A rare case of thyrotoxic periodic paralysis precipitated by hydrocortisone

Subrata Chakrabarti

Department of General Medicine, IPGMER, Kolkata, West Bengal, India

Address for correspondence:
Dr. Subrata Chakrabarti, Doctor's Hostel, IPGMER, A. J. C Bose Road, Kolkata - 700 020, West Bengal, India.
E-mail: subratachakrabarti2011@gmail.com

Abstract

Thyrotoxic periodic paralysis (TPP) is a rare, but serious condition characterized by acute paralytic attacks and hypokalemia in association with thyrotoxicosis. Although carbohydrate rich meals, strenuous exercise, alcohol, emotional stress are known precipitants of TPP, steroid treatment has rarely been reported to induce TPP. We report a case in which a patient with previously untreated Grave's disease developed TPP following administration of Intravenous hydrocortisone for control of severe anaphylaxis, which to best of our knowledge is very rare.

Key words: Anaphylaxis, hydrocortisone, hypokalemia, thyrotoxic periodic paralysis

INTRODUCTION

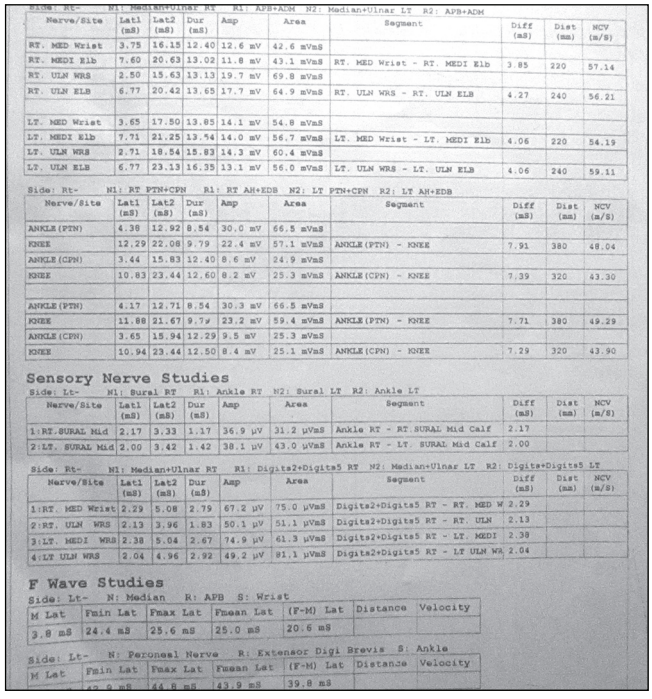
Thyrotoxic periodic paralysis (TPP) is mainly reported in young Asian males in their 3rd-4th decade of life,[1,2] classically evident as acute paralytic attack and hypokalemia in the background of thyrotoxicosis.[3] TPP should be considered as a cause of acute weakness to avoid missing a treatable and curable serious condition when established (heavy meal, exercise) or probable (beta 2 agonists, insulin, steroids) clinical history is evident.

CASE REPORT

A 32-year-old female not on any medication was rushed to the emergency unit with severe dyspnea along with intense wheezing, pruritus, and swelling of face for ½ h following multiple bee-stings. She did not complain of any myalgia or muscle weakness of any part of the body or passage of dark colored urine. Examination revealed the presence of generalized urticarial rash, angioedema, nasal congestion, tachypnea, rapid thready pulse, and hypotension (blood pressure [BP]: 96/66 mmHg at admission). A clinical diagnosis of anaphylactic shock was made and patient was administered high flow oxygen, nebulization with levosalbutamol and intravenous fluids (crystalloids). As her respiratory distress was not being alleviated following 1 h of this treatment and epinephrine injection not being available locally, it was decided to administer corticosteroids to diminish her dyspnea. Hydrocortisone (100 mg) was injected intravenously in short push. Her urticaria and

