anatomy. ENT examination was normal; however, CT scan of her neck demonstrated a multinodular goitre causing some displacement of the pharynx. Thyroid function test demonstrated hyperthyroidism with TSH: <0.03 mIU/L (0.3–4.7) and Free T3: 8.8 pmol/L (3.5–5.5). Her treatment included intravenous and oral potassium replacement and Carbimazole and showed dramatic improvement in her symptoms with no further falls.

DISCUSSION

One of the rare complications of hyperthyroidism is Thyrotoxic periodic paralysis (TPP). Thyroid hormone can increase sensitivity of beta-adrenergic receptors which in turn increase action of sodium-potassium ATPase action in the skeletal muscle membrane which finally shifts potassium into the

cells. All this gives result to hypokalaemia and muscle paralysis. Asian population has a higher incidence of TPP. In countries like Japan, Philippines and China cases of TPP are reported frequently. The overall incidence of TPP in China and Japan is 1.8 and 1.9%, respectively. In western countries, it is difficult to find extensive studies about its incidence. According to a report, in North America, the incidence rate of TPP was around 0.1–0.2% in thyrotoxic patients.[4] Individual cases of TPP have also been found in populations of other geographical background.[5] Patients are usually adult males giving history of recurrent partial to complete muscle weakness mostly in lower limbs but may involve upper limbs also. Generally respiratory muscles are not affected but total involvement of respiratory, bulbar, and ocular muscles has been seen in an acute attack.[4,6] Level of consciousness is preserved during the attack. Patient might give history of thyrotoxic symptoms before the paralytic event. Frequency and duration of the attacks is variable. In some cases, a precipitating factor like exercise, carbohydrate rich diet or stress may be found.

Diagnosis of TPP can be established when a patient is received with complains of recurrent weakness of proximal muscles mainly involving lower limbs with no family history of such disease. Furthermore, patient might have signs and symptoms of hyperthyroidism and hypokalaemia which can be confirmed through laboratory investigations.

A myopathic pattern can be seen in electromyogram study. This phenomenon is only evident during active disease, i.e., during paralysis, while in remission, a normal electromyogram can be found. In some cases, rhabdomyolysis is found in acute attacks of TPP.[7] The most common electron microscopic changes are vacuolation and mitochondrial abnormalities are in skeletal muscles.[8]

Other conditions that can cause periodic paralysis must be ruled out like familial periodic paralysis, drug induced (tocolytics, chloroquine toxicity, barium poisoning).[9] Acute muscle paralysis such as Botulism, Myasthenia crisis and Guillain Barré Syndrome must also be included in the differential diagnosis.

Treatment is recommended for periodic paralysis with hypokalaemia. In cases where there is a high frequency of attacks, prophylactic treatment must be considered. Exacerbating factors must be avoided**.** The main pillars of treatment for TPP are; treatment of hyperthyroidism with antithyroid medications (thionamides), surgical treatment (thyroidectomy), or radioiodine therapy. To minimize the frequency and, to some extent, severity of an acute attack, beta blockers (propanolol) can be used. They reverse excessive shift of potassium into cells. Increased potassium intake, betablockers (propranolol), dichlorphenamide and potassium sparing diuretics like spironolactone can be effective modes of treatment for prophylaxis as well as during attacks.[10] There is need for increased awareness about this condition among patients at risk as well as among the physicians so that an early diagnosis is made in order to prevent these attacks.

REFERENCES

1. Lam L, Nair RJ, Tingle L. Thyrotoxic periodic paralysis. Proc (Bayl Univ Med Cent) 2006;19(2):126–9.
2. Lin SH, Huang CL. Mechanism of thyrotoxic periodic paralysis. J Am Soc Nephrol 2012;23(6):985–8.
3. Ali Chaudhry M, Wayangankar S. Thyrotoxic Periodic Paralysis: A Concise Review of the Literature. Curr Rheumatol Rev 2016;12(3):190–4.
4. Ahlawat SK, Sachdev A. Hypokalaemic paralysis. Postgrad Med J 1999;75(882):193–7.
5. Liu YC, Tsai WS, Chau T, Lin SH. Acute hypercapnic respiratory failure due to thyrotoxic periodic paralysis. Am J Med Sci 2004;327(5):264–7.
6. Lichtstein DM, Arteaga RB. Rhabdomyolysis associated with hyperthyroidism. Am J Med Sci 2006;332(2):103–5.
7. Magsino CH Jr, Ryan AJ Jr. Thyrotoxic periodic paralysis. South Med J 2000;93(10):996–1003.
8. Kornø MR, Hagen C. Hypokalemic thyrotoxic periodic paralysis--a rare differential diagnosis in patients presenting acute tetraparesis. Ugeskr Laeger 2008;170(39):3070.
9. Siddiqui FA, Sheikh A. Muscle paralysis in thyrotoxicosis. BMJ Case Rep 2015;2015:bcr2014207945.
10. Venance SL, Cannon SC, Fialho D, Fontaine B, Hanna MG, Ptacek LJ, *et al*. The primary periodic paralyses: diagnosis, pathogenesis and treatment. Brain 2005;129(Pt 1):8–17.

Submitted: 23 February, 2019	*Revised: 21 May, 2019*	*Accepted: 21 May, 2019*

Address for Correspondence:

Miqdad Haider, Department of Medicine, Fatima Memorial Hospital, Shadman, Lahore-Pakistan
Cell: +92 312 405 1408
Email: miqdad14@yahoo.com