Case Report

Thyrotoxic Periodic Paralysis: A Case Report with Patient Perspective

A Baranskaya, Y Zhang & B Lee

Abstract

We present a case report on a spot diagnosis of Thyrotoxic Periodic Paralysis (TPP) with a unique first-person account of events from the patient. It illustrates the importance of pattern recognition and exemplifies how timely treatment enables quick resolution of a life-threatening medical emergency. Patient X's account affirms the condition's insidious onset and rapid deterioration. This case highlights the need for raising awareness of diseases that are more prevalent in specific ethnic groups and is particularly crucial for work in culturally diverse environments. We hope by sharing our experience, readers will be prompted to consider TPP as a differential diagnosis for acute limb weakness in an acute setting; with prompt testing of thyroid function and initiation of the appropriate treatments.

Keywords

acute limb weakness, acute paralysis, hypokalaemia, thyrotoxicosis, thyrotoxic periodic paralysis

We provide you with both a first-person patient account of events, written in his own words in blue, as well as our medical transcript of events.

Patient X, a normally fit and well Chinese male in his late 20s, called NHS 111 service due to rapid onset lower limb weakness after waking up in the morning.

"I had been having nocturnal leg cramps and nocturia for over a month. On the night before admission, I had a small party with friends and was eating snacks and sweets constantly until midnight. When I woke up at 4AM for my usual toilet visit, I realised my legs had lost a lot of power. I asked my friend to help me stand up. I had to lock my knees and could barely manage to walk to the toilet. I went back to bed afterwards, hoping the leg cramps would be resolved the next morning like usual. At 8AM, I woke up again and I couldn't move my legs at all. I required two people to lift me up to move around. I called 111 and two ambulance crew members arrived shortly."

On arrival to hospital, Patient X was vomiting and mildly breathless in the absence of cough, wheeze or chest pain. He recalled a 6-week history of lower limb muscle cramps, generalised tiredness, high temperatures, cloudy urine with nocturia and increased frequency of micturition. Muscle cramps initially started at night and after exercise but then gradually began affecting him intermittently during the day. There was no history of trauma or back pain.

Patient X stated he had experienced noticeable unintentional weight loss over the last few months. Otherwise, he had no recent infections, foreign travel or unwell contacts.

"After arriving at the hospital, the paralysis had slowly spread to my upper body, where I started losing strength in my arms and neck. I was feeling really sick and couldn't keep my eyes wide open."

His first set of observations showed a heart rate of 86 bpm, blood pressure of 106/48 mmHg, respiratory rate 18 breaths/min, temperature 36.6°C and a capillary blood glucose 7.6 mmol/L. The patient's heart rate ranged between 86 to 117 (average 110bpm) during his time in the emergency department.

On examination, Patient X was alert but visibly uncomfortable from lower limb pain. Cardiovascular, respiratory and abdominal examinations were normal. Neurological examination showed upper limb power of 4/5 and lower limbs 1/5 bilaterally, with absent tendon reflexes and plantar responses. Sensation was intact on gross assessment with no spinal tenderness. He did not have any features of thyroid eye disease or goitre on examination.

A repeat ECG showed prolonged QTc, U waves and ST depression (Figure 1). These changes were non-dynamic on repeated testing.

On point of care testing, hypokalaemic alkalosis with a potassium of 1.4 mmol/L was noted which corresponded to the laboratory measurement of 1.5 mmol/L (Table 1). Additionally, he had hypomagnesaemia (0.61 mmol/L) and severe hypophosphataemia (<0.21 mmol/L). Intravenous electrolyte replacement was initiated promptly. He was placed on a cardiac monitor whilst admission to ITU was arranged for central electrolyte replacement and monitoring.

