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Review Article

Thyrotoxic periodic paralysis: a short clinical review

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ABSTRACT

Thyrotoxic Periodic Paralysis (TPP) is a potentially lethal manifestation of hyperthyroidism which is characterized by hypokalemia and muscular weakness. It mainly affects Asian men in the age group of 20 to 40 years. Immediate supplementation with oral or intravenous potassium will help to not only abort the acute attack of paralysis but will also prevent serious and life threatening cardiac arrhythmias. Non selective beta blockers like propranolol can also be used to ameliorate and prevent subsequent paralytic attack. Acetazolamide has no role in the treatment of TPP.

Keywords: Thyrotoxic periodic paralysis (TPP), Hypokalemia, Potassium, Propranolol

INTRODUCTION

Thyrotoxic Periodic Paralysis (TPP) is a rare but potentially lethal manifestation of hyperthyroidism which is characterized by muscular weakness due to intracellular shift of potassium and subsequent hypokalemia. This condition mainly affects Asian men despite the fact that the incidence of hyperthyroidism is much higher in females. TPP resolves once the patient becomes euthyroid, so definitive treatment of hyperthyroidism in form of radioactive iodine or thyroidectomy should be offered to these patients. Treatment with oral or intravenous potassium will help to abort an acute attack of paralysis. Non selective beta blockers like propanolol can also be used an alternative treatment to ameliorate the paralysis without the fear of developing rebound hyperkalemia.

EPIDEMIOLOGY

Thyrotoxic Periodic Paralysis (TPP) mainly affects male patients of Asian origin in the age group of 20-40 years. TPP is seen in Asian countries like China, Japan, Vietnam, Philippines.

Although the condition is rare in Caucasians but in the present time immigration of population between continents has led to an emergence of TPP as presenting feature of Hyperthyroidism in western countries as well.

The overall incidence of TPP in Chinese and Japanese thyrotoxic patients is 1.8 and 1.9% respectively.[1] However if you look at the incidence rates of TPP in North America, it is around 0.1-0.2% in thyrotoxic patients.[2] TPP is more common in males as compared to females. The male to female ratio ranges from 17:1 to 70:1. Okinaka et al. conducted a study in Japan in 1957 and found that the incidence of TPP was 8.67% among males and 0.4% among female thyrotoxic patients.[1]

CLINICAL FEATURES

Thyrotoxic Periodic Paralysis (TPP) usually affects young Asian males in the age group of 20-40 years. Some authors have reported TPP in a young boy of 14 years.[3] A

typical TPP attack is characterized by transient episode of muscular weakness usually involving the lower limbs.[4]

The muscular weakness may range from mild weakness to complete flaccid paralysis. Sensory functions, bowel and bladder are not affected.

Attacks of TPP are usually precipitated by events which lead to increased release of Insulin. Excess insulin causes influx of potassium into the cells and thereby causing hypokalemia.

High carbohydrate load is by far the most common precipitating factor for an attack of TPP in Indian population, high salt intake, trauma, strenuous exercise, exposure to cold and alcohol intake are some of other precipitating factors. Some drugs like diuretics, estrogens and laxatives may also precipitate the attack.

A seasonal variation is observed with more frequent attacks occurring in summer months especially in tropical and subtropical climate regions. The seasonal variation may be due to increased outdoor activity and consumption of sweet drinks like sugarcane juice in summers.

Neurological examination done at the time of attack usually demonstrates muscular weakness (Proximal more than distal). Decreased muscle tone is most common clinical finding. Deep tendon reflexes are markedly diminished.[5] Sometimes areflexia may also be present.

Some patients do present with quadreparesis and when this happens, other differential diagnosis like Gullain Barre's syndrome, transverse myelitis and spinal cord compression need to be ruled out. Some patients experience recurrent episodes of weakness in between the episodes, patient usually has complete recovery.[6]

PATHOGENESIS

Hypokalemia is the hallmark of TPP. It occurs due to the shift of Potassium into the cells from the extracellular space. The rapid influx of Potassium is due to increased activity of sodium-potassium adenosine triphosphate pump (Na/K-ATPase).[7]

High circulating levels of thyroid hormones in hyperthyroidism increases Na/K-ATPase activity leading to hypokalemia and subsequent periodic paralysis. Hyperthyroidism is also associated with increased adrenergic response, which in turn increases Na/K-ATPase activity.[8] This also explains the fact that treating patients with non-selective beta-blockers can prevent paralytic attacks in patients with TPP.

Androgens have reported to increase the activity and expression of Na/K-ATPase.[9] This may perhaps explain the high propensity of this condition in males as compared to females.

