DOI: 10.7860/JCDR/2023/61061.17590

Case Report

Internal Medicine Section

Thyrotoxic Periodic Paralysis Precipitated by Viral Hepatitis

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ABSTRACT

Thyrotoxic hypokalaemic Periodic Paralysis (TPP) is a medical emergency usually seen in Grave's disease, commonly in persons of oriental descent. The present case is a rare first time presentation of TPP in association with acute viral hepatitis A. A 46-year-old female presented with weakness, vomiting, fever, altered sensorium and yellow discolouration for 20 days. She was diagnosed to have hepatic failure due to viral hepatitis A. The patient's serum potassium level was 1.79 mmol/L. Treatment for hepatic failure and i.v. potassium chloride replacement was started. Sensorium improved but severe hypokalaemia and flaccid paralysis persisted. Thyroid functions were assessed and thyrotoxicosis due to Grave's disease was diagnosed. Carbimazole and systemic corticosteroids were also started and potassium infusion was continued. Serum potassium became normal only after thyroid hormones reached normal limits followed by improvement in muscle weakness. TPP can be precipitated in conditions of stress, thyroid functions should be assessed in cases of hypokalaemic periodic paralysis even in absence of overt thyroid disease.

Keywords: Altered sensorium, Grave's disease, Hypokalaemia

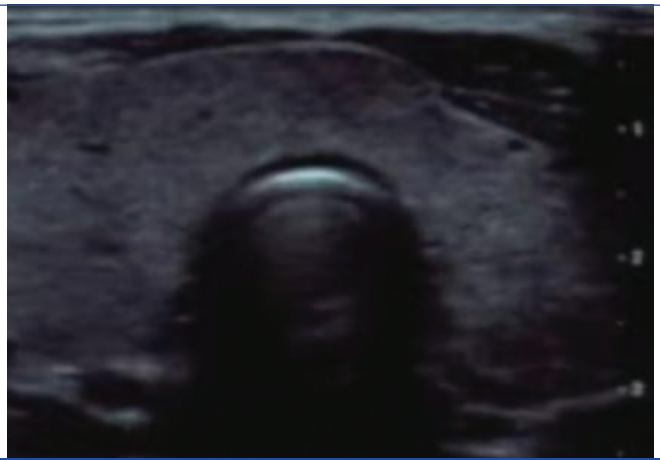
CASE REPORT

A 46-year-old female patient presented to emergency with history of generalised weakness for the last 20 days, yellowish discolouration of eyes and skin for six days and vomiting and altered sensorium since two days. Medical, personal and family history was unremarkable. Her pulse was 136 bpm, regular high volume; blood pressure was 100/50 mmHg; respiratory rate was 30/min and axillary temperature was 103ºF. General physical examination revealed cachexia, global alopecia, mild pallor, deep icterus, mild proptosis. On Cardiovascular System (CVS) examination, a short systolic murmur grade II best heard over pulmonary area radiating over the whole precordium was observed. Abdomen revealed soft, non tender hepatomegaly of 2cm from right costal margin and spleen tip palpable, with no shifting dullness. Bowel sounds were present. Respiratory system showed bilateral vesicular breath sounds and no added sounds. Central Nervous System (CNS) revealed E4M1V1. Patient was conscious but not following verbal commands. Because of generalised hypotonia, power could not be tested on admission and hypo-reflexia of deep tendon reflexes with flexor planter reflexes was observed.

On investigation, arterial blood gas analysis was suggestive of respiratory alkalosis with pH- 7.505, PCO2-20.6 mmHg HCO3-23.5 mmol/L with severe hypokalaemia (serum potassium 1.79 mmol/L) and i.v. potassium chloride replacement was initiated. Liver function test shows hyperbilirubinemia (total bilirubin 28.56 mg/dL, direct bilirubin 16.42 mg/dL, SGOT 80U/L, SGPT 149 U/L. Alkaline Phosphatase 172, protein 7 gm/dL and albumin 3 gm/dL, Prothrombin Time- 19.4 seconds (test), 10s control, INR-1.79, LDH-192 IU/L). Work-up for infective hepatitis was sent and anti-HAV IgM came out to be positive. Complete Blood Count (CBC), Kidney Function Test (KFT), glucose and other fever work-up was within limits as also chest X-ray. Electrocardiogram (ECG) was suggestive of hypokalaemia as T waves were flat.

