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Case Report

Internal Medicine Section

Normokalemic Thyrotoxic Periodic Paralysis with Preserved Reflexes- A Unique Case Report

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ABSTRACT

Although serum potassium levels are usually subnormal in Thyrotoxic Periodic Paralysis (TPP), but in exceptionally rare circumstances, it may be normal leading to the entity called normokalemic TPP. The diagnosis of normokalemic TPP is more often overlooked and/or delayed due to lack of awareness among the physicians and associated mild symptoms of hyperthyroidism. Here, the author describes the case of a 27-year-old male with newly diagnosed but untreated Grave's disease and TPP who was normokalemic during the acute phase of paralysis. Hypokalemia was documented only after resolution of paralytic attacks during subsequent days of admission. The importance of the case report is to highlight upon the fact that TPP should always be considered in an "previously asymptomatic" young Asian individual with acute paralysis with or without hypokalemia , and thyroid function and serial potassium values should be evaluated for diagnosing the usual hypokalemic type or the more rarer variant normokalemic TPP. This case report also deserves mention as the patient of TPP had a notable feature of having preserved reflexes in the face of hypokalemia.

Keywords: Hypokalemia, Paresthesia, Thyrotoxicosis

CASE REPORT

A 27-year-old non-smoker and non-alcoholic male was rushed to the emergency with acute onset and rapidly progressive bilaterally symmetrical lower limb muscle weakness followed by upper limb weakness which started 8 hours ago after waking up from sleep in the morning. He denied any pain or paresthesia. No prior history of fever or upper respiratory tract infection or spinal trauma or vaccination was documented. He had no difficulty in urination and he had clear sensorium without any seizures. No similar history of weakness was present in the other family members. He gave history that he had suffered repeated attacks of severe muscle weakness or limb paralysis for last three years prior to admission which required admission, and that each paralytic attack lasted from 16 h to 24 h, and resulted in complete inability to walk and stand without assistance. He had noticed that his paralytic attacks usually had their onset after meals and postexercise rest and resolved spontaneously without any medication after 2-3 d. He had no significant personal history and he was not taking any medications. There was no history of similar disorders or other endocrine or neurologic diseases in his family. He was recently diagnosed as having Grave's disease, three months ago and was advised oral Methimazole and propranolol but he did not begin intake of drugs. Classic complaints of hyperthyroidism namely palpitation, heat intolerance, diaphoresis, irritability, distal tremor were also provided by the patient.

On general examination, vitals were normal; resting tachycardia (112/min) diffuse thyromegaly without any nodules, thyroid eye signs were noted. On neurological examination, symmetrical flaccid weakness in both upper and lower extremities (lower> upper and proximal > distal; power 1/5 in all 4 limbs) was found. Deep tendon reflexes were normal in all limbs. Tests of sensorium, meningeal irritation, sensory examination and cranial nerves revealed no abnormality. Cardiovascular examination showed evidence of hyperdynamic circulation. Rest of the systemic examination was unremarkable.

Laboratory tests revealed normal complete blood counts as well as normal renal and liver function tests (including albumin), blood sugar and muscle enzyme levels (creatine kinase). Serum electrolytes including sodium, chloride, calcium, magnesium were also normal [Table/Fig-1]. Serum hypophosphatemia was also not noted.

Serial potassium concentrations at the time of admission was 4.2 mEq/L(normal 3.5-5 mEq/L). It progressively diminished over the next few hours and days as shown in [Table/Fig-2]. However, progressive drop in potassium was not associated with significant increase in weakness or disappearance of reflexes. Thyroid profile [Table/Fig-3] showed frank hyperthyroidism.

Thyroid radioiodine uptake scan revealed a diffuse homogeneous uptake.Urine sodium and potassium, and serum aldosterone and renin levels were measured to rule out adrenal involvement and were found to be normal. ECG revealed no abnormality on admission and Electro Myography–Nerve Conduction Study findings were unremarkable. MRI spine was normal.

A diagnosis of normokalemic TPP paralysis associated with Graves' thyrotoxicosis was made based on clinical and laboratory findings. Treatment with propranolol and methimazole was initiated and was counselled for thyroidectomy (to be performed after adequate control of hyperthyroid state). He was administered low-dose oral potassium chloride (KCl) tablets during the hypokalemic phase and advised a low carbohydrate diet and a caution to avoid heavy or strenuous exercise, to be followed life-long. He responded to this treatment and following the nadir on the 4th day of admission when its serum level dropped to 1.9 mEq/L, the serum potassium began to normalise. At six months of follow-up the patient was found to be clinically euthyroid and free from any further attacks of weakness.

