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A Rare Case of Thyrotoxic Periodic Paralysis After Epidural Steroid Injection: A Case Report and Literature Review

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
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Literature Search F
Funds Collection G

ABEF Kwame Ofori Affram
BE Tanya Luke Reddy
ABCDEF Kofi M. Osei

Department of Internal Medicine, Piedmont Athens Regional Medical Center, Athens, GA, U.S.A.

Corresponding Author: Kofi M. Osei, e-mail: kali_bonite@hotmail.com
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Patient: Male, 36
Final Diagnosis: Epidural steroid induced thyrotoxic periodic paralysis
Symptoms: Paralysis
Medication: —
Clinical Procedure: Epidural steroid injection
Specialty: Endorinology and Metabolic

Objective: Rare disease

Background: Thyrotoxic periodic paralysis (TPP) is a rare cause of acute paralysis, which if not promptly recognized and treated, can lead to significant morbidity and mortality. TPP can be precipitated by several factors, including a high carbohydrate diet and exercise. This report is of a rare case of TPP after epidural steroid injection in a young man, with a review of the literature of previous cases.

Case Report: A 36-year-old Asian man presented to the emergency department with sudden onset of paralysis of all his limbs following epidural steroid injection for traumatic low back pain. At presentation, he was found to have severe hypokalemia of 1.8 mEq/L. Further investigations led to the diagnosis of hyperthyroidism and Graves' disease. In the process of correcting his potassium, there was an unexpected rebound hyperkalemia that was successfully corrected. He had a rapid recovery and an early discharge from hospital.

Conclusions: Although several factors can lead to paralysis after an epidural steroid injection, TPP should be considered in the differential diagnosis, especially in individuals who have predisposing factors of ethnicity and gender. If patients have undiagnosed hyperthyroidism on presentation, the diagnosis of TPP can be delayed or missed. In the management of patients with TPP, care should be taken when correcting potassium levels.

MeSH Keywords: Glucocorticoids • Hyperthyroidism • Hypokalemia • Paralysis • Thyrotoxicosis

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Background

Severe hypokalemia of any cause can lead to muscle paralysis [1–3]. While treatment is aimed at correcting serum potassium, the pathophysiology of hypokalemia is critical to the therapeutic approaches required for safe and optimal correction and prevention of recurrence [4,5].

Here, we present a rare case of an acute thyrotoxic periodic paralysis (TPP) associated with severe hypokalemia in a young man after receiving an epidural steroid injection who had previously undiagnosed hyperthyroidism. A review of the literature identified one reported case of paralysis associated with hypokalemia following epidural steroid injection. To our knowledge, this is the first cases report of TPP following epidural steroid injection.

Case Report

A 36-year-old Asian man presented to the emergency department after physically collapsing at home without loss of consciousness. He recounted no previous similar episodes. Two months before this presentation, he developed low back pain following a motor vehicle accident. A chiropractor initially managed his back pain, but the pain continued. He then underwent an epidural steroid injection administered by his orthopedic surgeon, which had been performed on the morning of his physical collapse and hospital presentation.

Four hours after the epidural steroid injection, the patient noticed that his legs became weak, and he collapsed to the floor while urinating in the bathroom at his home. The weakness in the legs was more severe than that in his upper extremities, which allowed him to crawl back to his bedroom. He reported that, following his collapse, he vomited about four times. He was brought to the emergency department by family members.

On examination, the patient was drowsy. His vital signs included a blood pressure of 121/72 mmHg, a heart rate of 111 beats per minute, a respiratory rate of 21 breaths per minute, and his temperature was 36.6°C. His heart sounds were normal with no murmurs, gallops, or rubs. Neurologically, he was oriented to person, place, and time. His cranial nerves were grossly intact, and no sensory deficits were noted. His muscle tone was reduced in both upper and lower extremities, but the muscle bulk was adequate. Power was 1/5 in both lower limbs and 4/5 in his upper limbs. He had hyporeflexia of bicep, tricep, knee-jerk and ankle reflexes. He had no loss of perianal sensation on rectal examination, and sphincter tone was intact. He had diffuse thyroid enlargement without any further stigmata of thyrotoxicosis.

Table 1. Laboratory test results.

Laboratory test	Value	Reference ranges
Potassium (mEq/L)	1.8	3.5–4.5
Magnesium (mEq/L)	1.8	1.5–2.5
Sodium (mEq/L)	140	135–145
Calcium (mg/dl)	9.9	8.5–10.2
Random blood glucose (mg/dl)	176	
Free T4 (ng/dl)	3.72	0.46–1.42
T3 (ng/dl)	325	87–178
TSH (mciu/ml)	0.100	0.340–5.60
Aldosterone (ng/dl)	9.5	<16
Testosterone (ng/dl)	784	175–781
HbA1c	5.1	< 5.7%

T4 – thyroxine; T3 – triiodothyronine; TSH – thyroid stimulating hormone; HbA1c – glycated hemoglobin.

