ISSN 2307-8960 (online)

World Journal of *Clinical Cases*

Thrice Monthly Volume 13 Number 7 March 6, 2025

Published by Baishideng Publishing Group Inc

World Journal of Clinical Cases

Contents

Thrice Monthly Volume 13 Number 7 March 6, 2025

EDITORIAL

ORIGINAL ARTICLE

Retrospective Study

SYSTEMATIC REVIEWS

CASE REPORT

LETTER TO THE EDITOR

World Journal of Clinical Cases

Thrice Monthly Volume 13 Number 7 March 6, 2025

Contents

ABOUT COVER

Peer Reviewer of *World Journal of Clinical Cases*, Serghei Covantsev, MD, Surgeon, Department of Clinical Research and Development, Botkin Hospital, Moscow 125284, Russia. kovantsev.s.d@gmail.com

AIMS AND SCOPE

The primary aim of *World Journal of Clinical Cases* (*WJCC*, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING

The *WJCC* is now abstracted and indexed in PubMed, PubMed Central, *Reference Citation Analysis*, China Science and Technology Journal Database, and Superstar Journals Database. The 2024 Edition of Journal Citation Reports® cites the 2023 journal impact factor (JIF) for *WJCC* as 1.0; JIF without journal self cites: 0.9; 5-year JIF: 1.1; JIF Rank: 170/329 in medicine, general and internal; JIF Quartile: Q3; and 5-year JIF Quartile: Q3.

RESPONSIBLE EDITORS FOR THIS ISSUE

NAME OF JOURNAL
World Journal of Clinical Cases

ISSN
ISSN 2307-8960 (online)

LAUNCH DATE
April 16, 2013

FREQUENCY
Thrice Monthly

PUBLICATION DATE
March 6, 2025

World Journal of Clinical Cases

Submit a Manuscript: https://www.f6publishing.com

World J Clin Cases 2025 March 6; 13(7): 101214

DOI: 10.12998/wjcc.v13.i7.101214

ISSN 2307-8960 (online)

CASE REPORT

Insulin-induced severe thyrotoxic periodic paralysis: A case report

Yan-Li Wang, Jian Li

Specialty type: Medicine, research and experimental

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade B
Novelty: Grade B
Creativity or Innovation: Grade B
Scientific Significance: Grade A

P-Reviewer: Sharaf MM

Received: September 8, 2024
Revised: October 7, 2024
Accepted: November 19, 2024
Published online: March 6, 2025
Processing time: 77 Days and 19.9 Hours

Yan-Li Wang, Jian Li, Department of Endocrinology and Metabolism, Zigong First People's Hospital, Zigong 643000, Sichuan Province, China

Corresponding author: Yan-Li Wang, Doctor, Master's Student, Department of Endocrinology and Metabolism, Zigong First People's Hospital, No. 42 Shangyi Hao Road, Zigong City, Sichuan Province, China, Zigong 643000, Sichuan Province, China. wylisc@yeah.net

Abstract

BACKGROUND

Thyrotoxic periodic paralysis (TPP) is an endocrine emergency caused by thyrotoxicosis, manifesting mainly as periodic myasthenia and hypokalemia, and posing a serious threat to the patient's health. Fatigue, strenuous exercise, alcohol abuse, high carbohydrate intake and insulin injections are common triggers of paralysis. This article reports a case of severe TPP induced by insulin injection, elucidates the characteristics and pathogenesis of the disease, analyses the risk factors for triggering TPP, and hopefully provides more clinical data for TPP patients.

CASE SUMMARY

A 38-year-old Asian man presented to the emergency department with a one-week history of limb weakness and worsening half-day. His medical history included poorly controlled type 2 diabetes and he had been switched to Aspart50 a week earlier. He was alert and oriented with upper extremity strength grade 3 and lower extremity strength grade 1. Emergency department tests showed hypokalemia of 1.6 mmol/L. The paramedics administered 1.5 g of potassium intravenously, followed by 4.0 g orally. Weakness in the arms and legs improved. He was referred to endocrinology where he was diagnosed with Graves' disease, with suboptimal control and insulin injections possibly causing TPP. We stopped his insulin and he was discharged with a potassium level of 4.0 mmol/L.

