CASE REPORT

Reversible Thyrotoxic Dilated Cardiomyopathy

Tariq Nasser[1], ABIM, Faiza A. Qari[2], FRCP, ABIM, Ashraf Banna[3], ABIM and Aysha Tabbakh[4]

[1]Department of Medicine, Division of Endocrinology, King Saud bin Abdulaziz University for Health Sciences, Jeddah, Saudi Arabia
[2]Department of Medicine, Division of Endocrinology, Faculty of Medicine, King Abdulaziz University Jeddah, Saudi Arabia
[3]King Khalid National Guard Hospital, King Abdulaziz Medical City, Jeddah, Saudi Arabia
[4]Faculty of Medicine, Ibn Sina University, Makkah, Saudi Arabia

Correspondence
Prof. Faiza A. Qari
Department of Medicine
Division of Endocrinology
Faculty of Medicine, King Abdulaziz University
P.O. Box 80215, Jeddah 21589
Saudi Arabia
e-M: fgari@kau.edu.sa
faizaqari@gmail.com

Submission: 16 Oct 2019
Accepted: 02 Dec 2019

Citation
Nasser T, Qari FA, Banna A, Tabbakh A. Reversible thyrotoxic dilated cardiomyopathy. JKAU Med Sci 2020; 27(1): 83-88. DOI: 10.4197/Med. 27-1.11

Abstract

Thyrotoxic cardiomyopathy is a rarely diagnosed disease in patients coming into the hospital with hyperthyroidism for the first time. The objective of this case study is to present the rare case of a patient, who was diagnosed with a thyrotoxic cardiomyopathy for the first time.

A 47-year old Saudi male was presented in the King Abdulaziz Medical City in Jeddah, Saudi Arabia in March 2017, with a two-week history of progressive dyspnea, orthopnea, paroxysmal nocturnal dyspnoea, and atrial fibrillation. Following physical examinations and investigations, the diagnosis of thyrotoxicosis was performed. Initially, he was treated with Methimazole, fol-lowed by radioactive therapy, which resulted in the patient's full recovery from cardiomyopathy through the treatment of his thyrotoxicosis.

One of the first symptoms, the manifestation of thyrotoxicosis, is thyrotoxic dilated cardiomyo-pathy. In most cases, it may be completely reversible through the appropriate treatment of the thyrotoxicosis.

Keywords

Thyrotoxicosis; Cardiomyopathy; Congestive heart failure

Introduction

The abnormally elevated serum concentration of the thyroid hormone is responsible for the myocardial dysfunction seen in thyrotoxicosis patients[1]. However, only 1% of the patients with hyperthyroidism also manifests cardiomyopathy and symptomatic congestive heart failure.

The necessity of a normal level of the thyroid hormone is due to its participation in the regulation of the various physiological activities of the cardiac muscles, such as the heart rate, cardiac output, myocardial contractility and relaxation, initiation of the transcription of various genes, such as the α-myosin heavy chain fusion (MHC-α), and receptors, including the β1-adrenergic receptor[2].

In this case study, we present a case of hyperthyroidism-induced reversible cardiomyopathy, which was reversed, following the conventional therapy method. Looking upon such a case, it is clear that being aware of the cardiovascular complications of thyrotoxicosis is crucial, as it is an important cause of mortality in thyrotoxic patients, albeit being reversible.