DISCUSSION

TPP is a rare but life threatening condition characterized by acute paralytic attacks and hypokalemia in association with thyrotoxicosis. This uncommon medical condition mainly involves young Asian

Serum electrolytes and enzymes	Values
Sodium	138 mEq/L (N:135-145)
Chloride	100 mEq/L (N:96-106)
Calcium	5.1 mg/dL (N:4.4-5.3)
Magnesium	1.9 mg/dL (N:1.7-2.4)
Phosphate	3.1 mg/dL (N:2.4-4.1)
Creatine kinase	55 mcg/L (N:10-120)

[Table/Fig-1]: Showing different serum electrolyte values

Timing of measurement	Serum Potassium value
At admission	4.2 meq/L
18 hours after admission	3.6 mEq/L
36 hours after admission	2.8 mEq/L
4th day of admission	1.9 mEq/L

[Table/Fig-2]: Showing progressive drop in serum potassium following admission

Serum total thyroxine (T4)	19.6ng/dL(N: 5.13-14.1 ng/dL)
Serum free T4	3.97 ng/dL(N: 0.5–1.6 ng/dL)
Serum T3	2.5 ng/mL(N: 0.7–2.1 ng/mL)
Serum TSH	0.1 mIU/L(N:0.14–4.1mIU/L)
Serum Anti TPO Ab	754.7 IU/mL(N <50 IU/mL).

[Table/Fig-3]: Showing biochemical features of hyperthyroidism

males in their 3rd decade of life [1]. The index patient was a 27-year-old Indian male. Also, Patil et al., reported a case of TPP in a 33-year-old Indian male [2]. Patients developing normokalemic variants of TPP also tend to be young males [3].

Genetic association of TPP with HLA-DRw8 gene in Japanese patients and A2BW22, AW19B17 genes in Chinese patients have been noted [4]. Studies by Ryan et al., have also led to the discovery of mutations of an inwardly rectifying potassium (Kir) channel Kir 2.6 which is present in skeletal muscle and transcriptionally regulated by thyroid hormone and considered important in pathogenesis of TPP [5].

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 state, and hyperinsulinemia are some postulatory mechanisms to explain the disorder [4,6]. All these processes lead to potassium shift into the intracellular compartment causing hypokalemia, and precipitating the attacks but without changing the total body potassium level.

Deep tendon reflexes are decreased or absent in most patients but cases having normal jerks during acute paralytic attacks are documented as in the index case. Attacks of paralysis tend to occur during the night, as in the index patient, and may occur after stress, alcohol intake [7].

Our initial provisional diagnosis was THP and the differential diagnoses to be ruled out were Guillain-Barre syndrome (GBS), acute myelopathy, attack of any Familial Periodic Paralysis or channelopathy other than THP acute hypomagnesemia or hypophosphatemia, rhabdomyolysis. Normal sensory examination and sparing of bladder-bowel habits with normal MRI spine ruled out acute myelopathy. Demonstration of definite hypokalemia during the disease course with normal NCS excluded GBS. Normal electrolyte levels including Na+, Ca++, Mg++, phosphate and creatine kinase showed absence of the possibility of other channelopathy, hypomagnesemia, hypophosphatemia and rhabdomyolysis respectively as causes of the weakness.Another important differential diagnosis for TPP includes familial hypokalemic periodic paralysis (FHPP). Although both disorders are similar in their clinical presentation, TPP is rarely associated with a positive family history and has a later onset of presentation than FHPP. In the index case, there was no positive family history and attacks of weakness started from the age of 24 y and not from childhood thereby ruling out FHPP.

Although serum potassium levels classically decrease in most cases, it is not universal. Isolated cases of TPP are found to have normal or even increased potassium levels even in the acute paralytic phase [3,8,9]. Hypokalemia usually sets in after certain interval usually without further increase in weakness as seen this case. So, initial normokalemia during paralytic attacks dose not exclude the diagnosis of TPP. The index patient showed progressive decrease in serum K+ for 3 days and was reversed only after institution of potassium correction.

Normokalemic TPP is usually confused with other neurologic diseases such as Guillain-Barré syndrome (GBS), multiple sclerosis or even psychiatric ailments like hysteria, malingering, etc. Valizadeh et al., reported a case of normokalemic TPP in a 32-year-old Iranian male who was initially misdiagnosed as having somatization disorder [9]. Wu et al., reported normokalemic TPP in 2 young males who were initially treated as GBS and hysterical paralysis [3]. TPP should be kept in mind as a cause of acute muscle weakness to avoid missing a treatable and curable condition as unfamiliarity with the syndrome can result in a fatal outcome. Satam et al., reported a case of fatal normokalemic TPP in a 10-year-old girl [8]. It is especially dangerous in undiagnosed hyperthyroidism with mild features of thyrotoxicosis in which TPP is usually not considered as a diagnostic possibility causing undue delay in management and leading to respiratory failure, dysrhythmia, and death.

CONCLUSION

A diagnosis of TPP must be entertained in the setting of periodic paralytic attacks in a patient of hyperthyroidism with decreased or normal or even raised potassium levels. Serial monitoring of potassium is indicated to diagnose this normokalemic variant of TPP.

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