dyspnea responded remarkably and her angioedema started to resolve. Hypotension was promptly corrected within 20 min. However, 8 h after admission when her initial presenting complaints had subsided almost completely, the patient developed acute onset, rapidly progressive weakness first involving both lower limbs, mainly in the proximal aspects eventually progressing to proximal aspects of upper limbs within 1 h. She denied any pain or paresthesia and no prior history of fever or upper respiratory tract infection or spinal trauma or vaccination in the past 4-6 weeks was documented. She had no difficulty in urination or in passing bowels and possessed clear sensorium without any seizures. She had no significant personal history and she was not on any medications. There was no history of similar disorders or other endocrine or neurologic diseases in her family. However, she mentioned history of occasional irregular palpitation, heat intolerance, diaphoresis, irritability for the last 9 months following which she was diagnosed having primary hyperthyroidism resulting from diffuse toxic goitre by her local physician. She was admitted 5 months ago with similar presentation due to wasp bite. Both these episodes were controlled with oxygen, nebulization with levosalmutamol and IV fluids alone and did not require epinephrine or hydrocortisone administration. A rapid clinical examination revealed symmetrical flaccid weakness in both upper and lower extremities (lower >upper and proximal > distal; power 2/5 in all 4 limbs). Deep tendon reflexes were depressed in all limbs. Tests of sensorium, meningeal irritation, sensory examination, and cranial nerves revealed no abnormality. Her BP was 124/64 mm Hg and regular pulse rate of 112/min, which was collapsing in nature. Cardiovascular examination during this time showed apical impulse at left 6th intercostal space 0.5 cm lateral to the mid-clavicular line with forceful ill-sustained character. Together with a soft systolic murmur suggested hyperdynamic circulation. Diffuse enlargement of thyroid was noted. Rest of the systemic examination was normal.

Based on the clinical scenario, a diagnosis of TPP due to hypokalemia was considered most likely with guillain-barre syndrome, segmental myelitis, rhabdomyolysis, hypophosphatemia being the probable differential diagnosis. Serum potassium was 2.3 mEq/L (normal 3.5-4.5 mEq/L). Serum electrolytes including sodium, chloride, calcium, phosphate, and magnesium levels were normal. Other clinical biochemistry was also within normal levels. Electro myography and Nerve conduction study done within 1 h of evolution of the complete weakness ruled out any evidence of myopathy or acute inflammatory demyelinating radiculopathy, respectively [Figures 1 and 2]. Electrocardiography showed evidence of hypokalemia in the form of large U wave. Heart rate was 108/min and QTc interval was 0.32 s. Urine sodium and potassium and serum aldosterone and renin levels were measured to rule out adrenal involvement and were found to be normal. Urine spot potassium: Creatinine was 1.4 (i.e. <1.5) and transtubular potassium gradient was 2.6 (i.e. <3), both suggesting the absence of inappropriate potassium loss in urine. Magnetic resonance imaging brainstem and cervical spinal cord revealed no demyelination or acute vascular event or features suggestive of acute transverse myelitis [Figures 3 and 4]. She was treated with potassium supplementation initially intravenously (potassium chloride) followed by oral route upon which patient recovered completely within 10 h. She received 140 mEq of potassium (oral and intravenous forms altogether) before complete recovery of weakness. Recovery of muscle power was first noted in lower limbs within 2 h



Nerve/Site	Lat1 (mS)	Lat2 (mS)	Dur (mS)	Amp	Area	Segment	Diff (mS)	Dist (mm)	NCV (m/S)
RT. MED Wrist	3.75	16.15	12.40	12.6 mV	42.6 mVmS				
RT. MEDI Elb	7.60	20.63	13.02	11.8 mV	43.1 mVmS	RT. MED Wrist - RT. MEDI Elb	3.85	220	57.14
RT. ULN WRS	2.50	15.63	13.13	19.7 mV	69.8 mVmS				
RT. ULN ELB	6.77	20.42	13.65	17.7 mV	64.9 mVmS	RT. ULN WRS - RT. ULN ELB	4.27	240	56.21
LT. MED Wrist	3.65	17.50	13.85	14.1 mV	54.8 mVmS				
LT. MEDI Elb	7.71	21.25	13.54	14.0 mV	56.7 mVmS	LT. MED Wrist - LT. MEDI Elb	4.06	220	54.19
LT. ULN WRS	2.71	18.54	15.83	14.3 mV	60.4 mVmS				
LT. ULN ELB	6.77	23.13	16.35	13.1 mV	56.0 mVmS	LT. ULN WRS - LT. ULN ELB	4.06	240	59.11

