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Thyrotoxic periodic paralysis admitted to the medical department in Qatar

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ABSTRACT

Objectives: In this study we describe the clinical presentation and electrolyte disturbances of thyrotoxic periodic paralysis (TPP) in patients admitted to the Department of Medicine at Hamad General Hospital.
Methods: Retrospective descriptive study involving patients admitted to the medical department of Hamad General Hospital with paralysis and hyperthyroidism.
Results: Eighteen patients with TPP were identified over a three-year period (2004-2007). Their mean age was 32.4 ± 8.52 years (range 21 to 48 years); all were males. Eleven patients were from the Philippines, five were from Nepal, one was Indian and one was from Sri Lanka. Fourteen patients (77.8%) had the attack in the summer while the remaining four in winter. Nine had a history of severe exertion, five had ingested a heavy carbohydrate meal, two had a sore throat, one had ingested alcoholic and one was without a precipitating cause. Fifteen patients had no previous history of hyperthyroidism. Later on, all patients proved to have hyperthyroidism. All patients were hypokalaemic, while seven patients had hypophosphataemia and three had hypomagnesaemia. Urinary potassium was <20 mmol/l in all patients. Fifteen patients had ECG changes. All patients had proximal myopathy. Twelve patients had signs of hyperthyroidism in the form of goitre, warm sweaty palms, tachycardia, and tremor. Nine patients had attacks of paralysis before diagnosis. After discharge, ten patients had recurrences within one to seven months.
Conclusion: The causes of hypokalaemia and lower-extremity paralysis are numerous; TPP should be taken into consideration in the differential diagnosis of all acute episodes of motor paralysis, especially in young Asian male patients.

KEYWORDS

Hypokalaemia, periodic paralysis, thyrotoxicosis

INTRODUCTION

Thyrotoxic periodic paralysis (TPP) is an uncommon disorder characterised by simultaneous thyrotoxicosis, hypokalaemia, and paralysis. It is the most common acquired form of periodic paralysis,[1,2] which can present with acute, dramatic, life-threatening muscular weakness. It mainly affects males with a male-to-female ratio of 20:1[1,3] and the usual age of onset is between the second and fourth decades.[4] A significant number of patients can present in this way; however, this condition is not often suspected in our community because periodic paralysis is rare in ethnic Arabs. As there are increasing numbers of labourers from East Asia in our area, we must consider this diagnosis.
Here we describe 18 patients with thyrotoxic periodic paralysis over a three-year period.

PATIENTS AND METHOD

This was a retrospective observational study of patients admitted to Hamad General Hospital with hypokalaemic paralysis, during a period of three years (2004-2007). Data were collected from their files onto a special form adopted for this reason. The gathered information was transferred to the computer utilising the software EpiInfo 2000. Data were analysed using simple descriptive statistics.

RESULTS

Demographic data and precipitating factors

Eighteen patients with TPP were identified over a three-year period (2004 to 2007) in our medical department. Their mean age was 32.4 ± 8.52 years (range 21 to 48 years); all were male. Eleven patients were from the Philippines, with a median age of 36.27 years, five were from Nepal with median age of 22 years, one was Indian and one from

Sri Lanka. Fourteen patients (78%) had the attacks in the summer, between May and October, while four had attacks in winter. Thirteen patients presented early in the morning, four patients in the evening. All the patients were asked about precipitating factors: nine had a history of severe exertion, five had ingested a heavy carbohydrate meal, two had a sore throat, one had ingested alcoholic and one was without a precipitating cause (*table 1*).

Clinical presentation

All patients were asymptomatic the day before presentation, with the exception of one who had gradual symptoms developing over three days. Fifteen patients (83%) had no previous history of hyperthyroidism while three (17%) had documented hyperthyroidism, but their states were not controlled.

There was no family history of similar attacks. All patients complained of muscle pain and the physical examination showed a similar pattern of muscle weakness affecting the proximal muscles of the lower limbs more than the upper limbs. The ankle tendon reflex was absent in most cases. There was no sensory loss, cranial nerve palsy, respiratory weakness, laryngeal muscles involvement or sphincter involvement apart from one patient who had urinary retention. The patients were investigated for symptoms of hyperthyroidism; none of the patients had symptoms of palpitations, weight loss, heat intolerance and frequent bowel motions or increased appetite, but on clinical examination 12 patients (66%) had signs of thyroid disease in the form of goitre, warm sweaty palms, tachycardia and tremor. Nine patients (50%) had suffered attacks of paralysis before diagnosis (*table 2*).