Case Report

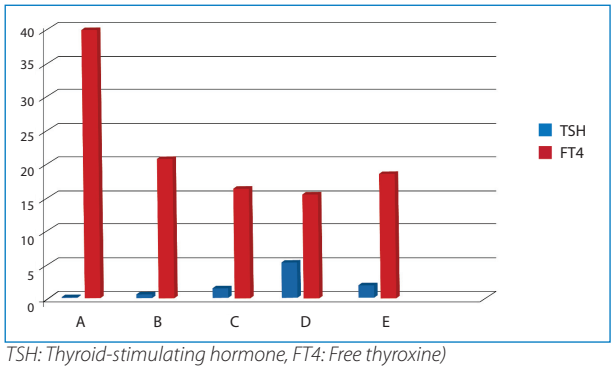
In March 2017, a 47-year old, healthy Saudi male was admitted in the King Abdulaziz Medical City with a two-week history of dyspnea, NYHA class 3- 4, in association with orthopnea, paroxysmal nocturnal dyspnoea, and palpitations. Upon physical examination, he was found with dyspneic condition, anxious, and tremulous, with a body temperature of 37°C, a blood pressure of 140/60 mm Hg, and an irregular pulse of 170 bpm. His Jugular Venous Pressure (JVP) was elected up to 10 cm and upon chest auscultation, bilateral crackles were heard. The thyroid gland was not palpable.

The investigations showed no abnormality in the renal profile or cardiac markers. The thyroid function test (TFT) revealed a suppressed thyroid-stimulating hormone (TSH) to less than 0.01 mIU/L (0.35–0.94), with a free thyroxine (FT4) of 40 pmol/L (9–19 pmol/L) and a free triiodothyronine (FT3) of 24 pmol/L (2.6–5.7 pmol/L). The thyroid-stimulating immunoglobulin level was observed at an elevated level of 20.7 U/L (negative < 1.0).

Furthermore, the electrocardiography (ECG) showed an atrial fibrillation (AF) with a rate of 170 beats/minute. The chest X-ray showed cardiomegaly and pulmonary oedema (cephalization of the lung vasculature, septal lines, and peribronchial cuffing). Through the transthoracic echocardiograms, these demonstrated a dilated left ventricular and a diffused global hypokinesia, with an ejected fraction of 26% and a moderate bi-atrial enlargement. The thyroid ultrasound demonstrated a diffused goiter.

As a result of the initial investigations, the patient was treated as a heart failure case with diuretics, digoxin, metoprolol, ARB, and heparin. However, following a later thyroid technetium scan, a diffused and increased thyroid uptake of technetium was clear. As a result, the patient was diagnosed with a dilated cardiomyopathy secondary to thyrotoxicosis, and he was treated with methimazole, and subsequently, with radioactive iodine, after which, he became hypothyroid, necessitating a replacement of the treatment to levothyroxine.

Three months later, the patient's condition improved, and he no longer suffered from heart failure. However, the atrial fibrillation was persistent, so he underwent electrical cardioversion, with a protocol of



TSH: Thyroid-stimulating hormone, FT4: Free thyroxine)

Figure 1. The thyroid function test during the admission and follow up. (A) On admission; (B) Four weeks after treatment and with methimazole (5 mg q8hr); (C) During the initiation of radioactive iodine therapy; (D) Post radioactive iodine therapy; (E) After the adjustment of Lthyroxine, with a daily dose at 100 mcg.

heparin infusion and anticoagulation for a duration of one week. The cardioversion was successful. His ECG was converted into sinus rhythm, and the administration of anticoagulant was discontinued.

The coronary angiography was planned for the patient for the treatment of ischemia-dilated cardiomyopathy as a cause of his tachycardia and heart failure. However, the patient's condition improved by controlling his thyrotoxicosis.

The echocardiogram was repeated after six months, revealing the resolution of the left atrium, the left ventricle's enlargement, and the left ventricular ejection fraction of 60%. The left ventricular ejection fraction by echocardiograph during admission and the graph showing the improvement of the left ventricular ejection fraction from 26%, followed by prevention in the emergency department to 60% within six months after the treatment with methiamethazole. Currently, the patient has a sinus rhythm and is only maintained on thyroxine for his hypothyroidism, with a regular follow-up in the endocrinology clinic (Fig. 1).

