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Case report

Thyrotoxic periodic paralysis together with thyrotoxic heart disease in a Ghanaian man: case report and literature review

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Abstract: Thyrotoxic periodic paralysis (TPP) is an uncommon symmetrical paralysis usually affecting proximal muscles, which occurs in the hyperthyroid state with associated hypokalemia. It is more prevalent in East Asian males and extremely rare in blacks. Data on TPP is scarce in Africa and no report has been made in Ghana. We report a case of a middle-aged Ghanaian man who had three episodes of paralysis in all four limbs occurring at night with the second and third episodes requiring hospital visit. He had no clinical signs of hyperthyroidism during his first hospital visit but had developed clinical and biochemical evidence of hyperthyroidism on the second visit with serum potassium levels of 1.9 mmol/l; and he was eventually diagnosed with TPP. His paralysis resolved with correction of the hypokalemia. It is important to evaluate patients presenting with paralysis comprehensively. Less common differential diagnosis such as TPP may also be considered in such patients to ensure early diagnosis and treatment which can prevent complications.

Keywords: thyrotoxic; periodic; paralysis; hypokalemia; case report

1. Introduction

Thyroid hormones are required by all nucleated cells in the body for normal metabolism. However, excess blood thyroid hormones leading to thyrotoxicosis causes dysfunction of various systems in the

body including the cardiovascular, nervous, musculoskeletal and other systems [1]. Thyrotoxicosis has a prevalence of 0.2–1.3% in developed countries where iodine is supplemented [2]. In Africa data on population-based true prevalence of thyrotoxicosis is lacking. However, in Ghana, thyroid disorders account for 13% of endocrine clinic visits [3].

One rare neurological complication of thyrotoxicosis is thyrotoxic perioid paralysis (TPP) [4]. TPP is a sporadic disease characterized by hypokalemia with acute reversible recurrent flaccid muscle weakness in patients with thyrotoxicosis due to increased shift of potassium into cells with the weakness usually lasting a few hours to three days [5]. TPP commonly affects Asian males having an incidence of 1.8 to 1.9% in this population [6,7] and an estimated incidence of 0.1% to 0.2% in Caucasians [5]. Increasingly, cases are being reported outside Asia attributable to increased migration and the fact that clinicians are increasingly becoming aware of the condition [8].

TPP presents similarly to other forms of hypokalemic periodic paralysis (HPP) such as familial hypokalemic periodic paralysis (FPP) and other acquired forms of HPP but differentiated on the basis of biochemical evidence of hyperthyroidism [9].

Treatment involves correcting the hypokalemia with intravenous or oral potassium, giving a non-selective beta blocker to stabilize the sodium-potassium ATPase and in the long term, treating the underlying thyrotoxicosis [10].

Although TTP is generally rare in blacks; a few cases have been reported in people of Afro origin living outside Africa [8,11–13] and also Africans living in Africa including Tanzania [14], Senegal [15] and Somalia [16]. However, no such report has been made in Ghana. We report a case of an adult Ghanaian black man who was eventually diagnosed with TPP after a year of delayed diagnosis.

2. Case presentation

A 43-year-old Ghanaian man presented to the Emergency Department of Komfo Anokye Teaching Hospital in Kumasi, Ghana at dawn with a third episode of weakness in all limbs which he noticed after waking up from sleep that dawn. He first noticed the weakness in his lower limbs which later progressed to involve his upper limbs a few hours prior to presentation.

He reported experiencing two similar episodes also occurring at dawn a year earlier. The first episode resolved spontaneously at home within a few hours. The second episode persisted for hours for which he was admitted at the hospital but regained full power spontaneously within a few hours on admission, discharged and followed up on out-patient basis but was lost to follow up.

He had not had any more paralysis over a year period until this third episode of paralysis that led to his second hospital admission. He had a preceding two months history of palpitations, dyspnea on minimal exertion and significant weight loss. He however was not on any medications, had no preceding diarrhea or vomiting and had no known history of any chronic illness. He had not taken an unusual amount of carbohydrate diet the preceding evening.

