Thyrotoxic periodic paralysis in a Saudi patient complicated by life-threatening arrhythmia

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ABSTRACT

مرض الشلل الدوري السمي الدرقي (TPP)، نادر لدى شعوب العالم من غير العرق الأصفر. هناك فقط 8 حالات مدونة لدى العرب، ثلاث منها في المملكة العربية السعودية. نستعرض في هذا التقرير حالة أخرى لهذا المرض النادر لدى رجل سعودي يبلغ من العمر 38 عام، بعد خمسة أسابيع من تشخيصه بداء غريف (Grave). ازداد نشاط الغدة الدرقية، وكان هناك نقص في البوتاسيوم (1.5mmol/L). أثناء التقييم المبدئي للمريض في الطوارئ حيث كان يعاني من حالة شلل رخو رباعي تام، تطور حالته إلى غشي وتوقف قلب مؤقت. تحسنت حالة المريض بشكل تام بعد الإنعاش وتعويض نقص البوتاسيوم. أكدت هذه الحالة إن الشلل الدوري السمي الدرقي (TPP) ليس مقتصرا على العرق الأصفر فقط بل ممكن أن يصيب أية مريض مصاب بفرط نشاط الغدة الدرقية.

Thyrotoxic periodic paralysis (TPP) is rare in non-Orientals, and sporadic case reports were reported world-wide. Eight cases were reported in Arabs, including 3 Saudis. We present an additional case of TPP in a 38-year-old Saudi man, and review the literature on TPP in Arabs. Our patient presented with complete flaccid quadriplegia, 5 weeks after he was diagnosed with Graves' disease that was treated with carbimazole and propranolol. He was hyperthyroid, and his potassium was extremely low (1.5 mmol/L). During initial evaluation in the emergency room, he developed transient asystole manifested by syncope. He was resuscitated and his hypokalemia was corrected, and he had a full recovery. This case emphasizes the notion that TPP can occur in patients of any ethnic background. The development of serious cardiac complications in our patient underscores the importance of early and correct diagnosis of this potentially life-threatening complication of hyperthyroidism.

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Thyrotoxic periodic paralysis (TPP) is an uncommon disorder characterized by simultaneous hyperthyroidism, hypokalemia, and quadriplegia, occurring mainly in males of Oriental (Southeast Asian) descent.[1] It was sporadically reported in non-Oriental ethnic populations from different countries,[1-7] and few cases of TPP were reported to occur in Arabs.[2-7] No cases of TTP were identified in Saudis through the late 1980's.[2,8] The first case was reported by Johnson and Hoque[2] in 1992, and 2 additional cases were added by Banzal et al[6] in 2004. Thyrotoxic periodic paralysis is expectedly associated with electrocardiographic (ECG) changes,[9] as hyperthyroidism is associated with various types of cardiac arrhythmias.[10] Likewise, hypokalemia is well-known to manifest stepwise progressive ECG changes.[11] Hence, TPP, a combination of the 2 disorders, may potentially present a wide variety of abnormalities in cardiac rhythm that can be serious. Various cardiac arrhythmias associated with TPP were reported.[12-14] We report herein, the case of an adult Saudi male who presented with rapidly progressive quadriplegia, severe hypokalemia, and mild hyperthyroidism, complicated by complete asystole and cardiac arrest.

Case Report. A 38-year-old Saudi man presented to the emergency room (ER) of King Fahd Armed Forces Hospital (KFAFH) in Jeddah, Kingdom of Saudi Arabia, with a history of sudden difficulty in moving his lower limbs since he woke up in the morning. The weakness progressed slowly until the patient became unable to move all limbs completely. He gave history of heavy exercise the day before presentation. He also gave history of a recent onset of reversible, mild recurrent episodes