CONCLUSION

Insulin is a trigger for TPP and should be avoided in patients with hyperthyroidism. Early recognition and treatment of TPP is crucial, especially in patients presenting with hypokalemic periodic paralysis.

Key Words: Thyrotoxic periodic paralysis; Potassium metabolism disorders; Insulin; Triggers of paralysis; Case report

Core Tip: Thyrotoxic periodic paralysis (TPP) is a severe endocrine emergency associated with potassium metabolism disorders. We report a case of severe TPP induced by insulin injection, which is rarely reported, and our study systematically elucidates the characteristics and pathogenesis of the disease, analyses the risk factors for triggering TPP, and hopefully provides more clinical data for TPP patients.

Citation: Wang YL, Li J. Insulin-induced severe thyrotoxic periodic paralysis: A case report. *World J Clin Cases* 2025; 13(7): 101214
URL: https://www.wjgnet.com/2307-8960/full/v13/i7/101214.htm
DOI: https://dx.doi.org/10.12998/wjcc.v13.i7.101214

INTRODUCTION

Thyrotoxic periodic paralysis (TPP) is a severe complication of thyrotoxicosis. Its clinical manifestations are dominated by metastatic hypokalemia and flaccid muscle paralysis. Although TPP can be caused by thyrotoxicosis for a variety of reasons, the most common aetiology is Graves' disease[1]. In contrast to the global distribution of Graves' disease, TPP shows significant racial and gender differences. TPP occurs at higher rates in Asian populations, ranging from 2% to 24%, but only 0.1% to 0.2% in non-Asian North Americans. It is also more common in males, with a male-to-female ratio of about 20:1, and the age of onset is usually 20–40 years[2,3]. Patients with TPP usually have subtle symptoms related to hyperthyroidism, and in about 75% of cases, it appears shortly after hyperthyroidism is diagnosed, but may precede its onset[4]. It is characterized by hypokalemia associated with acute proximal symmetrical weakness of the lower limbs and pelvic girdle, and may extend to all four limbs and the respiratory muscles[5]. Rapidly recognizing and stopping TPP is essential to avoid potentially fatal complications. Several factors can induce TPP, and a case of TPP induced by insulin injection is reported below.

CASE PRESENTATION

Chief complaints

One-week history of limb weakness and worsening half-day.

History of present illness

The patient had a history of primary hyperthyroidism and had been started on methimazole 10 mg Per Os daily without regular endocrine monitoring. At the onset of this episode his limb weakness was minimal, but in the last 12 hours the limb weakness has worsened dramatically.

History of past illness

His medical history included five years of poorly controlled type 2 diabetes mellitus treated with oral glimepiride and metformin. A week earlier, he had been switched to injectable insulin Aspart50.

Personal and family history

No family history of hyperthyroidism or related conditions, father had type 2 diabetes mellitus.

Physical examination

On clinical examination, the man was obese with clammy skin. He was alert and oriented with a respiratory rate of 20 breaths/min, heart rate of 91 beats/min, and blood pressure of 111/73 mmHg. Notable findings included grade II non-tender thyroid enlargement and an audible vascular murmur over both thyroid lobes. The patient had grade 3 upper extremity strength and grade 1 lower extremity strength. Deep tendon reflexes were reduced in the legs but normal in the arms.

Laboratory examinations

Laboratory tests in the emergency department showed hypokalemia of 1.6 mmol/L. The results of other biochemical investigations are shown in Table 1. Thyroid function tests were consistent with biochemical thyrotoxicosis (Table 1). Other hormones affecting blood potassium were all within normal ranges (Table 1).

Imaging examinations

The electrocardiogram showed sinus tachycardia with a flattened T wave (Figure 1), no electromyography information was available as the patient's muscle strength quickly returned. Thyroid ultrasound showed that the thyroid was regular shaped, internal echoes were coarse and heterogeneous, and blood supply was abundant. Left superior thyroid artery peak flow velocity was 120 cm/s, resistive index (RI): 0.56, and right superior thyroid artery peak flow velocity was 157 cm/s, RI: 0.63.