On examination, he was anxious, afebrile, anicteric and not pale. He had mild proptosis with thyroid eye disease clinical activity score of 1/10, diffuse goiter, tremulous hands and pitting bipedal edema. He was tachycardic with irregular pulse of 154 beats per minute (bpm) and a pulse deficit of 30 bpm. His blood pressure was 154/74 mmHg with respiratory rate of 22 cycles per minute. He had thrusting displaced apex beat, ejection systolic mummer and bibasal fine crackles. He was fully conscious, cranial nerves intact, power of 3/5 in both lower limbs and 4/5 in the upper limbs, with reduced muscle tone and deep tendon reflexes. The results of his investigations summarized in Table

1, Figures 1 and 2 below showed Graves' disease with severe hypokalemia (serum potassium of 1.9 mmol/l) and also dilated cardiomyopathy with reduced left ventricular systolic function and atrial fibrillation.

Table 1. Review of laboratory and imaging data.

Investigation	Admission	Month 2	Month 4	Reference range
Serum creatinine (umol/l)	81	-	75	44–106
Serum urea (mmol/l)	4	-	5	2.1–8.3
Serum potassium (mmol/l)	1.9	4.4	4.2	3.5–5.5
Serum sodium (mmol/l)	137	140	141	135–145
Serum chloride (mmol)	80	90	98	95–110
TSH (uIU/ml)	<0.015	<0.015	0.9	0.5–5.0
Free triiodothyronine (pmol/l)	>35	16	9	4.6–9.7
Free tetraiodothyronine (pmol/l)	>90	23	16	12–23
Anti TSH-receptor antibody (IU/l)	310.5	-	-	1.2–1.5
Thyroid ultrasonography	Diffusely enlarged thyroid gland with increased blood flow on color Doppler.			
Electrocardiogram	Atrial fibrillation with rapid ventricular response, left ventricular hypertrophy, ST/T changes and poor R wave progression			
Echocardiogram	Dilated cardiac chambers, global hypokinesia with LVEF of 45%, right ventricular systolic dysfunction (TAPSE 10 mm), normal valvular morphology with moderate to severe mitral and tricuspid regurgitation and severe pulmonary hypertension (RVSP 66 mmHg).			

Note: TSH: Thyroid stimulating hormone; LVEF: Left ventricular ejection fraction; TAPSE: Tricuspid annular plane systolic excursion; RVSP: Right ventricular systolic pressure; ST/T: ST segment and T wave.