Discussion

Thyrotoxic cardiomyopathy is a rare form of thyrotoxicosis, with around 1% of all thyrotoxicosis cases. Nonetheless, cardiovascular complications, such as cardiac arrhythmia, cardiomyopathy, heart failure, and other forms of myocardial dysfunction, are considered as the number one cause of death in patients with thyrotoxicosis[1,2].

Hyperthyroidism classically begins with non-specific symptoms, such as weight loss, heat intolerance, sweatiness, tremor, and anxiety. The condition may suddenly present itself as cardiovascular manifestations, such as dilated cardiomyopathy and atrial fibrillations, both of which had been observed in this patient[3].

To explain incidences of the dilated cardiomyopathy, one must delve into the realm of pathological cardiac changes. Dilated cardiomyopathy, which is seen in patients with hyperthyroidism, are caused mainly by the effects of triiodothyronine (T3) rather than by the effects of thyroxine (T4). Triiodothyronine exerts its effects in both nuclear and cellular levels. Triiodothyronine thyroid hormones affect the production, as well as the consumption and utilization of energy, using myocytes in three different mechanism[2].

Firstly, the alteration of the normal activity of the oxidative enzymes, namely, the creatine phosphate and the adenosine triphosphate (ATP), increases the consumption of oxygen by the myocytes. Secondly, the thyroid hormone can alter the synthesis of the heavy chain of myosin from its beta to its alpha forms by increasing the transcription of Ca^{++} ATPase gene and by enhancing the uptake of glucose and calcium, which leads to an increase in myocardial contractility with low efficiency[4]. Finally, the third mechanism involves the increase in the T3 levels, which leads to an increase in serum angiotensin-converting enzyme, as well as an increase in the serum erythropoietin. Consequently, this leads to the increased absorption of sodium by the kidneys and an increase of the erythrocytes mass, causing an expansion of the blood volume[5].

As for the causation of the atrial fibrillation (cardiac tachyarrhythmia) in thyrotoxicosis, it is due to the shortened action potential of the sinoatrial cells in combination with the fast-diastolic depolarization. However, relating to the reversibility of the disease, according to Siu *et al.*[6], two-thirds of the patients suffering from cardiac failure due to hyperthyroidism had recovered, following the achievement of the euthyroid state, while the remaining one-third had persistent dilated cardiomyopathy. Furthermore, according to Oliveros-Ruiz *et al.*[7], the recovery of patients suffering from thyrotoxic dilated cardiomyopathy for a shorter duration, *i.e.*, <13 months, is characterized by a response that is better than those who were given thyroidectomy and antithyroid medication. Also, in an experimental study, it was shown that chronic exposure to high levels of thyroid hormones had led to the permanent remodelling of the heart, and thus, the normalization of the thyroid hormone levels failed to induce complete recovery from dilated cardiomyopathy. It can be concluded that, if the patient is restored to his euthyroid state, it is likely that the thyrotoxic cardiomyopathy, due to the left ventricular dysfunction, will be reversed, provided that the disease was diagnosed during its early stages and that the patient was not exposed to high levels of the thyroid hormones.

In a study of a series of patients with hyperthyroidism and congestive heart failure, the mean left ventricular systolic ejection fraction had increased from 28% to 55% after their treatment for thyrotoxicosis. The ejection fraction had normalized in these patients, and an improvement from severe to mild systolic dysfunction was noted in other two patients.

The facts of this case directly support the application of the studies mentioned above. This patient was diagnosed within two weeks since the symptoms first began, and thus, was not exposed to high levels of thyroid hormones for a longer period of time. This may explain the dramatic response and the recovery this patient had to the antithyroid treatment with methimazole and radio-iodine therapies.

Albeit most of the thyrotoxic dilated cardiomyopathy cases are reversible. As mentioned above, reports also stated that some of these cases are irreversible. A possible explanation for the persistence of this condition may be due to the hyperthyroidisms and other cardiac diseases that can cause irreversible changes to the structure of the cardiomyocytes.