Table 1 Laboratory findings obtained of thyrotoxic periodic paralysis

Laboratory test	Patient's result	Normal value range
Hormonal data		
TSH (mIU/L)	0.013	0.35–5.1
FT4 (pmol/L)	32.6	6.44–18.02
FT3 (pmol/L)	12.8	2.76–6.45
TRAb (IU/L)	18.7	0–1.75
Renin (mIU/L)	18.63	4.67–47.59
Aldosterone (ng/dL)	12.77	3.1–35.1
Cortisol (nmol/L)	343.79	176.57–629.0
Blood biochemistry (mmol/L)		
Potassium	1.6	3.5–5.3
Calcium	2.18	2.11–2.52
Magnesium	0.64	0.75–1.02
TCO_2	21.3	23–29
Plasma glucose	10.36	3.85–6.11
Urinary biochemistry		
Potassium (U) (mosm/KgH_2O)	723	600–1000
Osmolarity (U) (mmol/L)	15.50	25–100

TSH: Thyroid-stimulating hormone; FT4: Free thyroxine; FT3: Free triiodothyronine; TRAb: TSH receptor autoantibodies; TCO_2: Total carbon dioxide.

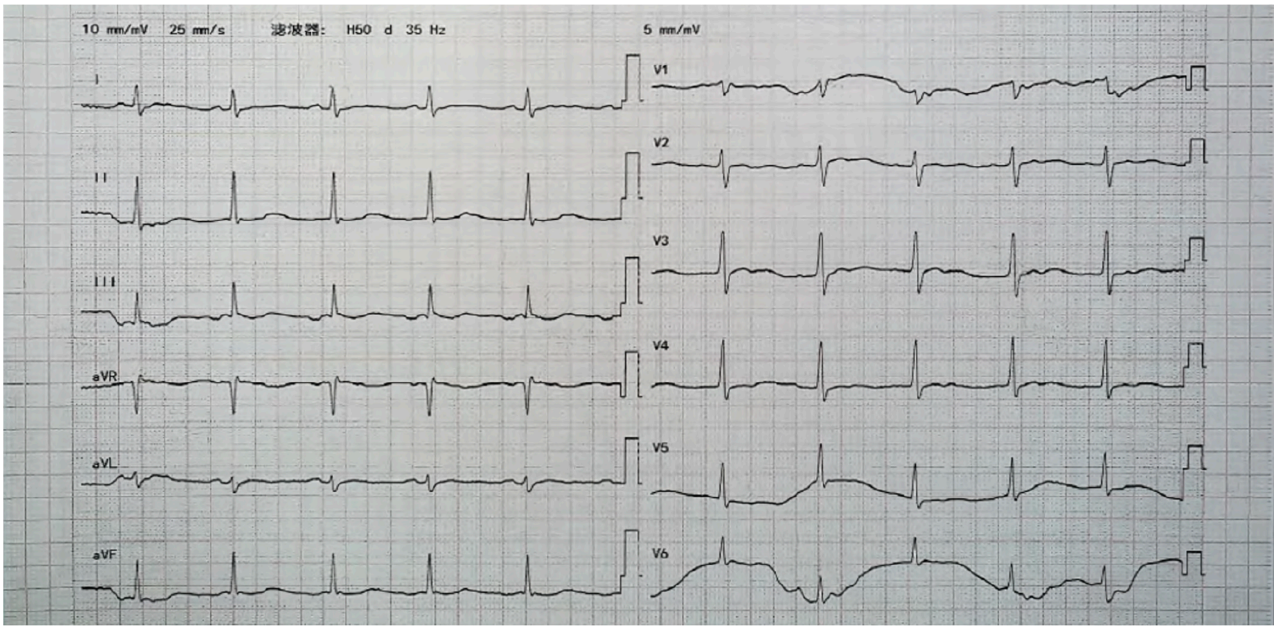

Figure 1 Electrocardiogram results.