Side: Rt- N1: RT PTN+CPN R1: RT AH+EDB N2: LT PTN+CPN R2: LT AH+EDB

Nerve/Site	Lat1 (mS)	Lat2 (mS)	Dur (mS)	Amp	Area	Segment	Diff (mS)	Dist (mm)	NCV (m/S)
ANKLE (PTN)	4.30	12.92	8.54	30.0 mV	66.5 mVmS				
KNEE	12.29	22.08	9.79	22.4 mV	57.1 mVmS	ANKLE (PTN) - KNEE	7.91	380	48.04
ANKLE (CPN)	3.44	15.83	12.40	8.6 mV	24.9 mVmS				
KNEE	10.83	23.44	12.60	8.2 mV	25.3 mVmS	ANKLE (CPN) - KNEE	7.39	320	43.30
ANKLE (PTN)	4.17	12.71	8.54	30.3 mV	66.5 mVmS				
KNEE	11.88	21.67	9.79	23.2 mV	59.4 mVmS	ANKLE (PTN) - KNEE	7.71	380	49.29
ANKLE (CPN)	3.65	15.94	12.29	9.5 mV	25.3 mVmS				
KNEE	10.94	23.44	12.50	8.4 mV	25.1 mVmS	ANKLE (CPN) - KNEE	7.29	320	43.90

Sensory Nerve Studies

Side: Lt- M1: Sural RT R1: Ankle RT N2: Sural LT R2: Ankle LT

Nerve/Site	Lat1 (mS)	Lat2 (mS)	Dur (mS)	Amp	Area	Segment	Diff (mS)	Dist (mm)	NCV (m/S)
1:RT.SURAL Mid	2.17	3.33	1.17	36.9 µV	31.2 µVmS	Ankle RT - RT.SURAL Mid Calf	2.17		
2:LT. SURAL Mid	2.00	3.42	1.42	38.1 µV	43.0 µVmS	Ankle RT - LT. SURAL Mid Calf	2.00		

Side: Rt- N1: Median+Ulnar RT R1: Digits2+Digits5 RT N2: Median+Ulnar LT R2: Digits+Digits5 LT

Nerve/Site	Lat1 (mS)	Lat2 (mS)	Dur (mS)	Amp	Area	Segment	Diff (mS)	Dist (mm)	NCV (m/S)
1:RT. MED Wrist	2.29	5.08	2.79	67.2 µV	75.0 µVmS	Digits2+Digits5 RT - RT. MED W	2.29		
2:RT. ULN WRS	2.13	3.96	1.83	50.1 µV	51.1 µVmS	Digits2+Digits5 RT - RT. ULN	2.13		
3:LT. MEDI WRS	2.38	5.04	2.67	74.9 µV	61.3 µVmS	Digits2+Digits5 RT - LT. MEDI	2.38		
4:LT ULN WRS	2.04	4.96	2.92	49.2 µV	81.1 µVmS	Digits2+Digits5 RT - LT ULN WR	2.04		

F Wave Studies

Side: Lt- N: Median R: APB S: Wrist

M Lat	Fmin Lat	Fmax Lat	Fmean Lat	(F-M) Lat	Distance	Velocity
3.8 mS	24.4 mS	25.6 mS	25.0 mS	20.6 mS		

Side: Lt- N: Peroneal Nerve R: Extensor Digi Brevis S: Ankle

M Lat	Fmin Lat	Fmax Lat	Fmean Lat	(F-M) Lat	Distance	Velocity
	43.9 mS	44.8 mS	43.9 mS	39.8 mS		

Figure 1: Normal motor and sensory nerve conduction velocity study including normal F wave and H reflex

