

THYROTOXIC PERIODIC PARALYSIS - A CASE REPORT

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Abstract: A 25 year old male patient having developed weakness of all the four limbs with signs/symptoms suggestive of hyperthyroidism and biochemical evidence of hypokalemia is being reported here for its rarity.

INTRODUCTION

Thyrotoxic periodic paralysis (TPP) is a thyroid related disorder that is manifested as recurrent episodes of hypokalemia and muscle weakness (hypokalemic periodic paralysis) lasting from hours to days. It is most commonly described among Asian men and is a well known complication of thyrotoxicosis. Proximal muscles are affected more severely than the distal muscles. Sensory function is preserved. Bladder symptoms are absent. In majority of patients, deep tendon reflexes are markedly diminished or absent although some patients may show evidence of normal or brisk jerks, even during paralysis[3]. TPP is identical to familial periodic paralysis (FPP), except for the fact that hyperthyroidism is an absolute requirement for the expression of the disease. Weakness rarely progresses to involve the muscles above the neck, thus sparing bulbar and respiratory musculature. Majority of patients have subtle or no symptoms of hyperthyroidism. Treatment consists of emergent correction of hypokalemia and management of thyrotoxic state.

CASE REPORT

A 25 year old non smoker, non diabetic, non-alcoholic male patient presented with signs and symptoms of thyrotoxicosis in the form of increased sweating, palpitation and fever. He gave history of weakness of four limbs 3 days ago with history of shooting pain in the legs while walking. No history of either respiratory, urinary problem, sensory loss in any limb, backache, involuntary movements, pain abdomen and drug intake, trauma or heavy exercise was available. His past history did not reveal similar episodes of pain, discomfort and weakness in all the four limbs. There was no history of similar illness in the family. On physical examination, he was conscious afebrile, anxious looking, had obvious exophthalmos bilaterally. Pulse was 94/min, regular and of good volume. BP was 150/70 mmHg in the right arm in the supine position. Respiratory rate was 22/min. Examination of respiratory and cardiovascular systems was normal. On neurological examination, higher mental functions and cranial nerves were normal. He had fine tremors of both hands, proximal weakness in both arms and legs associated with diminished deep tendon reflexes bilaterally. Power was grade 1/5 at both hip joints bilaterally and grade 1/5 at knee and ankle joints. Power at all joints in both upper limbs was 0/5. Tone was decreased in all four limbs. Sensory system and cerebellar functions were normal. Examination of neck revealed diffuse goitre with systolic bruit over it. His laboratory profile included Hb 9.6 g%; TLC 8100/mm³; DLC P83,

L17 B0, M0, E0; B.urea 26 mg%; Blood sugar 92 mg%; S.Na 126 mEq/L; S.K 2.0 mEq/L; S.Calcium 10.6 mg%; S.Phosphate 3.5 mg%; S.Magnesium 2.8 mmol/L and urine examination NAD. Thyroid profile revealed T3 246 mg/dl (normal 70-190); T4 18.1 mg/dl (normal 5-12); TSH 0.01 u IU/ml (normal 0.4-5). Arterial blood gases analysis showed no abnormality. X-ray chest was normal. Ultrasonography of thyroid revealed altered echotexture with increased blood flow. ECG showed prolonged QT interval. In view of unequivocal evidence of thyrotoxicosis, muscular weakness and documented hypokalemia, a diagnosis of hypokalemic thyrotoxic periodic paralysis (HTPP) was made. The patient was put on I.V potassium chloride (Kcl) and within few hours, he improved dramatically. He started moving all the four limbs the next day. Power improved to 5/5 in all four limbs and reflexes returned to normal. He was also given tablet propranolol 3 mg/Kg body weight and was advised for follow up. At 3 months period, he was found satisfactorily performing all routine activities of daily life.

DISCUSSION

TPP is most commonly described among Asian men in the age group of 20-40 years. However, recently it has been reported among white people, Native American Indians, black people and Aborigines. In Orientals, it occurs 75 times more frequently in males than females¹. This is despite the fact that there is much higher incidence of thyrotoxicosis in women. Patients usually present with clinical features of thyrotoxicosis and the attack is characterised by sudden recurrent transient episodes of muscle weakness that range from mild weakness to complete flaccid paralysis⁵. Proximal muscles are affected more severely than distal muscles. The paralytic attacks have a well marked seasonal variation usually occurring during the warmer months of May to October but less during the colder months of December to March¹. This is due to the fact that sweating is greatly increased during summer and the resulting hypokalemia may be responsible. In summer, the resulting thirst is commonly quenched by cold drinks with high sugar content, which may also precipitate attacks. Various precipitating factors include trauma, infection, emotional upset, menstruation, epinephrine, thyroid hormone, steroid, exercise, carbohydrate intake, alcohol and unaccustomed exercise. In majority of the patients deep tendon reflexes are markedly diminished or absent although some may show evidence of brisk or normal jerks even during paralysis³. The weakness also follows a diurnal pattern often occurring at night when the person is resting or during the resting period after exercise but does not occur during

