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CASE REPORT

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Thyrotoxicosis factitia: a rare cause of junctional rhythm and cardiac arrest

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ABSTRACT

Thyrotoxicosis factitia is a hyperthyroid state due to the accidental or deliberate thyroxine ingestion. It can have many complications depending upon the organ involved. We present a case of a heavy built athlete presenting with cardiac arrest, who was found to be abused the thyroxine hormone for bodybuilding. Electrocardiogram (EKG) was significant for junctional arrhythmias along with interval supraventricular tachycardia (SVT) and bradycardia. The patient ultimately expired due to a failed resuscitation. To our knowledge, this is the first reported case of junctional arrhythmias caused by exogenous thyroxine.

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Thyroid disease; endocrinology; arrhythmias; cardiovascular medicine

1. Introduction

Exogenous intake of thyroid hormone in the form of pills or supplements has various amounts ofthyroid hormone ranging from per capsule T3 content of 0.97 µg and a T4 content of 3.4 µg to 1.1 µg and 4.5 µg, respectively, [1]. It is most commonly used for the treatment of hypothyroidism; however, it has also been used as a recreational drug and has been abused in high quantities by athletes and gymnasts for body fitness. These levels of exogenous thyroid hormone preparations can easily cause alterations in normal hormone levels and even lead to iatrogenic thyrotoxicosis [2]. A number of complications have been observed, but little is known about the types and incidence of arrhythmias due to exogenous thyroxine. We are highlighting an unusual set of cardiac arrhythmias in a fairly healthy athlete who succumbed to the severe complication of exogenous thyroxine.

2. Case presentation

A 50-year-old female athlete was brought into the emergency department (ED) after a witnessed car accident. Per fiancé she was the only one in the car, was driving normally but all of a sudden she started driving haphazardly. She initially hit the curb on the roadside and was found to be gasped for air, staring into space, and had some irregular, jerky motions. The fiancé tried to pull her out of the car, but she unknowingly hit on the accelerator which led the car to fall into a deep puddle. She was pulled out of the car after this second impact. This time she was completely unresponsive and pulseless. On-site, CPR was started, and EMS was called. She was intubated on the field, had further two rounds of CPR and received six pushes of epinephrine along the way to the hospital. On presenting to the ER, her heart rhythm at this point showed the junctional rhythm. After a few minutes, she again went into the cardiac arrest. CPR was started, and repeat doses of epinephrine were given. Spontaneous circulation was established, but she went into supraventricular narrow complex tachycardia with a heart rate of 180 bpm (bpm) and blood pressure of 110/80. She then received two doses of adenosine and synchronized cardioversion at 100 J with no improvement in tachycardia. She was started on nicardipine gutta(gtt) to slowdown her heart rate, but it was futile, and the heart rate was continuously above 180 bpm, but her BP came down to 100 systolic. She was then started on 5 mg IV lopressor after being transferred to CCU, which resulted in a drastic drop in heart rate and another round of CPR had to be performed for 9 min, followed by two more rounds with the reestablishment of spontaneous circulation and systolic BP by doppler was 40. The patient at this time had bilateral fixed dilated pupils, was unresponsive with variable heart rate and rhythms. Her eyes were red and edematous, but there was no exophthalmos or thyromegaly. Her cardiovascular examination was unremarkable, but the abdomen was mildly distended with a lack of bowel sounds. Chest examination showed bilateral crepitation, while the neurological examination was remarkable for a GCS score of 3/15. Of note, per fiancé, her past medical history was significant for hypothyroidism for which she had been taking thyroid supplements (possibly 'nature thyroid') and prescribed levothyroxine. Her family also revealed that

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she was a very professional gym trainer and had a history of anabolic steroid intake (testosterone, Anavar and Primo). Further history from fiancé indicated that she has been using supplemental products by the name of 'Killer Bee's-fat burner' and thyroxine containing cardine supplements for weight loss and to energy boost up.