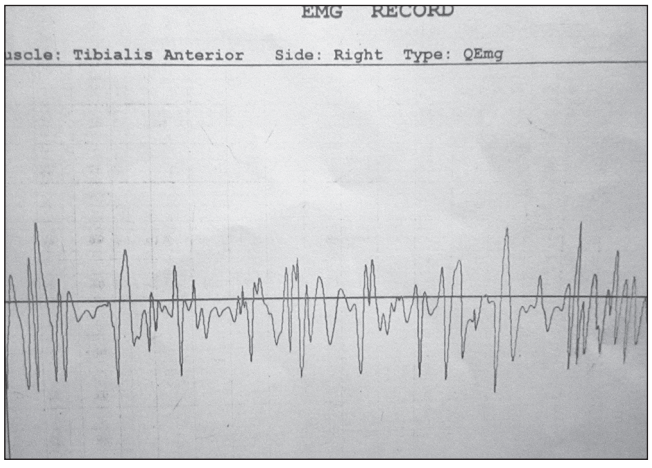


Figure 2: Normal pattern of electromyogram study (in tibialis anterior muscle)

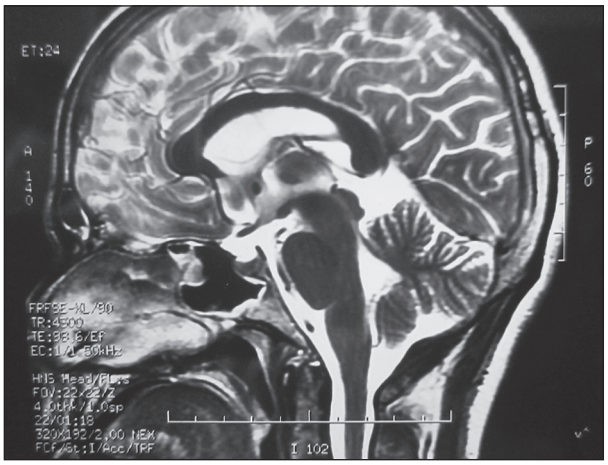


Figure 3: Normal brainstem in magnetic resonance imaging brain sagittal section (T2-weighted image) - no evidence of demyelination or acute vascular event

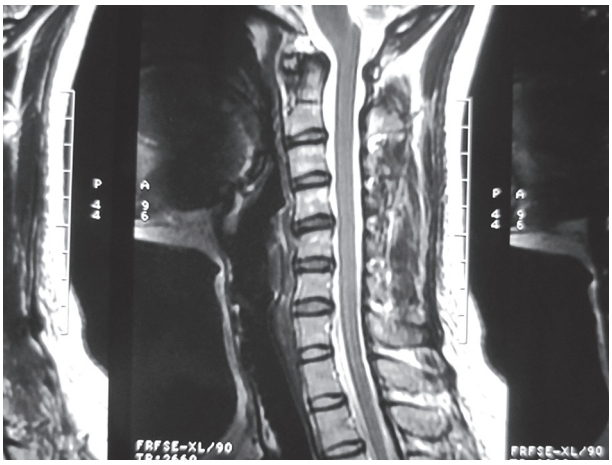


Figure 4: Normal cervical spinal cord in magnetic resonance imaging spine (T1-weighted image) - no evidence of acute transverse myelitis

(of initiating potassium supplementation) followed by upper limbs and was complete within 10 h with no residual deficit. Serum potassium at this time was 4.1 mEq/L. Thyroid profile was then obtained — Serum thyroxine (T4) of level 17.6 ng/dl (normal, 5.13-14.1 ng/dl) Serum-free T4 was 3.08 ng/dL (0.5-1.6); serum T3-2.9 ng/mL (0.7-2.1); serum thyroid-stimulating hormone: 0.1 mIU/L (0.14-4.1). Thyroid radioiodine uptake scan revealed a diffuse homogeneous uptake. A diagnosis of TPP associated with diffuse toxic goitre was made based on clinical and laboratory findings. Treatment with propranolol (40 mg/day) and methimazole (20 mg/day) was initiated on the 2nd day of admission. Oral potassium replacement at dose of 80 mEq/L was continued for another 4 days (total 5 days). Serial potassium values on day 2-5, were 3.9 mEq/L, 4.0 mEq/L, 4.2 mEq/L, and 4.0 mEq/L. Potassium replacement was stopped after 5 days, and she was followed up for next 3 days with daily potassium level checks which were in normal range (4.0 mEq/L, 4.0 mEq/L, 3.8 mEq/L). She was counseled for thyroidectomy (to be performed after adequate control of the hyperthyroid state). Alongside, she was advised a low carbohydrate diet and a caution to avoid heavy or strenuous exercise, to be followed life-long. She was discharged in a stable condition on the 9th day of admission.