Laboratory data

All patients were hypokalaemic with a potassium level between 1.6 and 3.3 mmol/l, mean 2.37 ± 0.53 mmol/l. All patients had hyperthyroidism with high free T4, free T3 and low thyroid-stimulating hormone (TSH); one patient had T3 thyrotoxicosis. Seven patients (39%) had hypophosphataemia and three (17%) had hypomagnesaemia. There were no sodium, potassium, or acid base abnormalities and the urinary potassium was <20 mmol/l in all patients. Fifteen patients had ECG changes in the form of tachycardia, ST-T changes, U wave, first-degree heart block, prolongation of the QT interval, multiple atrial ectopics and atrial flutter with variable block which resolved spontaneously (*table 3*).

Outcome

All our patients received 60 to 120 mmol intravenous potassium in saline on admission and were discharged after two to three days on β-blockers and carbimazole. Subsequently, ten patients (56%) had recurrences within one to seven months because of uncontrolled thyrotoxicosis that was due to an insufficient amount of medication and/or noncompliance but as they became euthyroid their condition improved. One patient continued to have recurrences for more than one year until he received radioactive iodine, after which he had no further relapse.

DISCUSSION

TPP is most common in Asian populations, with an incidence of approximately 2% in patients with thyrotoxicosis of any cause.[4-7] It has been recognised

Table 1. *Demographic data and precipitating factors*

Patient	Nationality	Sex	Age (years)	Precipitant factor	Month of presentation	Time of occurrence
1	Filipino	Male	32	Sore throat	July	5 am
2	Nepali	Male	23	Carbohydrate ingestion	June	11 pm
3	Filipino	Male	36	Heavy exertion	August	6 am
4	Filipino	Male	31	Carbohydrate ingestion	June	7 am
5	Nepali	Male	21	Exertion	August	6 am
6	Filipino	Male	48	Exertion	May	5 am
7	Filipino	Male	38	Exertion	August	6 am
8	Filipino	Male	29	Alcohol	June	5 am
9	Filipino	Male	39	Exertion	August	11 am
10	Nepali	Male	23	None	September	5 pm
11	Filipino	Male	45	Exertion	May	6 am
12	Nepali	Male	21	Exertion	June	5 am
13	Filipino	Male	29	Carbohydrate ingestion	June	6 am
14	Filipino	Male	33	Carbohydrate ingestion	December	6 am
15	Sri Lankan	Male	44	Exertion	November	3 days
16	Indian	Male	33	Exertion	December	3 pm
17	Filipino	Male	39	Carbohydrate ingestion	May	7 am
18	Nepali	Male	22	Sore throat	February	5 pm

Table 2. *Clinical presentation with recurrences and outcome*

Patient	Proximal muscle weakness power lower limb (L), upper limb (U)	Ankle tendon reflex	Signs of thyroid disease	Attacks before diagnosis	Recurrence	Known hyper-thyroidism	Stay in hospital
1	Proximal L 2/5, U 3/5	Normal	Yes	1	6	No	3 days
2	Proximal L 2/5, U 4/5	Normal	Yes	1	No	No	2 days
3	Proximal L 3/5, U 3/5	Normal	Yes	None	No	Yes	4 days
4	Proximal L 3/5, U 4/5	Decrease	Yes	10	3	Yes	2 days
5	Proximal L 2/5, U 4/5	Decrease	No	3	No	No	4 days
6	Proximal L 3/5, U 4/5	Normal	Yes	None	1	No	4 days
7	Proximal L 4/5, U 4/5	Decrease	No	None	No	No	3 days
8	Proximal L 2/5, U 3/5	Normal	Yes	2	No	Yes	1 day
9	Proximal L 1/5, U 2/5	Decrease	No	4	No	No	3 days
10	Proximal L 2/5, U 2/5	Decrease	No	None	7 within a month	No	2 days
11	Proximal L 2/5, U 3/5	Normal	No	None	1	No	2 days
12	Proximal L 2/5, U 3/5	Decrease	No	1	No	NO	1 day
13	Proximal L 3/5, U 3/5	Decrease	Yes	1 before 4 years	No	No	3 days
14	Proximal L 2/5, U 4/5	Decrease	Yes	None	1 after 4 months	No	2 day
15	Proximal L 2/5, U 4/5	Decrease	Yes	None	1	No	2 days
16	Proximal L 2/5, U 4/5	Decrease	Yes	1	2 attacks within 6 months	No	2 days
17	Proximal L 2/5, U 3/5	Decrease	Yes	None	1	No	2 days
18	Proximal L 3/5, U 4/5	Decrease	Yes	None	2	No	3 days