of muscle weakness. The patient was diagnosed to have hyperthyroidism 5 weeks prior to presentation, and was started on carbimazole and propranolol. There was no family history of a similar condition, or of thyroid or muscle disorders. The patient is a naval engineer, living in the Eastern Province. The physical examination revealed a healthy adult male, in no apparent distress. His pulse was regular at 80/min (on propranolol), and his blood pressure was 140/70 mm Hg. There were no tremors or rapid deep tendon reflexes. The examination of the head and neck revealed mild symmetric thyromegaly with no bruits and no gross ophthalmopathy. The examination of the heart, lungs and abdomen was unremarkable. The neurological examination showed normal mental status, cranial nerves, fundi, reflexes, and sensations. The motor examination showed no muscle tenderness, swelling, or fasciculation. There was profound weakness of the proximal muscles of both upper and lower limbs. The power was grade 0/5 in the proximal muscles, and grade 2/5 in the distal muscles of both lower limbs. In the upper limbs, the power was grade 2/5 in the proximal muscles, and 4/5 in the distal muscles. In view of the known history of hyperthyroidism, a clinical diagnosis of TPP was considered. The serum potassium was 1.5 mmol/L (range 3.2-5.0), phosphate 0.45 mmol/L (range 0.87-1.45), and magnesium 0.64 mmol/L (range 0.7-1.1). Thyrotropin (TSH) was <0.005 mIU/L (range 0.26-4.2), and total thyroxine was 26.35 pmol/L (range 12-22). The complete blood count, serum urea, creatinine, sodium, and liver functions test were normal. The ECG showed sinus rhythm with subtle U-waves, flat T-waves, mild first-degree heart block, and prolonged corrected-QT interval (**Figure 1**). While the patient was being evaluated and aggressively managed in the ER, (and before the result of potassium was known), he complained of severe dizziness, then fainted transiently and recovered spontaneously. Shortly thereafter, a similar episode occurred and the patient became unresponsive, while the cardiac monitor showed progressive bradycardia that culminated in a complete cardiac asystole (**Figure 2**). Immediate cardio-pulmonary resuscitation was initiated, and after a few external cardiac compressions, the patient regained consciousness, and the monitor showed a return to sinus rhythm. While proper airway was secured, intubation was not necessary. As soon as hypokalemia was noted within the first hour of presentation to the ER, intravenous potassium supplementation was instituted, as well as replacement of other deficient electrolytes. The patient was carefully stabilized and then transferred to the intensive care unit. He had then another episode of severe bradycardia, which responded to atropine. Over the subsequent 12 hours, the potassium level gradually increased to 4.1 mmol/L, and the patient regained full power in his extremities and was able to walk normally. A total of 170 mmols of potassium were infused. Replacement of phosphate and magnesium was also carried out. The patient had a full recovery and was discharged from the hospital in a healthy status the next day. He was advised to continue carbimazole and propranolol. On discharge, he was given detailed information regarding potential recurrence of the paralytic condition. He was instructed on diet and exercise, and was asked to follow closely with his doctor at home, (he was planning to return home as he was on vacation in Jeddah) in the Eastern Province, and therefore he was not given follow up appointment at KFAFH.

Discussion. Thyrotoxic periodic paralysis is the main non-familial form of hypokalemic periodic

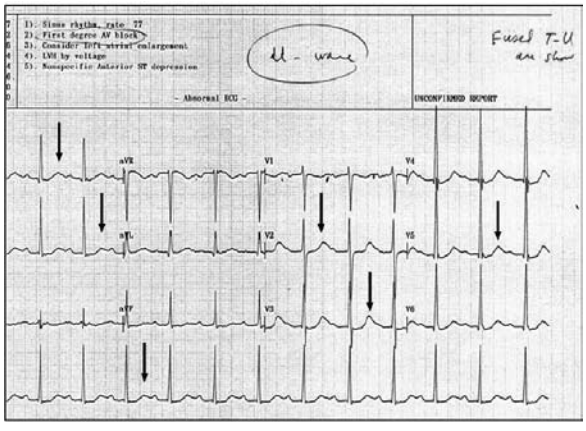

Figure 1 - Electrocardiogram of the patient showing sinus rhythm with prominent U-waves (fused-T and U-waves), flat T-waves, mild first degree heart block, and prolonged corrected-QT interval.

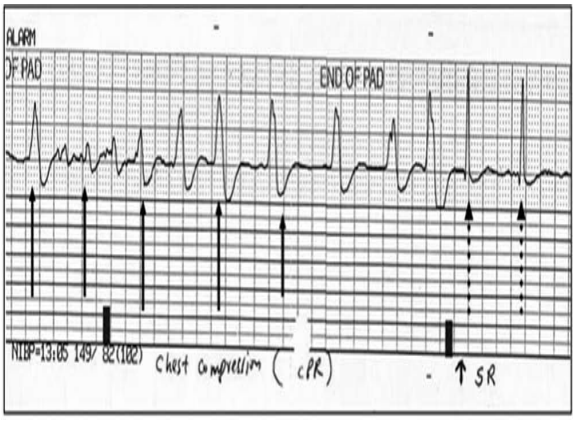

Figure 2 - Rhythm strip showing what was witnessed to be complete asystole by the treating physicians in the emergency room. The irregular, erratic complexes seen here are the external chest compressions applied during resuscitation. The resumption of sinus rhythm is seen on the right of the figure.