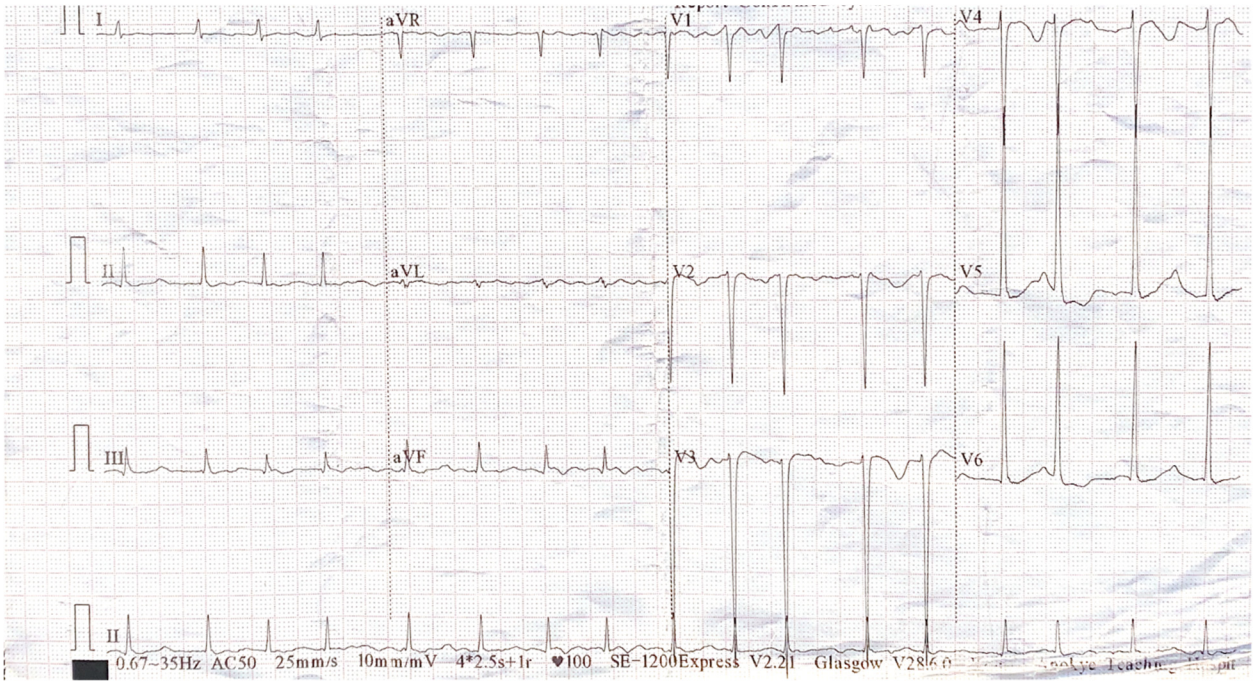

Figure 1. Resting electrocardiogram showing atrial fibrillation with rapid ventricular response, left ventricular hypertrophy, ST/T changes and poor R wave progression.

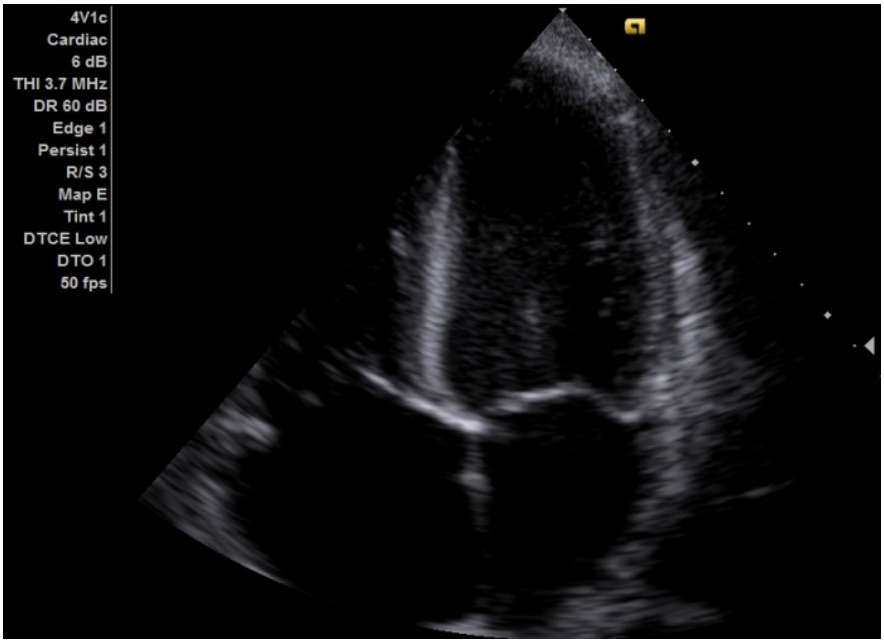

Figure 2. Epical 4 chamber view echocardiogram showing dilated cardiac chambers.

A diagnosis of Graves' disease with thyrotoxic periodic paralysis and heart failure secondary to thyrotoxic cardiomyopathy with atrial fibrillation was made. Patient regained full power in all the limbs with the correction of hypokalemia with 100 mEq of intravenous potassium chloride infused over 24 hours. He was then started on oral potassium (slow K 8 mEq three times daily), furosemide 40

mg daily, sacubitril/valsartan 50 mg twice daily, bisoprolol 5 mg daily, spironolactone 25 mg daily and anticoagulation with warfarin starting at 5 mg at night for the heart failure and atrial fibrillation. He was also put on oral carbimazole 20 mg twice a day and discharged on admission day 4.

At four months post discharge, repeat thyroid hormones were within normal ranges. His atrial fibrillation had spontaneously converted to sinus rhythm. Repeat echocardiography showed improved cardiac dimensions, LVEF had increased from 45% to 51%, right ventricular systolic function also improved (TAPSE increased from 10 mm to 16 mm) and RVSP had reduced from 66 mmHg to 47 mmHg. His heart failure symptoms had resolved and he has since not reported further paralytic episodes. He preferred to continue the thyrotoxicosis treatment with medical therapy rather than surgery or radioiodine therapy.