FINAL DIAGNOSIS

TPP and Graves' disease.

TREATMENT

The paramedics immediately administered 1.5 g of intravenous potassium, followed by 4.0 g of oral potassium. The weakness in the arms and legs was progressively reduced, with full recovery of muscle strength approximately 10 hours. The patient was referred to endocrinology for further evaluation as his serum potassium level normalized to 3.8 mmol/L. The clinical presentation and laboratory findings supported the diagnosis of Graves' disease, with suboptimal control and insulin injections possibly causing TPP. We stopped his insulin and he was discharged with a potassium level of 4.0 mmol/L without potassium supplementation.

OUTCOME AND FOLLOW-UP

The patient was discharged from hospital and scheduled for radioactive iodine treatment at the Nuclear Medicine Department. The patient was cured of hyperthyroidism with no hypokalemia during the six months of follow-up and normal thyroid hormone levels were monitored. The patient is at risk of developing hypothyroidism and needs to be followed closely.

DISCUSSION

TPP is closely associated with impaired potassium metabolism; maintaining normal total body potassium levels suggests that hypokalemia is caused by translocating potassium into the intracellular space[6]. Thyroid hormones can increase skeletal muscle Na/K ATPase activity, thereby accelerating potassium space transfer. Hyperthyroidism can amplify the b2 adrenergic pump by increasing intracellular cAMP. Insulin induces cellular K+ shifts by stimulating the intrinsic activity or membrane insertion of the Na/K ATPase[7]. Studies have shown that mutations and functional defects in the skeletal muscle-specific inward rectifier potassium ion channel Kir2.6 are the cause of this disease. Deletion of Kir2.6 has been found in approximately 33% of TPP patients[8,9]. TPP is also associated with genetic mutations (*e.g.*, *KCNE3*) and certain leukocyte antigen subtypes (A2BW22, AW19B17, B5, BW 46, DRw8) that increase Na/K ATPase pump activity or alter other potassium channels in skeletal muscle cells[10]. In addition, hyperthyroid patients have calcium channel abnormalities, which can affect muscle contraction coupling, leading to muscle paralysis[7]. Young and middle-aged adult males appear to be most affected by TPP, possibly due to the stimulatory effect of testosterone on the Na/K ATPase, while estrogen reduces its activity[11]. Unfortunately, we do not have the genetic test results in this case, which we hope to obtain during subsequent follow-up.

TPP is rare. Other conditions to consider include familial hypokalemic periodic paralysis and myasthenia gravis. Familial hypokalemic periodic paralysis is familial and easy to identify. Hyperthyroidism and myasthenia gravis are autoimmune diseases that may occur together in patients with autoimmune deficiencies[12]. Hyperthyroidism is present in 3%-5% of patients with myasthenia gravis, which is 20-30 times more common in women. Patients usually present with hyperthyroidism, leading to missed diagnoses of myasthenia gravis. This is similar to myasthenia gravis in general, but milder, with ocular muscle involvement and anti-acetylcholine receptors not readily detected in serum[13].

Initial symptoms of TPP are non-specific and include cramps, pain, or stiffness. Typically, muscle involvement is most severe in the proximal lower limbs, and upper motor neuron involvement may cause respiratory paralysis[5]. Paralysis can last from minutes to days and occur from a few times a year to several times a day, often more frequently at night or when resting after exercise[5]. In some cases, severe hypokalemia can cause fatal arrhythmias, such as ventricular fibrillation. Rapid intravenous potassium replacement is necessary to reverse muscle weakness and prevent life-threatening cardiac complications. In acute hypokalemia without systemic K+ deficit, cells rapidly release potassium once the seizure resolves; aggressive treatment may cause rebound hyperkalemia, occurring in about 40%-60% of TPP[14]. Low-dose potassium supplementation is recommended in the absence of serious cardiovascular complications. Research has shown that beta-blockers can be used as an adjunct treatment, particularly in patients with hypokalemia related to high adrenal activity[15]. Potassium supplementation may relieve symptoms during episodes, but will not prevent them. The long-term goal of treating TPP is to normalize thyroid function and avoid triggering acute episodes.