The patient was initially managed as acute fulminant viral hepatitis and with anti hepatic coma regime which included rifaximin and lactulose. Differential diagnoses of familial periodic paralysis were ruled out by history and there was no history of ingestion of beta 2 agonists. Flaccid paralysis due to Guillain Barre Syndrome was considered but absence of respiratory paralysis despite quadriparesis made it unlikely and severe hypokalaemia was present so it was unlikely. Gastroenteritis with dehydration and hypokalaemia induced by vomiting and hyperventilation induced alkalosis, renal tubular disorders like Gitelmann and Barters syndrome were also kept in mind and inj. Ceftriaxone 1g i.v. 12 hourly was added. Malaria Ag test and Dengue serology were negative. Intravenous potassium chloride infusion replacement was continued. Despite a daily replacement of 180-200 meq serum potassium remained between 1.2-2.3 mEq/L.

In view of high grade fever, tachycardia, hyperdynamic circulation and mild proptosis thyroid function test was sent which was suggestive of hyperthyroidism {T3 2.51 ng/mL(0.6-1.81), T4 21.23 microgram/mL (4.5-10.9), TSH 0.005 uIU/mL(0.35-5.5)}. Free T3-7.45 pg/mL (2.3-4.5), Free T4-4.54 ng/dL (0.7-1.1) TRAb antibodies came out to be positive while anti-TPO antibody was negative. Ultrasonography (USG) thyroid gland showed heterogenous echotexture, normal size and vascularity with bulky isthmus [Table/Fig-1]. In view of high thyroid hormone levels, raised TRAb possible Grave's disease, acute hepatitis A with fulminant hepatitis and TPP was made. Oral carbimazole 20 mg 8 hourly, i.v. hydrocortisone 100 mg 8 hourly and oral propranolol 40 mg 12 hourly by nasogastric tube was initiated. In view of thyrotoxicosis and detection of TRAbs grave's disease, acute hepatitis A with fulminant hepatitis and TPP was considered. Oral carbimazole 20 mg 8 hourly, i.v. hydrocortisone and oral propranolol by nasogastric tube were administered.



[Table/Fig-1]: USG image showing diffusely bulky and mildly heterogenous echotexture of thyroid.

The patient became afebrile on eighth day, the second day of starting antithyroid drugs and steroids. Respiratory rate reduced to 15 cycles/minute and arterial blood gases analysis improved to pH-7.43, PCO2-37 mmhg and HCO3-22 mmol/L. She started responding to verbal commands on day 9 but deep icterus, hypokalaemia and proximal muscle weakness power 1/5 persisted necessitating i.v. KCl replacement. A 24 hour urinary potassium levels were sent which were normal (75 mEq) suggestive of transcellular shift thus possibility of TPP was kept. Despite replacing potassium per day, patient had persistent hypokalaemia and ever increasing doses of potassium up to 200 mEq potassium chloride i.v. was required for the next several days. Thyroid function test was repeated periodically. Thyroid function test improved to Free T3-2.81 pg/mL (2.3-4.2), T4-1.73 ng/dL (0.7-1.1) and TSH-0.05 Uiu/mL (0.35-5.5) on day 24 followed by decline in serum bilirubin and improvement in serum K+ levels to 3.7-4.5 meq/l with decline in requirement of potassium chloride (KCl). By day 29, total bilirubin declined from 28.56 mg/dL to 10.35 mg/dL, muscle weakness improved to 5/5.

The patient was discharged on day 34 on oral prednisolone, neomercazole, potassium chloride 30 mL 12 hourly, propranolol and vitamin supplements. Patient followed-up in Outpatient Department (OPD) after two weeks. She was found to have gained weight of 2.4 kg. She had no muscle weakness or icterus and was clinically euthyroid. Thyroid function tests were normal and serum potassium was 4.7 meq/l. Her KCL supplementation was reduced and stopped on subsequent visits.

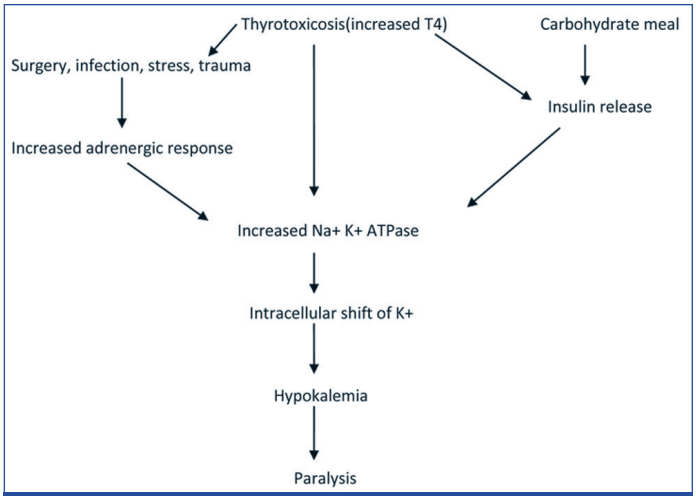
DISCUSSION

The Thyrotoxic hypokalaemic Periodic Paralysis (TPP) is a rare and potentially life threatening medical emergency most commonly due to Grave's disease. THPP/TPP is a rare neurological condition with an incidence of 2% in thyrotoxic Asian and 0.1-0.2% in non Asian patients [1-4]. It is characterised by transient episodes of paralysis and hypokalaemia during a thyrotoxic crisis usually triggered by infections, trauma, surgery or high carbohydrate diet [5]. It is most commonly associated with Grave's disease and predominantly affects predominantly males with male female ratio of 3:1 to 30:1 [5].