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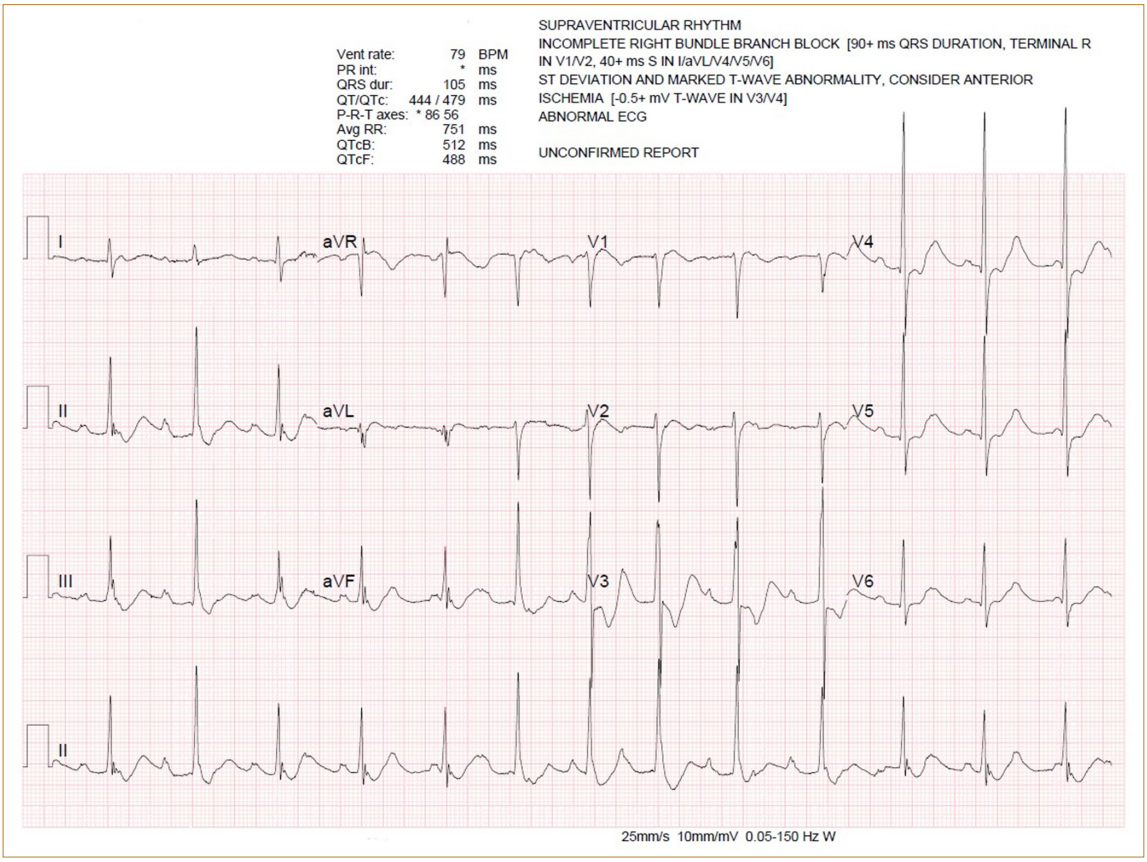


Figure 1. 12 lead ECG taken on admission to hospital.

The initial differential diagnoses considered were Familial Hypokalaemic Periodic Paralysis (FHPP), Thyrotoxic Periodic Paralysis (TPP), Gillian Barré Syndrome (GBS) and transverse myelitis.

Further investigations were arranged such as toxicology screening, thyroid function tests, parathyroid hormone (PTH) levels, urinary electrolyte measurements and blood borne viral (BBV) screen. Thyroid function test results were consistent with thyrotoxicosis, hence a diagnosis of TPP was made.

Following stabilisation of hypokalaemia, Patient X was commenced on carbimazole and propranolol. He had complete resolution of neuromuscular symptoms within a few hours following admission. Repeat potassium was 4.8 mmol/L and ECG changes normalised to sinus tachycardia. He made an uneventful recovery and was soon discharged from the hospital with outpatient endocrinology follow up; where a diagnosis of Graves' disease was confirmed by the markedly raised TSH receptor antibodies at 25.3 IU/L (normal reference <1.75 IU/L).