Table 3. *Laboratory data*

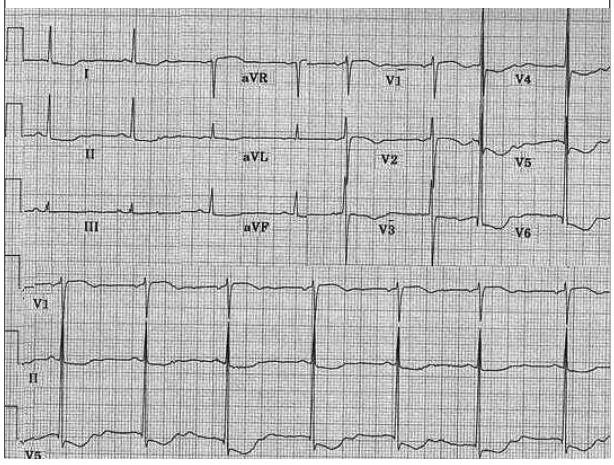
Patient	Potassium mmol/l	Free T4 pmol/l	Free T3 pmol/l	TSH mIu/l	Phosphorus mmol/l	Magnesium in mmol/l	ECG findings
1	3.3	61.07	33.06	<0.01	1.08	0.64	T wave inversion, U wave
2	2.5	40.7	28.2	<0.01	0.99	0.68	Multiple atrial ectopics and U wave
3	3.1	93.1	10.2	<0.01	0.72	1.53	None
4	1.6	34.2	33.9	<0.01	0.92	0.7	U wave
5	1.7	21.6	5.8	<0.01	0.47	0.79	Flat T wave
6	2.1	36.7	6.27	<0.01	0.66	0.82	Prolonged Q-T interval, inverted T wave
7	1.6	30.8	10.8	<0.01	0.89	0.95	Inverted T wave, U wave
8	2.2	29.9	12.7	<0.01	0.49	0.54	First-degree heart block, U wave
9	2.1	30.3	17.2	<0.01	1.01	0.69	U wave
10	2.2	29.7	10.1	<0.01	1.2	0.85	Inverted T wave, U wave
11	2.3	24.7	13.5	<0.01	0.76	0.74	Normal
12	1.8	16.4	7.1	<0.01	0.92	0.71	U wave
13	2.5	67.33	5	<0.01	0.53	0.81	Inverted T wave, U wave
14	2.7	76.73	46.08	<0.01	0.97	0.73	Normal
15	2.5	60.81	18.03	<0.01	0.81	0.74	Atrial flutter with variable block, U wave Inverted T wave
16	2.7	47.12	19.91	<0.01	0.62	0.93	Inverted T wave, U wave
17	3.3	29.14	11.56	<0.01	0.99	0.74	First-degree heart block, U wave
18	2.4	47.94	20.38	<0.01	1.11	0.59	Inverted T wave, U wave

Normal values: potassium: 3.5-5 mmol/l; free T4: 9-20 pmol/l; free T3: 3.4-6 p mol/l; thyroid-stimulating hormone (TSH): 0.45-4.50 mIU/l; phosphorus 0.87-1.45 mmol/l; magnesium: 0.65-1.05 mmol/l.

in Thai, Filipinos, Vietnamese, Koreans, Malaysians, Hispanics, African Americans, and Caucasians.[4-7] Our patients (eleven were Filipinos, five Nepali, one Sri Lankan and one Indian) represent the various involvement of the oriental male race. In other studies the male-to-female ratio ranged from 17:1 to 70:1.[4, 8-10] Our series did not include any females because most of the Asian workers here are men.

The attacks of paralysis have a well-marked seasonal incidence, usually occurring during the warmer months.[4] In our study 77.8% had attacks in the summer, between May and October, which may be due to increased sweating during the summer, probably related to increased outdoor exercise, and the consequent loss of potassium may have a part to play, which is similar to the findings of McFadzean

Figure 1. *Long QT interval, ST depression, low T waves, and TU wave fusion characteristic of hypokalaemia*



and his group.[4] A diurnal pattern of attacks also exists. Paralysis occurs when the patient is at rest and usually in bed at night and never during physical exertion. In our study, 83.3% of patients experienced the onset of symptoms between 5 pm and 8 am; these findings are similar to those of Yeo and colleagues, who reported that 88.5% of TPP patients in a Singapore series had symptom onset between 6 pm and 8 am.[11] The main clinical difference between familial periodic paralysis and TPP is the presence of thyrotoxicosis in the latter and the lack of positive family history, although familial TPP has been reported.[4] In our study there was no family history in any of the patients.