Factors such as high carbohydrate intake, excessive exercise, psychological stress, infection and trauma can trigger TPP. Chronic alcohol abuse may increase a patient's tolerance to profound hypokalemia, it may cause patients, particularly those with hyperthyroidism, to develop TPP[16]. Medications such as insulin, potassium-sparing diuretics, adrenaline, digitalis and propranolol should be avoided. Recent research suggests that new coronavirus infections may potentially cause TPP[17]. People with TPP have increased insulin release on oral glucose challenge, supporting the theory that insulin plays a role in the pathogenesis of hypokalemia[9]. Insulin has been shown to stimulate Na/K ATPase activity and the insulin response sequence is located in the upstream region of the *Na/K ATPase* gene[9]. This may explain why large carbohydrate intakes or insulin injections can induce TPP. In this case, the patient's flaccid paralysis was confirmed by elevated thyroid hormone levels and severe hypokalemia, excluding other possible causes. The patient suffered acute hypokalemia after insulin injection, suggesting insulin injection may indicate TPP. Future clinical practice should pay more attention to choosing hypoglycemic agents to avoid using insulin. There is currently no consensus on treatment recommendations for hyperthyroidism in patients with TPP. Radioiodine therapy can rapidly reverse thyrotoxicosis and prevent the recurrence of TPP, but lifelong hypothyroidism is a significant side effect. Oral anti-thyroid drugs have a slow onset of action, require long treatment periods, and can result in fluctuating thyroid hormone levels. Therefore, choosing the appropriate treatment regimen for hyperthyroidism in TPP patients remains a challenging issue

and decisions should be based on patient preference.

CONCLUSION

All patients with muscle weakness, especially middle-aged men of Asian descent presenting with acute muscle weakness or paralysis and hypokalemia, should be considered for TPP. Even if there are no overt symptoms or signs of thyrotoxicosis, thyroid function tests should be carried out. Treatment includes replacing potassium and controlling hyperthyroidism. Moderate potassium replacement to prevent rebound hyperkalemia, and beta-blockers for refractory symptoms. Avoidance of known triggers and restoration of euthyroid status with appropriate treatment may reduce relapses.

FOOTNOTES

Author contributions: Wang YL contributed to data collection and editing of the manuscript and to the literature review; Li J contributed to discussion and drafting of the manuscript.

Informed consent statement: Informed consent was obtained to publish this article.

Conflict-of-interest statement: No authors should declare any conflicts of interest.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

Country of origin: China

ORCID number: Yan-Li Wang 0000-0002-6683-357X.