Table 1 - Available case reports of TPP in Arabs according to year of publication.

Authors	Year of publication	Arabic sub-ethnicity	Age, years	K^+(mmol/L)	Severity of hyper-thyroidism*	Cardiac manifestations
Johnson et al[2]	1992	Saudi	26	1.8	Mild	ST, STd, TWi, pQT
Atar et al[3]	1996	Palestinian	29	NO	NO	NO
Siddiqui[4]	1998	Bahraini	33	1.8	Asymptomatic	UW
Redha et al[5]	1998	Omani	41	1.9	Moderate	ST, Non-Sp
Banzal et al[6]	2004	Saudi	25	NO	NO	NO
Banzal et al[6]	2004	Sudanese	30	1.9	Moderate	TWi
Banzal et al[6]	2004	Saudi	26	NO	NO	TWi
Atallah et al[7]	2007	Lebanese	38	2.4	Subclinical	pQT
Aldasouqi et al	(current case)	Saudi	38	1.5	Mild	SR, TWf, AV-1, UW, Asyst

K - potassium, NO - not obtainable from reference, *severity of hyperthyroidism - concluded from clinical description by authors, and/or from thyroid hormone levels (arbitrary categorization; subclinical - normal thyroid hormones, mild - double the upper limit, moderate - 3-time upper limit, severe - above 3-time upper limit), Asyst - asystole; TWf - flat T-wave; Non-Sp - nonspecific ST-T changes, pQT - prolonged QT, SR - sinus rhythm, ST - sinus tachycardia, STd - ST segment depression, TWi - T-wave inversion, UW - U-waves, AV-1 - first degree AV. All patients were males, and all recovered smoothly with appropriate treatment.

paralysis, affecting mainly hyperthyroid adult males of Southeastern Asian (Oriental) descent, with an incidence of 24%[1] of patients with hyperthyroidism. Nevertheless, TPP has been reported in non-Orientals worldwide.[1-7] The TPP affecting Arabs though, was scarcely been reported. Searching the English literature (Pub-Med/ Medline, Google, and Medscape), we found 8 published case reports of TTP in Arabs (**Table 1**), all from the Middle East.[2-7] While exact, population-based, epidemiological data on hyperthyroidism in the Kingdom of Saudi Arabia (KSA) are scarce, a retrospective review of thyrotoxicosis in a university hospital did not identify any case of TPP.[8] Between 1979 and 1986, 6 cases of TPP were identified in KSA, but all patients were of Oriental origin.[2] The first case report of TPP in a native Saudi patient was reported by Johnson and Hoque in 1992.[2] Two additional cases of TPP in Saudis were reported in 2004.[6] Our case is, thus, the fourth reported case of TPP in Saudis. It is prudent to point out though, that there may be other reported cases of TPP in Arabs that may not have been identified, and that cases of TPP may be underreported. Banzal et al[6] attributed this possible underreporting to a low index of suspicion of TPP, probably reinforced by previous reports of its rarity among non-Orientals, and to non-availability of biochemical tests in many health care centers. It could also be argued that other cases of TPP in Arabs may have been identified but were (simply) not reported. The clinical features of TPP classically include the occurrence of sudden and rapidly progressive limb weakness. The weakness typically occurs in males with hyperthyroidism, and usually in the morning upon awakening following rest after heavy exercise, or heavy carbohydrate intake.[1,2,9] The muscle weakness is usually symmetric and more marked in the lower extremities, lasting for a few hours to few days, and typically involves the skeletal muscles. The bulbar, ocular, and respiratory muscles are usually, but not always spared.[9] It is well established that various arrhythmias are associated with hyperthyroidism.[10] Hypokalemia, on the other hand, directly affects the cardiac conduction system and predictably manifests classical ECG findings, in a step-wise fashion matching the drop of serum potassium, ranging from prolonged P-R interval to the unique U-waves.[11] Combined, as the case is with TPP, hyperthyroidism, and hypokalemia may potentially result in a wide variety of cardiac arrhythmias and atrioventricular blocks. During the episodes of TPP, a variety of arrhythmias and conduction defects has been reported,[2,12-14] including ST segment depression, T-wave flattening, sinus tachycardia, prolonged QT interval, U-waves, sinus arrest, ventricular tachycardia, ventricular fibrillation, and Wenckebach atrioventricular blocks.