Precipitating factors of hypokalaemic thyrotoxic periodic paralysis include strenuous exercise followed by rest, excessive ingestion of carbohydrate-rich food, administration of insulin or epinephrine, trauma, exposure to cold temperatures, infection, menstruation, and emotional stress.[12] In our patients the main precipitant factors were rest after heavy exertion, heavy carbohydrate intake, infection and alcohol bingeing, all of which is in line with Lin's findings.[12]

The presentations of our patients correspond with those in most other studies such as Lin[12] and Goh.[13] All our patients had myalgia; flaccid paralysis involved the proximal muscle of the pelvic girdle more than the shoulder. All of them were conscious with normal mental function. There was no respiratory, ocular or bulbar muscle involvement or sensory signs nor cranial nerve palsy. These signs can help in differentiating from myasthenia gravis, Guillain-Barre syndrome, transverse myelitis and botulism. One of our patients had urinary retention; tests were carried out but no neurological cause could be found and it improved immediately after correction of his potassium. Ankle reflexes were diminished in most of the cases, which is in line with findings from other studies. Two of our patients had transient cardiac arrhythmia in the form of atrial ectopics and atrial flutter, which has been well reported.

We found that 66% of patients had signs of hyperthyroidism before the diagnosis, while McFadzean and Yeung found that the manifestations of the hyperthyroid state preceded the episodes of paralysis by three to nine years in 80% of affected subjects.[4]

The main biochemical abnormalities were high levels of thyroid hormones and hypokalaemia. On rare occasions only the total triiodothyronine level is elevated.[14] In our series, we have one patient with T3 thyrotoxicosis.

Pathogenesis of hypokalaemia was explained by some authors to be attributable to an intracellular shift of body potassium, which is catecholamine mediated.[15,16] Shizume and his group studied total exchangeable potassium which revealed that patients with thyrotoxic periodic paralysis were not significantly different from controls when the value was related to lean body mass.[15] The paralytic symptoms and signs improve as the potassium returns from the intracellular space back into the extracellular space.[17] The diurnal variation in potassium movement where there is nocturnal potassium influx into skeletal muscle would explain the tendency for thyrotoxic periodic paralysis to occur at night.[18] Hypophosphataemia and hypomagnesaemia are well known to occur in association with thyrotoxic periodic paralysis.[1,9,19-21] We note seven of our patients had hypophosphataemia and three had hypomagnesemia. The correction of hypophosphataemia without phosphate administration supports the possibility of intracellular shift of phosphate.[19]

Electrocardiographic findings supportive of a diagnosis of TPP rather than sporadic or familial periodic paralysis are sinus tachycardia, elevated QRS voltage and first-degree AV block (sensitivity 97%, specificity 65%).[22] In addition to ST-segment depression, T-wave flattening or inversion and the presence of U waves are typical of hypokalaemia. Most of our cases showed ST-T changes with U waves, two patients had first-degree heart block, another had prolongation of the QT interval and two had atrial ectopics and atrial flutter; all these resolved after correction of the hypokalaemia.

The management is to deal with the acute attack as well as treatment of the underlying condition to prevent future attacks. Rapid administration of oral or IV potassium chloride can abort an attack and prevent cardiovascular and respiratory complications.[12] A small dose of potassium is the treatment of choice for facilitating recovery and reducing rebound hyperkalaemia due to release of potassium and phosphate from the cells on recovery.[1-3] Rebound hyperkalaemia occurred in approximately 40% of patients with TPP, especially if they received >90 mmol of potassium chloride within the first 24 hours.[12] All our patients receive small doses of potassium between 60 and 120 mmol. Another mode of treatment is to give

propranolol, a nonselective β-blocker, which prevents the intracellular shift of potassium and phosphate by blunting the hyperadrenergic stimulation of Na^+/K^+–ATPase.[24] Hence, initial therapy for stable TPP should include propranolol.[23,25,26] None of our patients received intravenous propranolol because most of the cases reverted rapidly, but all of them were discharged on oral propranolol. The definitive therapy for TPP includes treatment of hyperthyroidism with antithyroid medications, surgical thyroidectomy, or radioiodine therapy. Our entire patients improved on carbimazole with exception of one patient who needed radioactive iodine.

CONCLUSION

Causes of hypokalaemia and lower-extremity paralysis are numerous; TPP should be taken into consideration in the differential diagnosis of all acute episodes of motor paralysis, especially in young Asian male patients. TPP should be treated by cautious replacement of potassium and achievement of a euthyroid state. Correction of thyrotoxicosis and avoidance of precipitating factors is the mainstay of treatment.

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