Thyrotoxic clinical features are usually absent. In medical literature TPP as a presenting feature of hyperthyroidism was reported by Younis A in a 34-year-old male in whom no precipitating factors were identified [6]. Bhavanathu T et al., also reported TPP as a presenting manifestation of Grave's thyrotoxicosis in a 40-year-old female in whom acute flaccid paralysis presented with hepatic abscess [7], while Sanyal D and Bhattacharjee S reported TPP as the first manifestation of thyroiditis in a 23-year-old male without any precipitating factors [8]. Soneji N et al., reported a 48-year-old Vietnamese male who presented with TPP and hypokalaemia induced ventricular fibrillation and Aseri ZA also reported TPP in a 29-year-old Chinese male as a first presentation of Grave's disease [9,10]. McFadzean AJ and Yeung R reported a Chinese male with TPP as first presentation of thyrotoxicosis Kumar S et al., reported a similar case from India [3,11]. Thus, TPP as a presenting feature of thyrotoxicosis has been reported only in Asian patients in third and fourth or fifth decade. In all reported cases potassium replacement and correction thyrotoxicosis with antithyroid drugs and steroids was followed by reversal of flaccid paralysis. In the present case, also the patient was 46 years of age and an Asian female in whom hepatitis A was identified as a possible trigger and was managed along similar lines with i.v. potassium chloride, antithyroid drugs and steroids and resulted in euthyroid status, normal serum potassium levels and reversal of paralysis.

Viral hepatitis was reported as a triggering event of TPP by Cui W et al., who described THPP as first presentation of Grave's disease in a 46-year-old patient suffering from hepatitis B [12]. Pastore F et al., opined an association between hepatitis C and autoimmune thyroid disorders and Kong SJ et al., reported 2 case of acute Hepatitis E with hyperthyroidism [13,14]. The hypothesised mechanism could be possible extra hepatic manifestations acting as a trigger for autoimmune stimulation of thyroid gland [14]. Thus, the present case is probably the first case in which TPP was reported in association with viral hepatitis A. The authors present a case of acute muscle weakness and refractory hypokalaemia and hyperthyroidism which presented for the first time in a female patient (who had no prior history of thyroid disease) with acute viral hepatitis A.

Hypokalaemia results in the setting of thyrotoxicosis due to increased transcription of genes which encode for Na+K+ ATPase in sarcolemmal membrane, enhanced beta 2 adrenergic stimulation and mutations in KCNJ18 gene inducing Kir 2.6 channels ,all of these causing intracellular shift of K+ in large amounts resulting in flaccid paralysis [5]. The liver is a major organ responsible for metabolising the thyroid hormones, as well as for producing thyroid binding proteins, such as thyroid binding globulin, transthyretin, and albumin. Conversely, thyroid hormones play a significant role in the activity of glucoronyl transferase involved in bilirubin metabolism [15,16]. In the present case, hypokalaemia was corrected only after correction of thyroid status [Table/Fig-2].



[Table/Fig-2]: Line diagram illustrating the pathophysiology of Thyrotoxic Periodic Paralysis.

CONCLUSION(S)

The authors present a rare case of Grave's Thyrotoxicosis presenting as Thyrotoxic periodic paralysis for the first time in association with hepatitis A which has never been reported in literature. Thyroid disease should be suspected and timely evaluation for the same should be done in all cases of hypokalaemic flaccid paralysis in persons of Asian descent even in absence of overt thyroid disease. Hypokalaemia in THPP is due to thyrotoxicosis induced transcellular shift of K+, thus i.v. KCL replacement is essential for the management of THPP but frequent monitoring may avert rebound hyperkalemia as euthyroid status is achieved.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Oct 28, 2022
- Manual Googling: Dec 30, 2022
- iThenticate Software: Jan 28, 2023 (4%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Oct 26, 2022**
Date of Peer Review: **Dec 05, 2022**
Date of Acceptance: **Feb 01, 2023**
Date of Publishing: **Mar 01, 2023**