3. Discussion

TPP is part of a group of diseases known as periodic paralysis characterized by episodes of sudden onset muscle weakness as a result of changes in the excitability of muscles membrane due to abnormal functioning of electrolyte channels which may involve potassium, calcium or sodium channels leading to hyperkalemic, normokalemic or hypokalemic paralysis [17]. The channelopathies are mostly genetic but may also be acquired. TPP is an acquired form of HPP and is differentiated from the familiar type, FPP, by the presence of elevated thyroid hormones which may also be associated with hypomagnesemia and hypophosphatemia [9,17]. Also, FPP is an autosomal dominant condition and there may be other family members with similar disease [10,18].

FPP is a genetic disease and may be due to genetic mutation in CACNA1S which is a dihydropyridine-sensitive calcium channel resulting in type 1 FPP and or SCN4A which is a voltage-gated sodium channel in skeletal muscle resulting in type 2 FPP. Also, mutations in the KCNJ2 and KCNJ18 genes that code for inward rectifier potassium channel have also been implicated [18–24].

Although TPP is an acquired disorder, there is growing evidence of genetic involvement. Particularly, patients with Graves' disease who possess the following genetic mutations DCHS2 on 4q31.3, C11orf67 on 11q14.1 and 17q24.3 near KCNJ2 have a higher risk of developing TPP than those without these mutations [25–28].

TPP by definition is a triad of hyperthyroid state, hypokalemia and paralysis. However, only 45% of patients have overt clinical findings of hyperthyroidism at the time of presentation [29] which can lead to the diagnosis being missed in favor of other closely related differential diagnosis as in the case of this patient at the first presentation. Abnormal electrocardiographic (ECG) findings are found in most patients with TPP either due to the elevated sympathetic activity caused by the excess thyroid hormones or changes related to hypokalemia [29]. Arrhythmias are common with atrial arrhythmias occurring frequently, however ventricular arrhythmias such as ventricular fibrillation can also occur [30]. This patient had atrial fibrillation with ST/T changes on the ECG which may be due to the hypokalemia.

Hypokalemia in TPP results from intracellular shift of potassium. Elevated thyroid hormones increase tissue responsiveness to beta–adrenergic stimulation, which along with insulin and androgens, increases the sodium-potassium ATPase activity in skeletal muscle membranes leading to intracellular shift of potassium, hyperpolarization of the muscle membrane and relative inexcitability of the muscle fibers [18,31]. For this reason, activities that increase insulin or cortisol action such as high

carbohydrate meals, alcohol abuse, infections, strenuous exercise and emotional stress are known triggers of TPP [5].

TPP typically occurs in males in the second to fourth decades of life [5] which is consistent with the age and gender of our patient. A few cases however, have been reported in females [13]. Our patient's episodes of paralysis occurred at night which is in keeping with the classic attacks of TPP explaining why this disease was originally described as nocturnal paralysis [32]. The nocturnal presentation of TPP may be explained by the fact that, serum potassium level is influenced by the body's circadian rhythm, such that, serum potassium levels are naturally lower at night and hypokalemia from any cause may be exaggerated at night [33,34]. The pattern of the muscle weakness is symmetrical and involves the proximal muscles commonly affecting the lower extremity muscles [5,10]. However, muscles of the other parts of the body may also be affected including bulbar and respiratory muscles [35].

The diagnosis of TPP involves demonstrating biochemical evidence of elevated thyroid hormones in the context of hypokalemia and paralysis [1,18].

Treatment of TTP involves correcting the underlying hypokalemia with potassium replacement and stabilizing the sodium-potassium ATPase with non-selective beta blockers. The definitive therapy is rendering the patient euthyroid with medical therapy, radioiodine or thyroidectomy [8,10,18,36,37].

4. Conclusions

TPP is increasingly being diagnosed in non-Asians including blacks. It may precede overt clinical manifestation of hyperthyroidism which may pose a diagnostic challenge. However, having a comprehensive approach towards patients with symmetrical paralysis and considering other less common differential diagnosis such as TPP would help ensure early diagnosis and treatment which can avoid complications.

Ethical approval

Patient gave written informed consent for publication of this case report. The case report including the electrocardiogram and echocardiogram images were de-identified to protect patient's privacy and maintain confidentiality.

Conflict of interest

All authors declare no conflicts of interest in this paper.

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