RESEARCH PAPER | MEDICAL SCIENCE | Volume : 6 | Issue : 2 | FEBRUARY 2016 | ISSN - 2249-555X

Thyrotoxic Periodic Paralysis : A Case Series And Literature Review

KEYWORDS: Hyperthyroidism, Hypokalemia, Thyrotoxic Periodic Paralysis.

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ABSTRACT *Thyrotoxic Periodic Paralysis(TPP) is a rare complication of hyperthyroidism characterised by episodes of muscle weakness and hypokalemia.TPP is often not recognized at first attack usually due to mild symptoms of hyperthyroidism. We describe a series of 12 cases of Hyperthyroidism with periodic paralysis. Hypokalemia was documented in all the cases and managed with syrup Potchlor. Hyperthyroidism was diagnosed during that episodes. The patients were subsequently diagnosed as having thyrotoxic periodic paralysis. Treatment with propanalol and methimazole was initiated and presently they were under follow up. Thyrotoxic periodic paralysis is a rare disorder but should be considered in patients with acute paralysis and hypokalemia and thyroid function should be evaluated.*

Aim of presentation:

- To highlight the importance of thyroid function evaluation in patients with sudden onset periodic paralysis
- To review the literature regarding thyrotoxic peridic paralysis.

CASE SERIES:

Here we report 12 cases of thyrotoxic periodoc paraysis. The patients presented with symptoms of sudden onset weakness ranging from paraparesis to quadriparesis which on clinical examination happened to be acute areflexic flaccid paraparesis or quadriparesis in all the cases. Predominant proximal muscle weakness was there in all the cases. 6 out of 12 patients reported weakness in the early morning hours. There is no history of any excess work in sunlight nor any intake of high carbohydrate diet. 3 patients reported recurrence of symptoms before presenting to us. Weight loss,distal tremor,palpitations,excess sweating,and heat intolerance was reported on retrospective questionnarie in 4 cases . They had no personal or family medical history and was not taking any medication.

Labaratory evaluation showed moderate to severe hypokalemia in all the patients. Routine work up for hypokalemia was started as per the guidelines and the patients were supplemented with potassium syrup (syrup potchlor 60 millieq in divided doses). 2 pateints were managed with intravenous potassium supplementation owing to severe hypokalemia. The patients showed mild relief in ssymptoms with the supplementation of potassium. Thyroid profile was done in all the patients and TSH was low in all of them. Beta blocker therapy was initiated in all of them which helped in complete recovery in all of them. Anti thyroid drugs were started and was maintained. Patients were under follow up and was asymptomatic then.

ECG changes ranged from sinus tachycardia to ST T changes suggestive of hypokalemia .The laboratory studies revealed normal renal and hepatic function.rest of the parameters were with in normal limits.

Table 1:Age,Sex,presentation &examination findings, Serum potassium, TSH and ECG changes in the patients

No	Age (yr)	Sex	Clinical presentation	Examination findings	Serum potassium (mmol/L)	Serum TSH mIU/ml)	ECG changes
1	42	Male	Acute onset weakness of all four limbs at 5 AM.	Areflexia	3.2	0.006	Sinus tachycardia ST depression T inversion
2	32	Female	Acute weakness of both ower limbs progressed to upper limbs in 4 hours. Tremors, palpitations and sweeting with weight loss	Deep tendon r flexes diminished Power 3/5	2.9	0.0051	Non specific ST T changes Sinus tachycardia
3	40	Male	Weakness of all four limbs at about 6 AM Similar complaints 2 months back	DTR lost Power 3/5	2.6	0.0062	Sinus tachycardia No specific abnormality else
4	35	Female	Weakness of all four limbs with similar complaints in past 2-3 times h/o tremors and palpitations present	DTR 1+ Power 3/5	3.1	0.0053	Sinus tachyardia ST depression Flat T waves

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5	55	Male	Weakness of all four limbs Sudden onset at about 6 AM	DTR absent Power 3/5	3.2	0.0058	COPD changes ST depression T inversion
6	24	Male	Weakness of both lower limbs Sudden onset With h/o palpitations weight loss , tremors	DTR absent Power 3/5	3.0	0.0025	Sinus tachycardia ST T changes
7	32	Female	Weakness of all the four limbs at about 5AM	DTR absent Power 3/5	2.2	0.0052	Non specific changes
8	19	Female	Weakness of all limbs Similar complaints in the past	DTR absent Power 3/5	3.0	0.0024	ST T changes of hypokalemia
9	36	Male	Weakness of both lowe limbs at 6AM Tremors , palpitations ,weight loss	DTR 1+ Power 3/5	2.8	0.0063	ST T changes
10	28	Male	Weakness of all limbs	DTR absent Power 3/5	2.6	0.0065	Non specific changes
11	24	Female	Weakness of both lower limbs progressed to upper limbs	Absent DTR Power 3/5	3.2	0.0052	Sinus tachyardia ST depression Flat T waves
12	36	Male	Weakness of all the four limbs	Absent DTR	2.6	0.0065	Sinus tachycardia

DISCUSSION:

Thyrotoxic periodic paralysis is characterised by recurrent muscular weakness of four extremities,mainly lower extremities.Onset of attack usually coincides with onset of hyperthyroidism though overt findings of thyrotoxicosis are rarely present with initial paralytic attack.