DISCUSSION

Thyrotoxic periodic paralysis is a dangerous, but preventable and curable disorder mainly observed in young Asian males with thyrotoxicosis. In the undiagnosed hyperthyroidism, mild features of thyrotoxicosis are easily overlooked resulting in a delay in clinical management leading to death by respiratory failure and dysrhythmia.[1,2]

Hypokalemia caused by potassium shift into the intracellular compartment[3] due to overstimulation of Na^+/K^+-ATPase pump in cell membranes of skeletal muscles caused by excess thyroid hormone levels, β2-adrenergic stimulation by catecholamines and thyroid hormones in thyrotoxic states are responsible for TPP. A high carbohydrate meal, warm weather, cold weather, diarrhea, viral illness, fatigue, or increased physical exertion, insulin, are usual precipitants of TPP.[4] Although Grave's disease is most commonly associated with TPP, any cause of hyperthyroidism (toxic adenoma/diffuse toxic goitre, etc.) may be responsible.[5] Treatment of TPP in the acute phase includes cautious potassium replacement therapy via intravenous or oral route based on the severity of hypokalemia.[1-3] Control of the hyperthyroid state is the mainstay of treatment. Nonselective β-blockers like propranolol are useful for both treatment and prevention of recurrence of attacks.[6] Transient hypophosphatemia and hypomagnesemia are often documented; however, the index patient had normal phosphate and magnesium levels ruling out hypophosphatemia as a cause or contributor of the weakness.[4]

There is a fall in serum potassium preceding weakness, but in some patients, the level may never fall below normal. Some patients experience severe weakness and/or cardiac instability with only mild hypokalemia (K + 3.0-3.5 mEq/L). Respiratory function may deteriorate rapidly in these patients. In the index patient who presented with significant quadriparesis (power in all 4 limbs 2/5) without bulbar involvement, the initial K^+ was 2.3 mEq/dL.[7,8]

Myotoxicity following bee-sting is unusual. If respiratory distress develops due to myotoxicity or neurotoxicity (bulbar involvement), it is not associated with wheezing, pruritus, or swelling of face. Suddenness of the onset of respiratory distress and association with intense wheezing, pruritus, and swelling of face favors anaphylaxis (bronchospasm) as the cause of her respiratory difficulty. However, neurotoxicity of wasp venom is well-reported.

Kinins in the venom cause presynaptic block of cholinergic transmission by means of irreversible depletion of acetylcholine, probably caused by noncompetitive inhibition of choline uptake resulting in development of weakness of different muscles including bulbar weakness. Several studies have suggested that besides the neurotoxic effect of wasp venom, delayed immunological response to wasp antigens followed by an allergy-triggered autoimmune reaction can resulting in weakness. Such cases respond well to intravenous administration of cholinergic agents (mainly neostigmine) and recovery occurs within about 24-36 h after neostigmine use. The index patient did not require such cholinergic agent for her recovery, which was complete within 10 h of potassium replacement. Moreover, corticosteroids are often used in the treatment of such cases with excellent results. The index patient developed weakness after administration of corticosteroids. This negates the possibility of neurotoxicity of the bee stings as the cause of her weakness.[9]

Certain medications alleged to precipitate TPP are acetazolamide, estrogen, diuretics, cortisol, adrenalin, beta-agonists, and potassium sparing diuretics.[5] Isolated case reports are available in the literature incriminating therapy with antiretrovirals[10] or interferon-alpha[11] as possible precipitating factors. Documentation of steroid therapy precipitating TPP is exceedingly sparse.[12-14] Among corticosteroids, hydrocortisone has not been previously reported as a precipitant for TPP. The exact role of steroids in causing TPP although not known may be due to increase in the number of Na^+/K^+-ATPase molecules (the main pathogenetic molecule of TPP) in skeletal muscle. They also increase insulin secretion both basal and the first phase which in turn activates Na^+/K^+-ATPase pump.[3,5]