DIAGNOSIS OF TPP

Biochemical parameters in TPP

Serum electrolytes

Hypokalemia is the hallmark of TPP. This hypokalemia is due to rapid shift of Potassium into the cells from the extracellular space.[10] Hypokalemia is not necessarily due to net loss potassium from the body. Sometime hypokalemia may be profound with serum potassium levels <3.0 meq/L. Severe hypokalemia may be associated with life threatening ventricular arrhythmias.

Hypokalemia in TPP may also be associated with hypophosphatemia and hypomagnesemia. Both hypophosphatemia and hypomagnesemia are due to intracellular shift.

TPP is also associated with increase in serum creatinine phosphokinase. The creatinine phosphokinase is of muscle origin.

ECG finding which are typical of hypokalemia includes increased amplitude of P waves, widening of QRS complexes, prolong PR interval and appearance of U waves.

Electro-diagnostic studies in TPP

Electro myogram (EMG) performed during weakness at the time of acute attack reveals typical myopathic pattern.[11] The amplitude of compound muscle action potential is markedly reduced. Nerve conduction studies are normal.

TREATMENT

The treatment of TPP has two main objectives

(i) Immediate correction of hypokalemia.

(ii) Definitive treatment of hyperthyroidism to prevent further attacks.

Immediate correction of hypokalemia

As patients with TPP have marked hypokalemia, immediate potassium replacement is warranted to prevent the life threatening arrhythmias. Depending on the general condition of the patient potassium supplementation is given either orally or intravenously. Immediate potassium supplementation is absolutely essential to prevent cardiopulmonary complications. Potassium chloride can be given intravenously or orally or both.[12] The dose may vary between 50 and 200 mmol. The only caution with overzealous and excessive potassium replacement is the fear of developing rebound hyperkalemia. Potassium supplementation should be done at a slow rate.

Potassium supplementation has no role in prevention of further paralytic attacks and therefore should not be prescribed to patients in between attacks.

Non selective beta blockers like propranolol can be given at the time of acute attacks and also to prevent recurrence[13]. Propranolol can be given both orally and intravenously. Propranolol acts by decreasing the activity of Na/K-ATPase. It can be given in a dose of 20 -80 mg every eight hourly. Acetazolamide, which has been reported to decrease the frequency of paralytic attacks in FHPP, should never be given to patients with TPP as it may actually worsen the attack.

Prevention of recurrent attacks

Avoidance of precipitating factors and achievements of euthyroidism are of utmost important for prevention of further attacks. Patients should avoid intake of heavy carbohydrate meals, alcohol, high salt content in diet and strenuous exercise until the hyperthyroid state is adequately controlled[14]. Apart from these dietary and life style precautions some medications like acetazolamide, diuretics, estrogen, laxatives and liquorice can also precipitate an acute attack and should be avoided.

Since TPP does not occur once the patient has achieved euthyroid status, so adequate and definitive control of hyperthyroidism is the mainstay of treatment to prevent subsequent attacks.[15] The patients who suffer from Graves' disease, toxic multi nodular goiter or toxic adenomas should be treated with radioactive iodine or thyroidectomy .The aim of treatment in such patients is to render them euthyroid.

Table 1: Precipitating factors for TPP.

Serial No.	Triggers of periodic paralysis
1.	High carbohydrate diet
2.	High salt intake
3.	Stress: -Infection -Surgery/emotional stress
4.	Hypothermia/cold
5.	Undue exertion
6.	Drugs: -Diuretics -Acetazolamide -Estrogens -Corticosteroids

CONCLUSION

TPP is a potentially lethal complication of hyperthyroidism occurring in Asian men in the age group of 20-40 years. With lot of population migration, cases of TPP are rising in western countries as well. Early diagnosis and treatment will prevent serious and hazardous cardiac complications. At the time of acute attacks treatment should be initiated with low dose of potassium supplements. Non selective beta blockers like propranolol can also be given. Levels of serum potassium should be frequently monitored to prevent rebound hyperkalemia. Patients with TPP should be treated with definitive therapy like radioactive iodine or thyroidectomy and all efforts should be aimed at achieving of euthyroid state as early as possible.

Learning points

- TPP is a potentially lethal manifestation of hyperthyroidism encountered in Asian men in the age group of 20 to 40 years.
- Treatment with low dose potassium and non-selective beta blockers should be initiated immediately on diagnosis.
- Serum potassium levels should be measured frequently to prevent the occurrence of re-bound hyperkalemia.
- The underlying cause of hyperthyroidism should be treated with anti-thyroid drugs, radioactive iodine or thyroidectomy, if indicated.

Abbreviations

TPP: Thyrotoxic periodic paralysis

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