Even if the thyrotoxic dilated cardiomyopathy is caused by a disease other than that of hyperthyroidism, the treatment of the hyperthyroidism in these patients is a key factor in the resolution of the cardiomyopathy. In a report made by Umpierrez *et al.*[8], which consisted of a series of seven cases with hyperthyroidism, complicated by heart failure and dilated cardiomyopathy, the patients were given antithyroid medications, and the treatments for heart failure and the rapid improvement of the cardiac function followed. Five out of seven patients recovered completely, the other two showed

relative improvements from severe to a mild degrees of cardiac failure and cardiomyopathy. This indicates that, had the hyperthyroidism in the patients not been recognized, the possible outcomes would have either been the progression of the cardiomyopathy to a severe level or the patient's death.

Thus, it is essential to increase the awareness of physicians, such as primary care physicians or cardiology specialists, about the importance of examining and investigating the patients for hyperthyroidism. The early diagnosis and effective treatment of hyperthyroidism in such patients would save them from the burden of being admitted to the hospital and would also save resources, which would otherwise have been lost in the treatment of the consequences (see above Magner *et al.*[9]).

It should also be noted that it is necessary to differentiate between the two types of tachycardiomyopathy: the rate-related cardiomyopathy that develops as a consequence of cardiac rhythm abnormality, specifically atrial fibrillation, and the cardiomyopathy that develops as a result of the direct toxic effect of the thyroid hormones on the cardiac myocytes. The tachycardiomyopathy responds to the restoration of normal cardiac rhythms by antiarrhythmic medications or cardioversion. However, the distinction is vital in determining when the cardioversions should be given. In the former case, cardioversions should be given as soon as possible, while in the latter case, the patient must reach a euthyroid state, before the cardioversions are given. Here, we would like to recall the case, which was reported by Tsai *et al.*[10], where the cardiomyopathy caused the death of a patient, who was presented with atrial fibrillation due to the cardioversions being given prior to the patient's thyrotoxicosis being treated, thus, reaching a euthyroid state.

The patient in this study was initially treated with methimazole and radioactive iodine, which treated the hyperthyroidism but, instead, made the patient hypothyroid. As a result, the team had to treat him then with levothyroxine, until he had reached the desired euthyroid state after three months of such treatment. Following on, the arterial fibrillation could only then be controlled via electrical cardioversions. What this proved to us was that the patient's arterial fibrillation was not related to thyrotoxicosis.

Conclusions

Following this analysis of thyrotoxic cardiomyopathy and its effects, it is clear that the screening for subclinical or overt hyperthyroidism in all patients with insidiously or abruptly developing cardiac symptomatology should be a part of the guidelines and/or the protocols that are used in all emergency and cardiology units.

Acknowledgments

The authors would like to acknowledge the work and efforts of Ms. Khawla Alnajafi in the initial editing of the spelling, grammar, and structure of this case report.

A written informed consent was obtained from the patient for the publication of this case and the accompanying images.

Conflict of Interest

The authors declares that they have no conflict of interest that is related to this study and this article.

Disclosure

The authors did not receive any type of commercial support either in forms of compensation or financial for this study. The authors have no financial interest in any of the products or devices, or drugs mentioned in this article.

Ethical Approval

The study design was reviewed and approved by the Unit of Biomedical Ethics Research Committee at King Abdulaziz University, Jeddah, Saudi Arabia.

References

[1] Panagoulis C, Halapas A, Chariatis E, Driva P, Matsakas E. Hyperthyroidism and the heart. Hellenic J Cardiol 2008; 49: 169–175.

[2] Veselka J. Thyrotoxic cardiomyopathy: In *Cardiomyopathies - from Basic Research to Clinical Management*. Babenko AY, Bairamov AA, Grineva EN, Ulupova EO, eds. Shanghai: INTECH, 2012. 553–580.

[3] Seigel SC, Hodak SP. Thyrotoxicosis. Med Clin North Am 2012; 96(2): 175–201.