Initial investigation showed severe hypokalemia of 1.8 mEq/L, magnesium of 1.8 mEq/L, sodium of 140 mEq/L, calcium of 9.9 mg/dl, random blood glucose of 176 mg/dl, and glycated hemoglobin (HbA1c) of 5.1%. Blood urea nitrogen (BUN) and creatinine were within normal limits. Aldosterone was 9.5 ng/dl, urine potassium was 12.8 mEq/L, urine creatinine was 168.22 mg/dL (14.87 mmol/L) and the urine potassium to creatinine ratio was 7.61 mEq/g (0.81 mEq/mmol). On review of his previous medical records, it was noted that the patient had seen his primary care physician one month prior to this presentation, for erectile dysfunction. Laboratory results at that time showed a thyroid stimulating hormone (TSH) level of 0.100 mciu/ml and a testosterone level of 784 ng/dl. His potassium level at the time was 3.7 mEq/L. The patient was unaware of the test results, as he was awaiting a follow-up visit at the time of the episode of paralysis that resulted in his hospital admission. Table 1 shows his repeat blood test results, with their corresponding reference ranges.

The electrocardiogram (ECG) showed a rate of 95 bpm, regular sinus rhythm with left axis deviation, and a prolonged QRS complex of 125 ms. There was flattening of T-waves, but no U waves were noted (Figure 1). Magnetic resonance imaging (MRI) of his lumbar spine showed bulging intervertebral discs but no nerve impingement or other causes for his paraplegia.

The patient had mild dysphagia and failed a bedside swallow screen in the emergency department. Therefore, he received potassium in the form of an intravenous (IV) potassium chloride (KCL) infusion. Hypokalemia was rapidly overcorrected with the serum potassium rising from 1.8 mEq/L to 6.3 mEq/L after receiving 100 mEq of potassium. The rapid correction of

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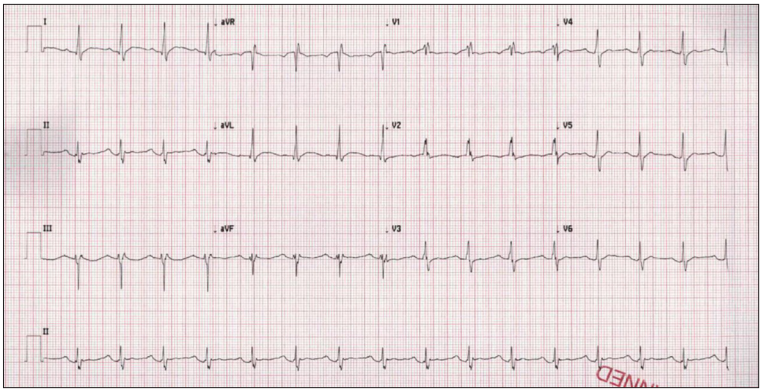

Figure 1. The electrocardiogram (ECG) on admission to hospital when the patient's potassium was 1.8 mEq/L.

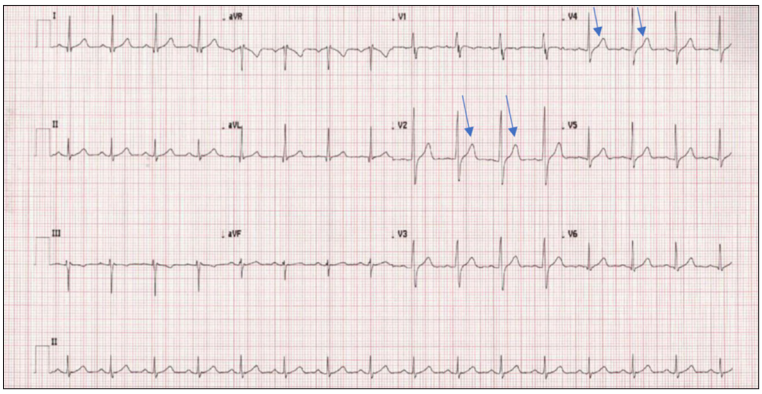

Figure 2. The electrocardiogram (ECG) when the patient was hyperkalemic with potassium of 6.3 mEq/L. The arrows show relatively pronounced T waves when compared with Figure 1

potassium was significantly out of proportion to the expected increase in potassium levels.