S-Editor: Liu H
L-Editor: A
P-Editor: Zhang XD

REFERENCES

1 **Kung AW**. Clinical review: Thyrotoxic periodic paralysis: a diagnostic challenge. *J Clin Endocrinol Metab* 2006; **91**: 2490-2495 [PMID: 16608889 DOI: 10.1210/jc.2006-0356]
2 **Ko GT**, Chow CC, Yeung VT, Chan HH, Li JK, Cockram CS. Thyrotoxic periodic paralysis in a Chinese population. *QJM* 1996; **89**: 463-468 [PMID: 8758050 DOI: 10.1093/qjmed/89.6.463]
3 **Elston MS**, Orr-Walker BJ, Dissanayake AM, Conaglen JV. Thyrotoxic, hypokalaemic periodic paralysis: Polynesians, an ethnic group at risk. *Intern Med J* 2007; **37**: 303-307 [PMID: 17504277 DOI: 10.1111/j.1445-5994.2007.01313.x]
4 **Madurga A**, Ceacero-Marín D, González-Peiro C. Thyrotoxic periodic paralysis: a case report and review of relevant pathophysiology. *Emergencias* 2024; **36**: 230-231 [PMID: 38818990 DOI: 10.55633/s3me/025.2024]
5 **Chang CC**, Cheng CJ, Sung CC, Chiueh TS, Lee CH, Chau T, Lin SH. A 10-year analysis of thyrotoxic periodic paralysis in 135 patients: focus on symptomatology and precipitants. *Eur J Endocrinol* 2013; **169**: 529-536 [PMID: 23939916 DOI: 10.1530/EJE-13-0381]
6 **Patel M**, Ladak K. Thyrotoxic Periodic Paralysis: A Case Report and Literature Review. *Clin Med Res* 2021; **19**: 148-151 [PMID: 34531272 DOI: 10.3121/cmr.2021.1610]
7 **Lin SH**, Huang CL. Mechanism of thyrotoxic periodic paralysis. *J Am Soc Nephrol* 2012; **23**: 985-988 [PMID: 22460532 DOI: 10.1681/ASN.2012010046]
8 **Ryan DP**, da Silva MR, Soong TW, Fontaine B, Donaldson MR, Kung AW, Jongjaroenprasert W, Liang MC, Khoo DH, Cheah JS, Ho SC, Bernstein HS, Maciel RM, Brown RH Jr, Ptácek LJ. Mutations in potassium channel Kir2.6 cause susceptibility to thyrotoxic hypokalemic periodic paralysis. *Cell* 2010; **140**: 88-98 [PMID: 20074522 DOI: 10.1016/j.cell.2009.12.024]
9 **Cheng C**, Lin S, Lo Y, Yang S, Hsu Y, Cannon SC, Huang C. Identification and functional characterization of Kir2.6 mutations associated with non-familial hypokalemic periodic paralysis. *J Biol Chem* 2011; **286**: 33707 [DOI: 10.1074/jbc.a111.249656]
10 **Salifu MO**, Otah K, Carroll HJ, Ifudu O, Friedman EA, Oh MS, Aytug S. Thyrotoxic hypokalaemic paralysis in a Black man. *QJM* 2001; **94**: 659-660 [PMID: 11704698 DOI: 10.1093/qjmed/94.11.659]
11 **Garla VV**, Gunturu M, Kovvuru KR, Salim SA. Thyrotoxic periodic paralysis: case report and review of the literature. *Electron Physician* 2018; **10**: 7174-7179 [PMID: 30214699 DOI: 10.19082/7174]
12 **Zhang Q**, Bi Z, Yang M, Gui M, Bu B. Differences in immunophenotypes between myasthenia gravis patients with and without thyroid antibodies. *Muscle Nerve* 2022; **65**: 553-559 [PMID: 35147983 DOI: 10.1002/mus.27517]

13 **Amin S**, Aung M, Gandhi FR, Pena Escobar JA, Gulraiz A, Malik BH. Myasthenia Gravis and its Association With Thyroid Diseases. *Cureus* 2020; **12**: e10248 [PMID: 33042687 DOI: 10.7759/cureus.10248]

14 **Mahon-Daly F**, Liegeois C, Carter JP. Thyrotoxic periodic paralysis (TPP): assessment in the emergency department. *BMJ Case Rep* 2022; **15** [PMID: 35217552 DOI: 10.1136/bcr-2021-245830]

15 **Banavathu T**, Tripathi S, Sukhadiya P, Ahari K, Meena DS, Garg MK. Thyrotoxic Periodic Paralysis with Thyroid Storm as the First Presentation of Graves' disease; a Case Report. *Arch Acad Emerg Med* 2021; **9**: e19 [PMID: 33870206 DOI: 10.22037/aaem.v9i1.1083]

16 **Lin YY**, Hsieh YS. Chronic Alcohol Abuse-Induced Hypokalemia Might Lead to Delayed Diagnosis or Misdiagnosis of Thyrotoxic Periodic Paralysis. *Cureus* 2021; **13**: e15880 [PMID: 34336407 DOI: 10.7759/cureus.15880]

17 **Lu A**, Chen CC, Lin C, Wu TJ, Lin SH. Artificial Intelligence Electrocardiography Detecting Thyrotoxic Periodic Paralysis Following a SARS-CoV-2 Infection. *Am J Med* 2024; **137**: e91-e93 [PMID: 38280555 DOI: 10.1016/j.amjmed.2024.01.018]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com