3. Investigations

Laboratory workup revealed hemoglobin of 14 g/dL with a white blood cell count of 8000. Serumcreatinine was 2.07 mg/dL, sodium was 155 mEq/L, serum calcium was 6.7 mg/dL, serum phosphorus was 6.5 mg/dL. Thyroid workup revealed a TSH level of 0.057 mmol/L. These investigations are given in Table 1. Her urine drug screening turned out negative. An arterial blood gas showed pH 7.21 with bicarbonate of 18.9 and pCO2 of 19. Her initial EKG showed junctional rhythm with diffuse ST depressions (Figure 1) whereas her 2D echocardiography showed an ejection fraction of 55–60% and impaired LV relaxation. There was mild mitral and tricuspid regurgitation. Chest X-ray showed mixed interstitial and alveolar opacities within the mid and upper lung zones, more on the left side with no cardiomegaly or mediastinal shifting. Chest CT scan revealed extensive dependent airspace disease which could point out to atelectasis or aspiration pneumonia. A head CT scan was performed which revealed global loss of intracranial sulci, slit-like ventricles, and diminished gray-white differentiation, concerning for global anoxic injury and cerebral edema (Figure 2).

Table 1. Laboratory investigations performed on admission.

S. no	Investigation	Result	Normal range
1	Hemoglobin	14 g/dL	12–14 g/dL
2	White blood cells (WBCs)	4.2/L	4.5–11/L
3	pH	7.21	7.35–7.45
4	Blood urea nitrogen (BUN)	32 mg/dL	5–20 mg/dL
5	Lactate	2.1 mmol/L	0.5–1 mmol/L
6	Creatinine	2.07 mg/dL	0.7–1.2 mg/dL
7	Sodium	155 mEq/L	135–145 mEq/L
8	Potassium	4.2 mEq/L	3.5–5 mEq/L
9	Calcium	6.7 mg/dL	8.5–10.5 mg/dL
10	Phosphorus	6.5 mg/dL	2.5–4.5 mg/dL
7	CO_2	19	23–29 mEq/L
8	AST	1291 units/L	10–40 units/L
9	ALT	732 units/L	5–40 units/L
10	Albumin	2.5 g/L	3.5–5.5 g/L
11	TSH	0.057 mmol/L	0.4–4 mmol/L
12	Free T3	>30	75–200 ng/dL
13	Free T4	16 ng/dL	0.7–1.9 ng/dL
14	PO_2	128 mmHg	80–100 mmHg
15	HCO_3	18.9 mEq/L	22–28 mEq/L
16	Troponin T	5.13 ng/mL	<0.4 ng/mL

4. Treatment

An initial diagnosis of cardiogenic shock was made, and the patient was transferred to the CCU. She was put on broad spectrum antibiotics vancomycin, cefepime and levaquin. Norepinephrine was started as the first pressor as she was unable to maintain her blood pressure due to cardiogenic shock. Her mean arterial pressure (MAP) was 63 after being on norepinephrine. Her cerebral edema was managed gradually by monitoring the serum sodium levels and starting patient on low dose hypertonic saline. It was not considered safe by the neurologists to bring her serum sodium level down quickly, as it could worsen her brain edema. Since there was evidence of acute kidney injury, she was started on aggressive fluid therapy and was started on keppra for seizure prophylaxis. Due to respiratory failure, the patient was kept on ventilatory support.

5. Outcome and follow-up

Discussion with the neurologist made it clear that the patient had sustained severe anoxic brain injury with extremely poor prognosis and was brain dead. Planar scintigraphy made evident that there was no

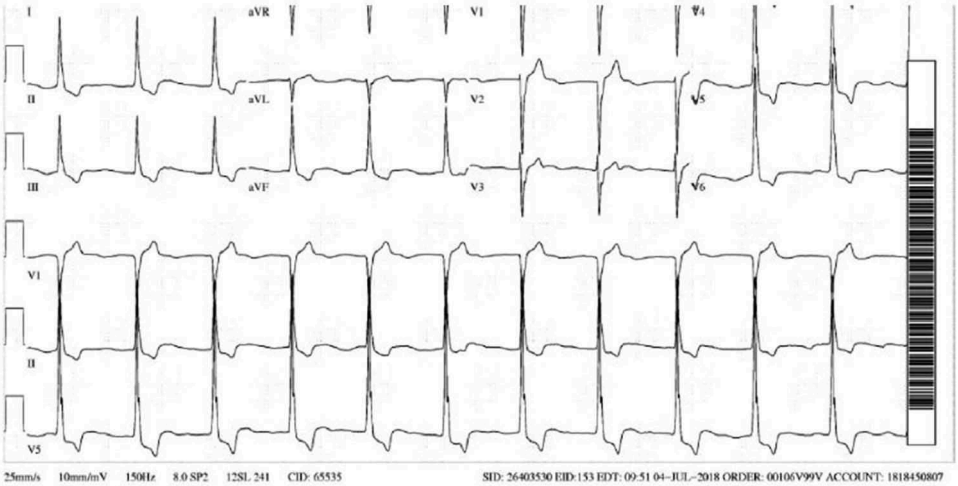

Figure 1. ECG showing the junctional rhythm with some evidence of left ventricular hypertrophy.