This patient had received beta-agonist (in the form of levosalbutamol), which is a known precipitant of TPP. While most of the cases of TPP reported in the literature have developed following multiple doses. The index patient developed TPP after single dose of levosalbutamol, although the patient did receive levosalbutamol 5 months back without any episode of TPP. Interestingly, single or pulse dose of steroid (hydrocortisone) precipitated TPP, although it is difficult to pinpoint which drug among the two was the real precipitant or if a drug synergy had a role.[15] To prevent further episodes of TPP, health care professional and patients are strongly advised to avoid the established precipitating drug (in this case corticosteroids) lifelong and inform the attending physician regarding this fact in every hospital admission or other health-care contacts.

REFERENCES

1. Miller D, delCastillo J, Tsang TK. Severe hypokalemia in thyrotoxic periodic paralysis. Am J Emerg Med 1989;7:584-7.
2. Kelley DE, Gharib H, Kennedy FP, Duda RJ Jr, McManis PG. Thyrotoxic periodic paralysis. Report of 10 cases and review of electromyographic findings. Arch Intern Med 1989;149:2597-600.
3. Magsino CH Jr, Ryan AJ Jr. Thyrotoxic periodic paralysis. South Med J 2000;93:996-1003.
4. Kung AW. Clinical review: Thyrotoxic periodic paralysis: A diagnostic challenge. J Clin Endocrinol Metab 2006;91:2490-5.
5. Manoukian MA, Foote JA, Crapo LM. Clinical and metabolic features of thyrotoxic periodic paralysis in 24 episodes. Arch Intern Med 1999;159:601-6.
6. Birkhahn RH, Gaeta TJ, Melniker L. Thyrotoxic periodic paralysis and intravenous propranolol in the emergency setting. J Emerg Med 2000;18:199-202.
7. Griggs RC, Resnick J, Engel WK. Intravenous treatment of hypokalemic periodic paralysis. Arch Neurol 1983;40:539-40.
8. Lin SH, Lin YF, Halperin ML. Hypokalaemia and paralysis. QJM 2001;94:133-9.
9. Piek T. Neurotoxic kinins from wasp and ant venoms. Toxicon 1991;29:139-49.
10. Brown JD, Kangwanprasert M, Tice A, Melish J. Thyrotoxic periodic paralysis in a Polynesian male following highly active antiretroviral therapy for HIV infection. Hawaii Med J 2007;66:60, 62-3.
11. Cesur M, Gursoy A, Avcioglu U, Erdogan MF, Corapcioglu D, Kamel N. Thyrotoxic hypokalemic periodic paralysis as the first manifestation of interferon-alpha-induced Graves disease. J Clin Gastroenterol 2006;40:864-5.
12. Wongraoprasert S, Buranasupkajorn P, Sridama V, Snabboon T. Thyrotoxic periodic paralysis induced by pulse methylprednisolone. Intern Med 2007;46:1431-3.
13. Sabeer T, Sudheeran. Hyrotoxic periodic paralysis after administration of methyl prednisolone. Thyroid Res Pract 2007;4:82-3.
14. Liu Z, Braverman LE, Malabanan A. Thyrotoxic periodic paralysis in a Hispanic man after the administration of prednisone. Endocr Pract 2006;12:427-31.
15. Haffner CA, Kendall MJ. Metabolic effects of beta 2-agonists. J Clin Pharm Ther 1992;17:155-64.

How to cite this article: Chakrabarti S. A rare case of thyrotoxic periodic paralysis precipitated by hydrocortisone. J Nat Sc Biol Med 2015;6:271-4.

Source of Support: Nil. **Conflict of Interest:** None declared.

Access this article online	
Quick Response Code:	Website: www.jnsbm.org
	DOI: 10.4103/0976-9668.149236