"On arrival to ITU, there was great discomfort on my legs as I couldn't move them at all. Although I have a strong mentality, the situation was very distressing and I couldn't help but let some tears out. When the IV electrolytes were nearly finished, my condition improved immediately. I could suddenly move all my limbs again and all the discomfort was gone. All the ITU staff treated me extremely well. I felt safe on the unit and trusted treatments that were offered."

Discussion

Thyrotoxic Periodic Paralysis (TPP) is a rare complication of thyrotoxicosis. While thyroid disorders are more common in females, this rare disease predominantly affects young males between 20-40 years of age[1]. The prevalence of TPP is low among Caucasians and is 10 times more common among the Asian population, with the overall incidence of 1.8% among the Chinese thyrotoxic population[2,3]. TPP is associated with the human leukocyte antigen DRw8 isotype, hence suggesting a genetic component to the disease. Due to population mobility, presentations of TPP are becoming increasingly more common in Western countries. Therefore, it is crucial for all clinicians to have up-to-date knowledge of the condition to avoid delay in diagnosis and potentially life-threatening complications.

TPP typically presents with acute attacks, varying from mild weakness to total paralysis. Our case demonstrates a typical presentation of TPP as it often starts at night or in the early morning, thought secondary to the catecholamine surge. Other precipitants include hyperinsulinemia following a

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Table 1. Patient X's blood test results on admission. Abnormal results are denoted with (H) for higher than normal and (L) for lower than normal reference range, where appropriate.

		On Admission	Reference ranges
FBC	White blood cell count, blood	(H) 12.8 10*9/L	(4.0-11.0 10*9/L)
	Haemoglobin level, blood	150 g/L	(125-180 g/L)
	Platelet count, blood	218 10*9/L	(150-450 10*9/L)
	Neutrophil count, blood	(H) 10.76 10*9/L	(1.70-7.50 10*9g/L)
Biochemistry	Sodium level, blood	141 mmol/L	(133-146 mmol/L)
	Potassium level, blood	(L) 1.5 mmol/L	(3.5-5.3 mmol/L)
	Chloride level, blood	108 mmol/L	(95-108 mmol/L)
	Urea level, blood	5.3 mmol/L	(2.5-7.8 mmol/L)
	Creatinine level, blood	61 umol/L	(44-133 umol/L)
	C-reactive protein (CRP) level, blood	<1 mg/L	(Normal <5 mg/L)
	Troponin I level, blood	38 ng/L	
	Albumin level, blood	40 g/L	(35-50 g/L)
	Adjusted calcium level, blood	2.53 mmol/L	(2.20-2.60 mmol/L)
	Phosphate level, blood	(L) <0.21 mmol/L	(0.80-1.50 mmol/L)
	Magnesium level, blood	(L) 0.61 mmol/L	(0.70-1.00 mmol/L)
	Creatine kinase (CK) level, blood	136 U/L	(40-320 U/L)
Thyroid Function Test	Thyroid stimulating hormone, blood	(L) <0.01 mU/L	(0.35-4.94 mU/L)
	Free T4 level, blood	(H) 48 pmol/L	(9-20 pmol/L)
	Free T3 level, blood	(H) 28.4 pmol/L	(2.4-6.0 pmol/L)
	TSH receptor antibody level	(H) 25.30 IU/L	(normal <1.75 IU/L)
	Thyroid peroxidase (TPO) antibody – *checked in outpatient setting following discharge.*	(H) 128 iu/mL	(<34 iu/mL)

heavy meal, alcohol abuse or strenuous exercise[2,4]. Muscle paralysis is often transient, lasting up to 72 hours, with patients often presenting with recurrent episodes. During attacks, the proximal lower limbs are more affected than other muscle groups with the bulbar, respiratory and ocular muscles spared in most cases. As observed, the patients typically have lower motor neuron signs, with diminished or absent deep tendon reflexes, and normal sensory function. Reflecting on our case, the patient reported a few months history of multiple episodes of lethargy and significant leg cramps following exercise. Possibly these were mild attacks of the condition that have previously been overlooked by the patient.