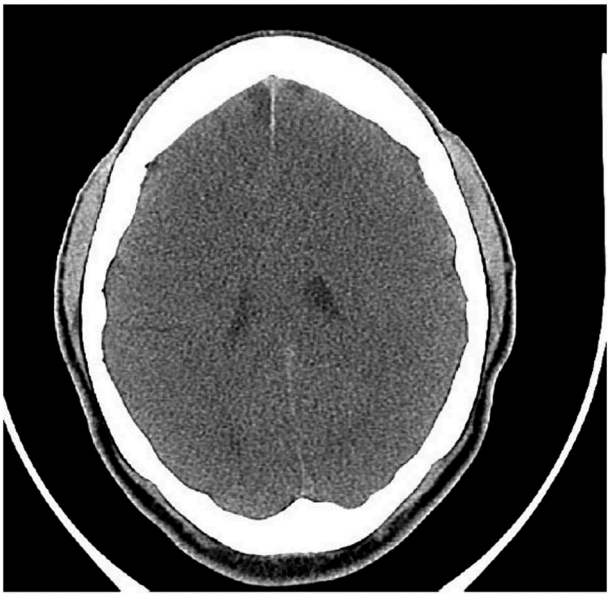

Figure 2. Head non-contrast CT scan showing global loss of intracranial sulci, slit-like ventricles and diminished gray-white differentiation.

detectable blood flow to any part of the brain, and the findings were consistent with brain death. The family was counseled accordingly. She was extubated, and all treatment was withdrawn leading to patient's sad demise.

6. Discussion

A hyperthyroid state can be divided into two main categories, thyrotoxicosis, i.e. hyperfunctioning of the thyroid gland or exogenous intake of thyroid hormone. The thyrotoxicosis state is well known for its numerous adverse effects on the body however little is known regarding the exogenous thyroid hormone toxicities. It can have a variety of adverse effects depending on the system involved and the amount of intoxication. Although the symptoms of hyperthyroidism from factitious ingestion can be similar to the symptoms from thyrotoxicosis including weight loss, heat intolerance, tremor, palpitations, anxiety, increased frequency of bowel movements, or shortness of breath, there can be some physical signs specific to a specific cause. For instance, there will be no exophthalmos and thyromegaly in factitious hyperthyroidism while lid lag and stare can be seen in both exogenous and endogenous hyperthyroidism [3]. Our patient's eyes were red and swollen but since they were reported to be normal before the cardiac arrest that rules out Graves' disease and suggests that swelling of her eyes was as a result of brain edema after the cardiac arrest. Thyrotoxicosis in old age is notorious for cardiac complications while the adverse events related to factitious hyperthyroidism are still unknown.

Following table compares signs and symptoms of exogenous hyperthyroid state versus hyperfunctioning thyroid gland Thyroxine overdose or hyperthyroid state is known to be associated with tachycardia and atrial fibrillation, it can occasionally cause supraventricular tachycardia but there are no data to suggest the mechanism or association of thyroxine-induced junctional rhythm. Our case was unique as the junctional rhythm in the setting of thyroxine overdose was never been reported. Comparison with other reported cases and our approach to the article is described under the heading 'methods' In terms of initial presentation, our case was different as the initial presentation was cardiac arrest and unlike other reported cases our patient had junctional rhythm on presentation rather than tachycardia arrhythmias. Management in previously reported cases was with beta blockers, diazepam, and supportive care because they were having supraventricular tachycardia (SVT). One case responded well and recovered, while the other reported by Bacci et al. was an old-aged patient with nonspecific changes who died. Our case was unique not only in terms of presentation but also the management; she required multiple resuscitative measures, intubation and ultimately had brain death. The characteristics of these cases are shown in Table 2 [4,5].