[4] Pearce EN, Yang Q, Benjamin EJ, Aragam J, Vasan RS. Thyroid function and left ventricular structure and function in the Framingham heart study. Thyroid 2010; 20(4): 369–373.

[5] Wang YY, Jiao B, Guo WG, Che HL, Yu ZB. Excessive thyroxine enhances susceptibility to apoptosis and decreases contractility of cardiomyocytes. Mol Cell Endocrinol 2010; 320(1-2): 67–75.

[6] Siu CW, Yeung CY, Lau CP, Kung AW, Tse HF. Incidence, clinical characteristics and outcome of congestive heart failure as the initial presentation in patients with primary hyperthyroidism. Heart 2007; 93: 483–487.

[7] Oliveros-Ruiz L, Vallejo M, Canseco LFD, Cárdenas CM, Hermosillo JAG. Determinants of thyrotoxic cardiomyopathy recovery. BioMed Res Intern 2013; 452709: 1–7.

[8] Umpierrez GE, Challapalli S, Patterson C. Congestive heart failure due to reversible cardiomyopathy in patients with hyperthyroidism. Am J Med Sci 1996; 410: 99–102.

[9] Magner JA, Clark W, Allenby P. Congestive heart failure and sudden death in a young woman with thyrotoxicosis. West J Med 1988; 149: 86–91.

[10] Tsai SH, Chu SJ, Wu CP, Tsai TN, Cheng SM. Acute right ventricular dysfunction after cardioversion in an unrecognized thyrotoxicosis patient. Am J Emerg Med 2006; 24: 631–633.

الشفاء التام من مرض إعتلال عضلة القلب المتسعة بعد علاج تسمم الغدة الدرقية

طارق ناصر[١]، فايزة أحمد قاريح[٢]، أشرف بناع[٣]، عائشة طاب باخ[٤]
[١]قسم الطب قسم الغدد الصماء، جامعة الملك سعود بن عبد العزيز للعلوم الصحية، جدة - المملكة العربية السعودية
[٢]قسم الطب الباطني، وحدة الغدد الصماء، كلية الطب، جامعة الملك عبد العزيز، جدة - المملكة العربية السعودية
[٣]مستشفى الملك خالد للحرس الوطني بمدينة الملك عبدالعزيز الطبية، جدة - المملكة العربية السعودية
[٤]كلية الطب، جامعة ابن سينا، مكة المكرمة - المملكة العربية السعودية

المستخلص. من النادرأن يشخص مريض تسمم الغده الدرقية بإعتلال في عضلة القلب المتسعة ويكون سبب دخوله للتنويم في المستشفي للمرة الاولي.

والهدف من عرض هذه الحالة النادرة جدا، هو سرد قصة مريض شخص بمرض إعتلال عضة القلب المتسعة بسبب تسمم الغده الدرقية لأول مرة في مرضه.

نوم المريض السعودي البالغ من العمر ٤٧ عاما في مدينة الملك عبد العزيز الطبية بجده في المملكة العربية السعودية في مارس ٢٠١٧ م بسبب معاناته للمره الأولي من ضيق في التنفس وخاصة اثناء النوم، و خفقان بسبب الرجفان الأذيني، وبناءا علي الفحص السريري والمخبري شخص بمرض إعتلال عضلة القلب المتسعة بسبب تسمم الغدة الدرقية.

تلقي المريض العلاج اللازم لتسمم الغده الدرقية بدواء الميثامزول، و بعد فتره عولج بجرعة يود مشع، حيث تعافي المريض تماما من مرض إعتلال عضلة القلب المتسعة بعد علاج تسمم الغدة الدرقية.

وخلاصة دراسة هذه الحالة من الأعراض المهمة لتسمم الغدة الدرقية، هو في ظهور مرض إعتلال عضلة القلب المتسعة، وقصور القلب لأول مرة، والتي من الممكن أن يشفى منها المريض تماما بعد علاج تسمم الغده الدرقية.