The patient was asymptomatic from the hyperkalemia, and the ECG showed a reduction in QRS complex duration to 105 ms, with relatively pronounced T-waves (Figure 2 compared with Figure 1). Hyperkalemia was treated with calcium gluconate and insulin. His flaccid paralysis rapidly improved within three hours of potassium correction. He was able to ambulate with assistance within six hours of treatment and was back to baseline potassium levels within nine hours of treatment.

Additional history after his recovery revealed that he had a recent history of weight loss of 30 lb in the previous six months, despite having a good appetite. However, he had no other signs suggestive of hyperthyroidism with no tremors, palpitations, or heat intolerance. There were no signs of ophthalmopathy or pretibial myxedema. He also denied any diuretic use or knowledge of a family history of paralysis. Further investigation of his thyroid function showed elevated levels of antibodies to thyroglobulin, a thyroid peroxidase antibody, and an anti-TSH receptor antibody. Ultrasonography confirmed a diffusely enlarged thyroid gland. He was discharged from hospital with a diagnosis of thyrotoxic periodic paralysis (TPP) secondary to Graves' disease and treated with propranolol. He was referred to endocrinology for outpatient management of his hyperthyroidism.

Discussion

Thyrotoxic periodic paralysis (TPP) is a rare cause of acute paralysis, which is reported to be more common in Asian males [4,6]. Although the incidence of TPP in the United States is unknown, published reviews and case report indicate that the incidence may be on the rise due to changing demographics [4,6]. TPP has several triggers, including high carbohydrate diets, exercise, and steroid treatment. While several instances of steroid-triggered TPP have been reported (Table 2), epidural steroid injection represents a rare association with TPP, with no previously published case report found on review of the literature. However, there has been one reported case of hypokalemic paralysis following epidural steroid injection, but this was not associated with thyrotoxicosis, and there have been other reports of paralysis following epidural steroid injection, including trauma and hemorrhage [7,8]. It is likely that the paralysis from TPP is mediated by sudden and transient hypokalemia.

Pathophysiologically, hypokalemia can occur as a result of reduced potassium intake, or increased loss via the gastrointestinal tract, sweat, and renal routes. Shifts of potassium into the intracellular compartment can also cause hypokalemia. Factors that enhance intracellular potassium shift include alkalosis, hyperthyroidism, beta-adrenergic activity [9], elevated levels of testosterone and insulin [10]. These factors increase the expression or activity of sodium potassium ATPase on cell membranes [11].

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Table 2. Steroid doses from similar cases.

Authors	Trigger	Dose	Route
Tahmasbi et al., 2017 [17]	Dexamethasone	10 mg	Epidural
Wongraoprasert et al., 2007 [18]	Methylprednisone	1 g	IV
Büyükcam et al., 2011 [19]	Methylprednisone	80 mg	IV
Genek, 2016 [20]	Dexamethasone	8 mg	IV
Soriano et al., 2017 [21]	Methylprednisolone	Not provided	Tendon
Tigas et al., 2011 [22]	Methylprednisolone	1 g	IV

IV – intravenous.

To better understand the mechanism of hypokalemia, 24-hour urine potassium or the urine potassium to creatinine ration (K/Cr) can be used to determine the route of potassium loss [12,13]. High 24-hour urine potassium is an indication of renal loss, which could be due to loop diuretic or thiazide diuretic use, or hereditary renal channelopathies, such as Bartter syndrome, Gitelman syndrome, and Liddle syndrome [1], hyperaldosteronism or renal tubular acidosis [3]. Due to difficulties in assessing 24-hour urine potassium, the use of the urine potassium to creatinine (urine K/Cr) ratio is a reasonable alternative to 24-hour urine correction. A urine K/Cr ratio of less than 13 mEq/g (1.5 mEq/mmol) in the setting of hypokalemia is indicative of potassium loss from the gut, or transcellular shift [5,13]. The patient in this report had a low urine K/Cr ratio of 7.61 mEq/g (0.81 mEq/mmol), which ruled out renal loss as a possible etiology. The patient reported vomiting that occurred after developing flaccid paralysis, which was likely to be a symptom rather than a cause of his hypokalemic state.