Our case is the third reported case of thyroxine therapy related to any cardiac arrhythmia and the

System	Symptoms	Signs	Hyper- functioning thyroid gland	Exogenous hyperthyroid state
Cardiovascular	heat intolerance, sweating, and polydipsia, palpitations,	Tachycardia, systolic hypertension, atrial fibrillation, weight loss	Present	Present
Neuromuscular	Tremors, anxiety, Reduced sleep, Nervousness	Hyperactivity, Hyperreflexia, Muscle tenderness	Present	Present
Skin	Increased perspiration	Warm and moist skin	Present	Present
Graves dermopathy	Red, swollen skin on shins and top of feet	Orange peel like skin called pretibial myxedema	Present in Graves disease	Absent
Ocular	Redness and swelling in both eyes	Lid lag, lid retraction	Present	Present
Graves exophthalmos	pain, dryness and photophobia in both eyes	Conjunctivitis, bulging eyes	Present in Graves Disease	Absent
Neck	Dsyphagia, dyspnea, cough, neck tightness	Thyromegaly, hoarseness	Present	Absent

Table 2. Previously reported cases of thyroxine-induced cardiac arrhythmias.

S. no	Author	Age /Sex	Presentation	T3, T4, TSH	Comorbids	EKG	Echo	Treatment	Outcome	FU
1	Bacci V et al [4]	63/F	Lethargy, Unconsciousness	T4 1.2 ug/dL	Hypothyroidism	NSST	LV dilatation	Resuscitation	Death	N/A
2	Hack JB et al [5]	34/M	Vomiting, Diaphoresis, Insomnia, Incoherent speech	T4 13 mcg/dL,	N/A	SVT	N/A	Intubation, Hydration, Activated charcoal, Haloperidol, Diazepam, Phenobarbital, Propranolol	Recovered	N/A
3	Our case	50/F	Cardiac arrest	T3 > 30 mcg/dL, TSH 0.057 mm ol/L	Hypothyroidis m, Anabolic steroid intake	Diffuse ST depression	55–60% EF, Impaired LV relaxation. Mild mitral, tricuspid regurgitation.	Ventilatory support, Antibiotics, Vasopressors, Hypertonic saline, Correction of acidosis, Fluid therapy, Levetiracetam	Death	N/A

first reported case of junctional rhythm in association with thyroid hormone treatment. Moreover, our case for the first time unmasks the reality that thyroid hormone abuse for weight loss and energy boost up just like steroid hormones in athletes can lead to arrhythmias and surprisingly junctional rhythm. Loose et al. postulated that the myocytes mainly depends on T3 as it does not have significant intracellular deiodinase activity [6]. T3 then travels into the myocytes via channels and reaches the nucleus to alter the genetic expression [7]. This explains the thyrotoxicosis induced cardiac complications, but the ingested thyroxine is mostly in T4 form and is not known for severe cardiac complications. Moreover, thyroxine pills rarely cause any arrhythmias as the dosages are well controlled and monitored in the clinical settings. In our case thyroxine was abused for weight loss and energy boost up causing junctional arrhythmias leading to cardiac arrest. The mechanism of these arrhythmias is unknown; however, the generally observed effects of ingested thyroxine on cardiac myocytes are similar to the effects of catecholamines such as tachycardia, increased contractility, increased stroke volume and ejection fraction [8]. This can eventually cause persistent tachycardia, atrial fibrillation, eventually causing a high output heart failure [9–11]. What caused junctional arrhythmias in our case is unknown. Our patient had raised T4 at presentation in the setting of chronic abuse of thyroxine products indicating its role in the causation of junctional arrhythmias.

Palpitations are the most common presenting symptom of hyperthyroidism, in about 10–25% of the patients, more likely in the population age 60 years and above, and usually caused by atrial arrhythmias, e.g., atrial fibrillation [9]. Almost 55% to 75% of the patients with AF secondary to hyperthyroidism without any underlying cardiac disease usually return to normal sinus rhythm within 3 to 6 months after treatment of hyperthyroidism [12]. Other types of arrhythmias can be sinus tachycardia, ventricular tachycardia, SVT, ventricular fibrillation and rarely cardiac arrest can also happen [13–15]. There has been no report of thyroxine-induced junctional rhythm leading to cardiac arrest reported so far.

The mechanism responsible for any possible arrhythmias can be generalized to the effect of thyroxine on the cardiac conduction system. Thyroxine causes early repolarization changes and also increases coronary vascular spasm. A study conducted on 403 patients with various kinds of hyperthyroidism evaluated the types of arrhythmias [16]. Eighty-seven patients (21.5%) had cardiac disturbances. The frequency of the arrhythmias was atrial fibrillation (4.00%), ventricular premature beats (2.77%), paroxysmal supraventricular tachycardia (2.23%), atrial flutter (1.00%). Congestive heart failure occurred in 10.42% of the cases [16]. A forensic analysis of six cases of sudden cardiac death revealed increased cardiac

weight, dilatation of cardiac chambers, diffuse myocardial hypertrophy and focal areas of necrosis [17]. Our case was unique not only because of its presentation but also because thyroxine was abused rather than being used for medical purposes, and this highlights the importance that it should be taken in the therapeutic range only.