Hypokalaemia is the precipitant for paralysis and a biochemical hallmark of TPP. This finding is a significant clue to diagnosis, however in acute setting alternative causes need to be excluded. Hypokalaemia occurs due to an intracellular shift that occurs either as a direct response to thyroid hormone or indirectly via adrenergic stimulation, insulin or exercise. All the above increase cellular sodium/potassium-ATPase pump (Na-K pump) activity which in combination with reduced potassium output disrupts potassium homeostasis, leading to hyperpolarization and paralysis. In addition, there is evidence to suggest that mutations in potassium efflux channels are implicated in development of TPP; as TPP is a rare manifestation seen in small portion of patients with thyrotoxicosis[5].

The diagnosis of TPP is driven by clinical presentation. High serum triiodothyronine (T3) and thyroxine (T4) with completely suppressed serum thyroid-stimulating hormone (TSH) level are in keeping with thyrotoxicosis. Raised TSH receptor antibodies are decisive in the diagnosis of Graves' disease. It is worth noting that elevated thyroxine peroxidase (TPO) antibody levels are present in 90-95% of patients with autoimmune thyroid disease, with detectable levels in up to 70-80% of patients with Graves' Disease[6].

Other supporting diagnostic findings are low spot urine potassium and hypophosphataemia with low

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phosphaturia. Unlike in our case, hypomagnesaemia tends to be mild to moderate[7]. Typical ECG changes include hypokalaemia associated changes, tachycardia, atrial fibrillation, high QRS voltage and atrioventricular block.

Differential diagnoses of the neurological presentation of TPP include Familial Hypokalaemic Periodic Paralysis (FHPP), GBS and transverse myelitis. FHPP is a competing differential that presents with similar clinical presentations and biochemical markers. It is an autosomal dominant condition that typically affects Caucasians. FHPP tends to present at an earlier age, typically before the age of 16[8]. Importantly, it is differentiated from TPP by absence of clinical and biochemical features of thyrotoxicosis.

Even though cases are regularly reported in the literature, TPP remains a diagnostic challenge. This case illustrates the importance of pattern recognition of rare conditions. Whilst clinician's ability to separate the usual from the rare disease is vital, with the advance of technology one can utilise computerised disease pattern recognition software such as Orphanet[9] for diagnostic support. If one keys in a search term hypokalaemic paralysis, then thyrotoxic hypokalaemic periodic paralysis will come up as a differential diagnosis.

Once TPP is diagnosed, the management is straightforward. It involves potassium replacement with close monitoring for cardiac arrhythmias. Immediate administration prevents serious cardiopulmonary complications such as arrhythmias and may hasten the recovery of muscle weakness[10]. A paradoxical fall in serum potassium can occur following initiation of replacement, which requires close monitoring[11]. Potassium supplementation should stop once serum level is normalised and be administrated with caution due to the high risk of rebound hyperkalaemia, as the potassium shifts extracellularly[7]. Following clinical stabilisation, antithyroid medication such as carbimazole can be initiated to treat the thyrotoxicosis. Beta blocker propranolol is given in conjunction to inhibit peripheral T4 conversion to T3 and antagonise beta-receptor mediated adrenergic activities. Both levothyroxine and propranolol are thought to reduce Na/K–ATPase activities. Definitive therapy such as surgery (thyroidectomy) or radioactive ablation can be considered once the patient is stabilised.

Once diagnosed and treated, TPP has a good prognosis with no evidence that prophylactic potassium supplementation prevents further episodes[2].

Acknowledgement

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Declaration of competing interests

Nothing to declare.

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