Hypokalemic paralysis in the patient presented in this report could be explained by systemic effects of steroids from the epidural steroid injection he received. Systemic effects of steroids after epidural steroid injections are not uncommon and can have significant effects on metabolism [14–16]. Although rare, hypokalemia with paralysis has been reported after epidural steroid injection [17]. Recently, Tahmasbi Sohi et al. reported a case of a 30-year-old man who developed hypokalemia, hyperglycemia with quadriplegia 4 hours after intrathecal steroid injection [17]. This case was similar to ours regarding gender, the latency of symptom development, and patient management [17]. What distinguishes the case presented in this report from the case reported by Tahmasbi Sohi et al. is the absence of thyrotoxicosis, with the hypokalemia in their case solely attributed to the direct effects of the steroids and hyperglycemia [17]. In the case reported by Tahmasbi Sohi et al., epidural steroid injection was performed with dexamethasone [17]. Unfortunately, the procedure in the case reported here was done at another hospital, and we were unable to acquire external records of the details of the nature of the steroid used and the dose administered.

There are several mechanisms by which steroids by themselves can induce hypokalemia. First, steroids can directly induce the expression of Na/K ATPase to facilitate intracellular potassium shifts [23]. Steroids can also facilitate intracellular potassium shift indirectly by inducing hyperglycemia that induces insulin release [24]. Transient hyperinsulinemia and hyperglycemia then lead to activation of Na/K ATPase, which drives potassium into the cells [25]. Evidence for such a mechanism in this case report was indicated by a high blood glucose level with a normal HbA1c. A previous blood sugar level in the patient's records was within normal range. The third possible mechanism is a mineralocorticoid effect of the injected steroid leading to hypokalemia via increased urinary excretion [26]. However, the K/Cr ratio of the patient was low, making this possibility unlikely. Hyperaldosteronism with hypokalemic paralysis via renal salt wasting has previously been reported in a patient with hyperthyroidism, emphasizing the need to rule out secondary causes [27]. Hyperaldosteronism as an underlying factor in this case presentation was ruled out by a normal serum aldosterone level and the absence of hypertension.

Other potential causes of paralysis in this patient could have included conus medullaris syndrome from infarction [28], or an epidural hematoma, all of which have been reported as causes of paralysis after epidural steroid injection [7,8]. However, in this patient, these diagnoses were unlikely given the time course of his symptoms and the resolution of paralysis after potassium replacement.

The patient's laboratory investigations were diagnostic of Graves' disease. Hyperthyroidism can cause hypokalemia by activating Na/K ATPases and thus driving potassium intracellularly [29]. However, triggers are usually required to induce the extent of hypokalemia required for TPP [30,31]. Many triggers for TPP have been identified, with the most common being high carbohydrate diet, alcohol, and exercise [30,31]. Steroids are a relatively rarely reported trigger for TPP, and when they are involved, they are usually administered intravenously with the most common steroid being methylprednisone (Table 2).

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No previous case of epidural steroid injection associated with TPP has been reported. Hypertestosteronemia also creates an environment for the development of TPP as it increases muscle bulk and can induce the expression of Na/K ATPase in muscles, thereby explaining the increased incidence of TPP in men, although women have a higher incidence of Graves' disease [29,31]. The patient in this report had some risk factors for the development of TPP, including hyperglycemia, hypertestosteronemia, steroid injection, and being a young adult male of Asian origin. Hyperglycemia can drive insulin release which drives potassium into cells [29,31]. The likely trigger of his TPP was the epidural steroid injection with its systemic effects facilitated by an environment of hypertestosteronemia.

Overcorrection of potassium is not an uncommon problem during the management of TPP. This patient had an initial overcorrection of his potassium, which supports that caution is needed during potassium correction in TPP.

The management of this case illustrates an essential clinical learning point. The patient had rebound hyperkalemia despite receiving just 100 mEq of potassium chloride. To normalize his overcorrected potassium level, he was given insulin and glucose. It is therefore important to ascertain the mechanism of hypokalemia during patient management, as this determines the strategy for correction. Rapid overcorrection of serum potassium levels should prompt consideration of an intracellular shift as a potential mechanism for hypokalemia. The rebound hyperkalemia observed in the patient was likely to have been due to a transient reversal of sodium-potassium ATPase stimulation. Conversely, refractory hypokalemia or paradoxical worsening of hypokalemia, despite adequate correction of potassium, also supports total body potassium depletion or ongoing sodium-potassium ATPase mediated intracellular shifts. Iatrogenic overcorrection of potassium in hypokalemic periodic paralysis has been reported [13].

Conclusions

Epidural steroid injection is a rare precipitant of thyrotoxic periodic paralysis (TPP) in genetically predisposed individuals who have subclinical hyperthyroidism but should be considered in patients who develop paralysis after this procedure. When correcting hypokalemia related to TPP, rebound hyperkalemia is a potential complication that should be anticipated.

Department and Institution where work was done

Department of Internal Medicine, Piedmont Athens Regional Medical Center, Athens, GA, U.S.A.

Conflict of interest

None.

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