exercise⁶. Sensory function is normal. In majority of the patients, deep tendon reflexes are markedly diminished or absent, although some may show evidence of brisk or normal jerks even during paralysis³. In TPP, hypokalemia is the underlying biochemical disturbance which provokes paralysis². Hypokalemia occurs due to a massive shift of potassium into the cells rather than a net loss from the body. In addition to hypokalemia, hypophosphatemia and hypomagnesemia have been reported. Rebound hyperkalemia after therapy may occur in about 40% of patients⁷. Electromyography during a paralytic attack, reveals myopathic changes in the form of decrease in the duration of compound muscle action potential, increase in polyphasic potentials, and reduced amplitude of evoked muscle action potential on nerve stimulation. Peripheral nerve function is normal⁸. The pathophysiology of TPP remains unclear. Hypokalemia occurs due to rapid and massive shift of potassium from the extracellular into the intracellular compartment mainly into the muscles. This is probably due to increased Na/K-ATPase pump activity in patients of TPP⁹. Development of paralysis is partly influenced by the hyperadrenergic state characteristic of thyrotoxicosis thereby, further increasing Na/K-ATPase activity. Exercise releases potassium from the skeletal muscles whereas rest promotes influx of potassium. This explains why paralytic attacks occur only during recovery from exercise and resumption of exercise can abort an attack⁴. Regarding role of genetics in the development of TPP there is association with HLA-DRW8 gene as revealed in Japanese men¹⁰. Treatment consists of emergent correction with I.V KCl and management of thyrotoxic state alongwith ECG monitoring. Oral propranolol in doses of 3 mg/Kg is given to reverse paralysis, hypokalemia and hypophosphatemia¹¹. Genetic counselling and

prenatal testing may be helpful in few patients of TPP because it may be inherited in autosomal dominant manner.

CONCLUSION

Early diagnosis and prompt treatment are important. Clinically TPP mimics many common diseases which must be excluded. It is a curable disorder that resolves when an euthyroid state is achieved.

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DRUG PROFILE

Aliskiren

Pharmacology: Aliskiren 2(S),4(S),5(S),7(S)-N (2-carbamoyl-2- methylpropyl)-5-amino-hydroxy- 2-7-diisopropyl-8(4-methoxy-3-13-methoxypropyl) octanamide, is the first in a new class of orally active non peptide, , molecular weight (551.8 g/mol) rennin inhibitor. The active with four chiral carbons, but exists as a single diastereoisomer. It is a highly affinity and specificity for human renin. It binds to the S1/S3 conversion of angiotensinogen to Ang I. Aliskiren, is first DRI with bioavailability of 2.5% and has shown to be generally well tolerated when given as single or multiple dose. **Pharmacokinetics:** The plasma concentration of aliskiren increased in a dose dependent manner, following oral administration in healthy volunteers, with peak concentration reached after 3-6 hours. Oral bioavailability of aliskiren was about 5% (for 95% it is excreted unchanged in faeces) and plasma steady state level were reached after 5-8 days of treatment. An average plasma half- life of 23.7 hours (range 20-45 hours) makes drugs suitable for once daily administration. Aliskiren is not metabolized by cytochrome P450 system and interact with warfarin, and a number of other compound. Drug showed no clinically, valsartan. HCTZ and ramipril, in healthy volunteers. **Mechanism of Action:** Elevated PRA has been identified independent predictor of morbidity and mortality (p=0.0025) in a large scale trial of 4300 patients with congestive heart failure. Aliskiren inhibits the rennin by directly targeting the renin enzyme, at the point of activation and blocking the conversion of angiotensinogen to Ang I and decreasing levels of Ang I and II. Aliskiren decreases PRA by approximately 50-08% and provides similar reduction when administered in combination with drugs know to increase PRA such as the ACE inhibitor ramipril, the ARB valsartan or the diuretic HCTZ. **Efficiency & indication:** Aliskiren decrease PRA, Ang I and Ang II levels in normotensive volunteers in a dose dependent manner, decrease in plasma and urine aldosterone levels were also noted with daily aliskiren doses of 80 mg and above. Aliskiren 160 mg and enalapril 20 mg doses were comparable in terms of their inhibitory effects on Ang II levels BP nor heart rate was affected by aliskiren and enalapril in these normotensive subjects, In a within -study, 12 sodium-depleted normotensive subjects were randomly given placebo, aliskiren 300 mg/day, valsartan (150 mg/day, +80 mg/day, As expected, aliskiren along decrease PRA while valsartan along increased PRA, Ang I and Ang II. The combination of aliskiren and valsartan completely eliminated the rise in PRA elicited by valsartan.