The high incidence of this disorder in Asians and the association with the presence of HLA-DRw8 suggests that the basic defect may be genetically determined, but the precise pathogenesis of TPP remains unclear.[3]Familial cases are inherited in an autosomal dominant manner. Mutations in CACNA1S and SCN4A gene adversely affect the function of calcium and sodium ion channels servicing muscle cells, respectively . The KCNJ2 gene codes for inward rectifying potassium channels (Kir 2.1) that moves potassium ions into the cells of skeletal and cardiac muscles. Mutations of this gene have been known to cause familial periodic paralysis with arrhythmias and Andersen-Tawil syndrome .

It can present as a medical emergency. Patients often have an abrupt onset of paralysis which could affect all four limbs traditionally associated with hypokalaemia. Suspected cases of TPP with normal potassium levels during an attack have been reported . The classical presentation is of ascending lower limb paralysis in the early hours of the morning, or after rest following strenuous exercise and a high carbohydrate meal, leaving the patient unable to move. Acute episodes may be preceded with muscle aches, cramps, or stiffness. It is rare to observe ocular, bulbar, or respiratory muscle involvement. Tendon reflexes are generally diminished or absent with intact sensation and consciousness .Recession of paralysis occurs in reverse order of appearance.

TPP occurs during attacks of thyrotoxicosis .Most common cause is Grave's disease , others Jod Basedow , TSH secreting pituitary tumour, abuse of thyroid hormone ,solitary toxic thyroid adenoma. Specific cause of thyrotoxicosis is not a critical factor for expression of attack.

Table 2: Triggers of periodic paralysis attacks.

Triggers	Examples	Notes
High glycaemic index foods	Sweetened drinks, pasta, certain fruits, white bread, certain cereals and fruits, for example, watermelon, rice, potatoes	High glycaemic index foods promote release higher insulin levels
Salt/high sodium intake	High-salt-containing foods	Promotes diuresis and loss of potassium
Stresses	Infection, psychological, surgery	Release of catecholamines which can activate Na/K/ATPase pump
Ambient temperature	Cold weather	
Physical activity	Rest after significant exertion	Weakness maybe apparent first thing in the morning
Gastrointestinal	Diarrhoea	Loss of potassium
Drugs	Acetazolamide, oestrogen, diuretics, laxatives, liquorice, cortisol, aminoglycosides, acrolides, fluoroquinolones	Listed antibiotics adversely affect neuromuscular transmission
		Liquorice and cortisol promote potassium excretion
		Oestrogen can increase insulin resistance

The Na/K+/ATPase pump located on the sarcolemma of muscle cells prevents accumulation of intracellular sodium. It pumps out 3 Na+ for every 2 K+ ions it pumps into the cell. The influx of potassium into the cells alters the resting potential of the muscle cell leaving it unable to depolarise because it is hyperpolarised. The pump is activated by catecholamines (via beta-2 receptors) and therefore in susceptible patients, thyroid hormones since they sensitise the circulation to circulating catecholamines. Thyroid hormones can also directly stimulate Na/K/ATPase activity, and thyrotoxicosis (with or without periodic paralysis) has been shown to increase pump numbers . This pump is also activated by androgens, and men are approximately 10–20 times more likely to be affected than women, with onset in the 4-5th decade of life.

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An electrocardiogram may show characteristic features of hypokalaemia. Unlike hypokalaemia from other causes, sinus tachycardia predominates in TPP patients. Other findings include atrial fibrillation, atrioventricular block, ventricular fibrillation, and asystole . The electrolyte disturbance can be severe enough to cause asystole and cardiac arrest .

The underling hyperthyroid state has to be addressed in order to definitively rectify the condition; however initially potassium replacement may be needed to hasten muscle recovery and prevent cardiopulmonary complications . Potassium chloride is the preferred salt as its is less irritant . Supplementation must be given with caution (not faster than 10mmol/hour) as there is a risk of rebound hyperkalemia once the muscle cells recover releasing potassium and phosphate into the circulation . Administration of potassium is not done to correct hypokalemia but mainly to prevent cardiac arrhythmias.

A nonselective beta blocker such as propanolol can rapidly promote recovery without the risk of rebound hyperkalaemia. Propranolol blunts the hyperadrenergic stimulation of the Na-K-ATPase pump. Patients should be educated to avoid precipitating factors and continue propranolol until a euthyroid state is achieved so as to prevent symptoms.

Summary :
Throtoxic periodic paralysis is one of the rare cause of hypokalemia due to redistribution of potassium in the cells and extracellular compartment because of the high adrenergic levels. It is one of the correctable causes and reversible cause. High index of suspicion is necessary due to lack of classical thyrotoxic symptoms at presentation. Routine screening of patients with periodic paralysis for thyroid function is helpful.

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