While mortality from TPP-related arrhythmia is probably unheard of, a fatal case of dysrhythmia has been recently reported in a patient with TPP.[12] On careful review of this report, however, we noted that the fatal arrhythmia was not temporally associated with TPP, as the author concluded. The diagnosis of TPP is straightforward when a high index of suspicion is kept in mind. The characteristic presentation and metabolic findings discussed earlier are difficult to overlook. However, TPP has been underdiagnosed and underreported.[6] The difficulty sometimes is to differentiate TPP from the familial form of periodic paralysis,[6] and therefore, careful review of family history is prudent. Other confusing situations include extremely rare cases of TPP occurring in euthyroid patients.[15]

The molecular basis for TPP has been elucidated. Increased sodium-potassium ATPase activity in

the skeletal muscle potassium channels seems to be responsible for the marked hypokalemia observed during the transient paralytic attacks of TPP.[6,9] Similarly, the genetic basis of TPP was recently suggested as a mutation in the potassium ionic channel gene KCNE3, and differences in the HLA types were speculated as possible causes for the observed ethnic variation.[9]

The cornerstone in the treatment of TPP is timely recognition and diagnosis. High index of suspicion is crucial, as hyperthyroidism is often subtle and other more common differential diagnoses, such as Guillaine Barrett syndrome, may be incorrectly considered early on, and especially before hypokalemia is noted. In one retrospective series of 24 episodes of TPP occurring in 19 patients,[16] the diagnosis was correctly made in one patient only. Although in strict pathophysiological terms, the paralytic attack should resolve spontaneously over time with reversal of the redistribution mechanism, it is not expected that any physician, especially ER physicians, would leave hypokalemia untreated. Therefore, it is recommended to administer potassium, with special relevant protocols being published, to ensure safety of such a critical therapeutic decision-making.[16] However, caution should be practiced herein, since rebound hyperkalemia had been reported.[3,5,16] The ultimate treatment as recommended by most authors, is achieving euthyroidism.

Propranolol has been used in the prophylaxis[17] and treatment of TPP.[16] The clinical outcome of TPP has reportedly been benign with full recovery, however, mortality from TPP has been reported.[12] Our case is consistent in general, with other cases of TPP reported in the world literature. However, it yet presents certain unique features. This case adds the ninth reported case of TPP in native Arabs, and the fourth in Saudis. Of note, although hypokalemia in our case is considered extremely low (1.5 mmol/L), lower potassium levels (1.1 mmol/L) had been reported.[16] However, among TPP cases with identifiable potassium levels reported in Arabs (**Table 1**), no case displayed more severe hypokalemia than our case. The most peculiar aspect of our case is the life-threatening cardiac consequences that occurred in our patient, which happened precipitously and unpredictably. Fortunately, he was attended and resuscitated promptly (being well-monitored in the ER). It is therefore reasonable to suggest that TPP is a serious metabolic disorder with potential serious consequences. While our patient had a full recovery from his life-threatening asystole, a fatal case of dysrhythmia (asystole) has recently been reported in a Caucasian patient with TPP,[12] in which the dysrhythmia and mortality were conceivably attributed to TPP per se. However, the dysrhythmia in the aforementioned case[12] was not very well documented since the patient had a cardiac arrest at home, 3 weeks after radioactive iodine treatment of Graves' disease that had been complicated previously (3 weeks earlier) by TPP, with mild hypokalemia (potassium=2.9 mmol/L). However, at the time of the subsequent fatal cardiac arrest, and while the patient was reportedly in asystole, his potassium was 4.6 mmol/L, arguing against a diagnosis of TPP at the time. Therefore, it could be argued that the patient actually died from a malignant arrhythmia (such as, ventricular tachycardia or fibrillation) due to severe hyperthyroidism, as a rebound response to the radioactive iodine treatment, and not from TPP, as the authors concluded.[12]

In conclusion, we recommend that patients diagnosed with hyperthyroidism must have proper education on the rare occurrence of TPP. They must be given instructions to avoid progression of TPP, by seeking medical attention immediately upon the earliest suggestive symptom. Likewise, physicians should anticipate potential occurrence of serious cardiac arrhythmias, and should take appropriate and quick actions to prevent potentially fatal outcomes.

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