The management of thyroid induced cardiac arrhythmias can be divided into two steps. Establishing the normal rhythm and hemodynamic stabilization of the patient followed by treating the underlying hyperthyroid state. Beta blockers help in controlling the heart rate and decrease the peripheral conversion of T4 to T3. An antithyroid drug such as propylthiouracil is preferred over methimazole because of the additional effect of blocking T4 to T3 conversion, although there is some disagreement in avoiding methimazole in this setting since no data show the superior efficacy of propylthiouracil in thyroid storm [18]. Inorganic iodine decreases the release of preformed T4 and T3 and should be given 1 h after antithyroid drugs because iodine can increase hormone production by acting as a substrate for the thyroid synthesis of T4 and T3 if synthesis has not already been blocked with antithyroid drugs. In cases of thyroid storm, fever should be treated with paracetamol; salicylates should be avoided because they increase free T3 and free T4 concentrations by inhibiting T3 and T4 binding to serum proteins [19]. Other medications such as bile acids sequestrants, e.g. cholestyramine bind the free intestinal thyroid hormone and help in its fecal excretion in cases of thyroid storm [20]. Glucocorticoids reduce T4 to T3 conversion and treat the potential risk of adrenal insufficiency due to severe thyrotoxicosis [21]. Our patient, however, did not manifest signs of thyroid storm and presented with thyroid-induced cardiac arrest. She ultimately succumbed to the complications and could not be revived.

Our comprehensive search showed only a few reported cases on factitious thyroxine-induced cardiac complications. The available literature was searched systematically by three authors independently to retrieve all available material on thyroid-induced cardiac arrhythmias, cardiac arrest or myocardial complications. A total of 129 articles were initially obtained using the above search strategy. The titles and abstracts of all these articles were screened for their relevance to our study. One hundred and four articles described different cardiac rhythm problems associated with the hyperfunctioning thyroid gland. Seven of the total articles were about amiodarone-induced thyroid gland abnormalities leading to various arrhythmias while only two articles reported cardiac arrhythmias due to iatrogenic thyroid therapy. The schematic of this search is shown in Figure 3. The thyroxine therapy induced cardiac rhythm abnormalities were reported in one female and one male patient previously. All the patients including ours were young except one reported case of non-specific ST changes leading to the cardiac arrest with levothyroxine ingestion reported by Bacci et al. in a 63 years old patient [4]. Interestingly, the thyroxine levels were normal in this patient [5]

7. Conclusions

- Thyroxine-induced cardiac arrhythmias can range from sinus tachycardia to ventricular fibrillation, and surprisingly it can cause junctional rhythm due to an unknown mechanism.
- Thyroxine if abused for weight loss, energy gain or recreational needs can exceed the tolerated dose and can have detrimental effects on heart rhythm.

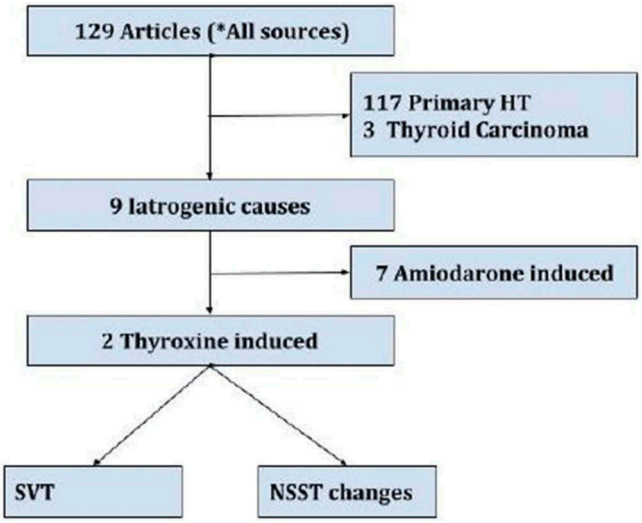

Figure 3. Flow Sheet of literature search and thyroxine-induced cardiac arrhythmias.

- Thyroxine dose regulation and proper disposition are imperative in patients on regular thyroxine therapy for any hypothyroid condition as unexpected side effects are life-threatening.

Disclosure statement

No potential conflict of interest was reported by the authors.

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