American Journal of Medical Case Reports, 2021, Vol. 9, No. 3, 194-197
Available online at http://pubs.sciepub.com/ajmcr/9/3/15
Published by Science and Education Publishing
DOI:10.12691/ajmcr-9-3-15

NON-ST-Segment Elevation Myocardial Infarction Associated with Inadvertent Thyroid Hormone Overdose

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Received December 02, 2020; Revised January 05, 2021; Accepted January 14, 2021

Abstract Thyroid hormone has a major role in cardiovascular function and cardiac hemodynamics. A slight change in thyroid affects ventricular function, serum cholesterol levels, increases the risk of coronary artery disease as well as cardiovascular mortality. In this report, we present a 62-year-old female with history significant for ischemic heart disease who was admitted for acute coronary syndrome (ACS) with persistent tachycardia, requiring urgent cardiac catheterization. Complete cardiac workup revealed that the patient had most likely suffered from vasospastic angina secondary to inadvertent overdose of her prescribed levothyroxine. This report emphasizes the significant cardiac complications caused by a deluged hyperadrenergic state secondary to overt hyperthyroidism. We conclude that thyrotoxicosis is a significant risk factor for cardiovascular disease and should be considered as a cause of life-threatening myocardial ischemia, especially in patients with known ischemic heart disease and thyroid disorders.

Keywords: *thyroid hormone, ischemic heart disease, acute coronary syndrome, levothyroxine, hyperthyroidism, cardiovascular disease*

Cite This Article: Andrew V. Doodnauth, Fadi Yacoub, Vaibhavi Solanki, Andrea Trimmingham, Lina Soni, and Samy I. McFarlane, "NON-ST-Segment Elevation Myocardial Infarction Associated with Inadvertent Thyroid Hormone Overdose." *American Journal of Medical Case Reports*, vol. 9, no. 3 (2021): 194-197. doi: 10.12691/ajmcr-9-3-15.

1. Introduction

Acute coronary syndrome (ACS) in the setting of hyperthyroidism is a well-described phenomenon; however, evaluation of thyroid function is quite often overlooked when assessing cardiovascular risk factors. Thyroid hormone has important effects on cardiac muscle, the peripheral circulation, and the sympathetic nervous system that alter cardiovascular hemodynamics in a predictable way. [1] Overt hyperthyroidism is characterized by low serum thyroid-stimulating hormone (TSH) concentrations and raised serum concentrations of thyroid hormones: thyroxine (T4), triiodothyronine (T3), or both. [2] We describe a case of a patient admitted to the cardiac intensive care unit (CICU) for ACS in the setting of overt thyrotoxicosis and known ischemic heart disease. Our discussion focuses on the clinical importance of evaluation of thyroid function as an independent risk factor for cardiovascular disease, particularly in patients with known, or at risk of thyroid disease.

2. Case Description

A 62-year-old female presented to the emergency department with atypical substernal chest pain that was sharp in nature, radiating to her back and worsening with movement. Past medical history was notable for significant triple-vessel coronary artery disease (CAD) with two stents placed in the mid-Left Anterior Descending artery (LAD) and distal Right Coronary artery (RCA), heart failure with reduced ejection fraction (HFrEF) with automated implantable cardioverter-defibrillator (AICD), HIV and hypothyroidism secondary to radiation therapy for esophageal cancer. Additionally, the patient reported a weight loss of eighty pounds over the past six months and multiple episodes of loose stools for several days prior to admission. Upon further review, there were no changes in medications, however, she stated that she missed a month of her prescribed levothyroxine due to insurance reasons and decided to double the dose for the last three weeks prior to admission. She denied the use of any illicit drug use, recent travel or exposure to sick contacts. No other pertinent findings on review of systems were documented.

Vitals were significant for resting tachycardia of 115 beats per minute (bpm). Mild distress was observed on the physical exam. Initial laboratory testing was positive for an elevated troponin I, free thyroxine (free T4) and a suppressed thyroid-stimulating hormone (TSH) level (Table 1). Chart review showed that all laboratory results were within normal limits on last admission just two months prior.

Table 1. Laboratory Data

Variable	Reference Range	On Arrival, The Hospital	12 hr after Arrival, CCU	Day 1, post Esmolol Drip	Day 2, post Esmolol Drip
Days after symptoms onset		0	1	2	3
Hemoglobin (g/dl)	12.0-16.0	11.1	11.1	10.7	10.8
Hematocrit (%)	37.0-47.0	35.1	33.6	32.5	33.6
White-cell count (K/uL)	3.50-10.80	6.88	7.22	5.12	5.07
Differential count (%)					
Neutrophils	40.0-74.0	80.2	53.9		48.4
Lymphocytes	19.0-48.0	11.6	36.5		36.1
Monocytes	0.0-9.0	5.8	5.5		7.3
Eosinophils	0.0-7.0	0.4	1.0		3.4
Platelet count (K/uL)	130-400	263	233	237	225
Sodium (mmol/liter)	136-145	138	135	137	137
Potassium (mmol/liter)	3.5-5.1	4.4	3.9	3.8	4.2
Chloride (mmol/liter)	98-107	102	102	107	107
Carbon dioxide (mmol/liter)	21-31	26	22	22	20
Urea nitrogen (mg/dl)	7-25	16	15	17	18
Creatinine (mg/dl)	0.70-1.30	1.15	1.08	1.24	1.28
Glucose (mg/dl)	70-99	361	233	146	253
Lactate (mmol/liter)	0.5-1.6	1.9			
Calcium (mg/dl)	8.2-10.0	8.8	8.5	8.6	9.0
Ionized calcium (mmol/liter)	1.15-1.29	1.10			
Magnesium (mg/dL)	1.9-2.7		1.6	1.7	1.8
Phosphorus (mg/dl)	2.5-5.0		3.8	4.3	3.7
Alanine aminotransferase (IU/liter)	7-52	17	14	12	
Aspartate aminotransferase (IU/liter)	13-39	20	20	13	
Creatine kinase (IU/liter)	30-223	510	284		
N-terminal pro–B-type natriuretic peptide (pg/ml)	≤100	597	285		
troponin I (ng/mL)	≤0.15	0.26	0.20	0.16	0.07
Thyroid Stimulating Hormone (uIU/mL)	0.38-4.70	<0.05			
T4, Free (ng/dL)	0.71-1.85		2.12		
Thyroxine (ug/dL)	5.2-10.5		14.9		
Prothrombin Time (second)	10.8-13.7				
INR	1.1				
APTT (second)	25.4-38.6		87.2		

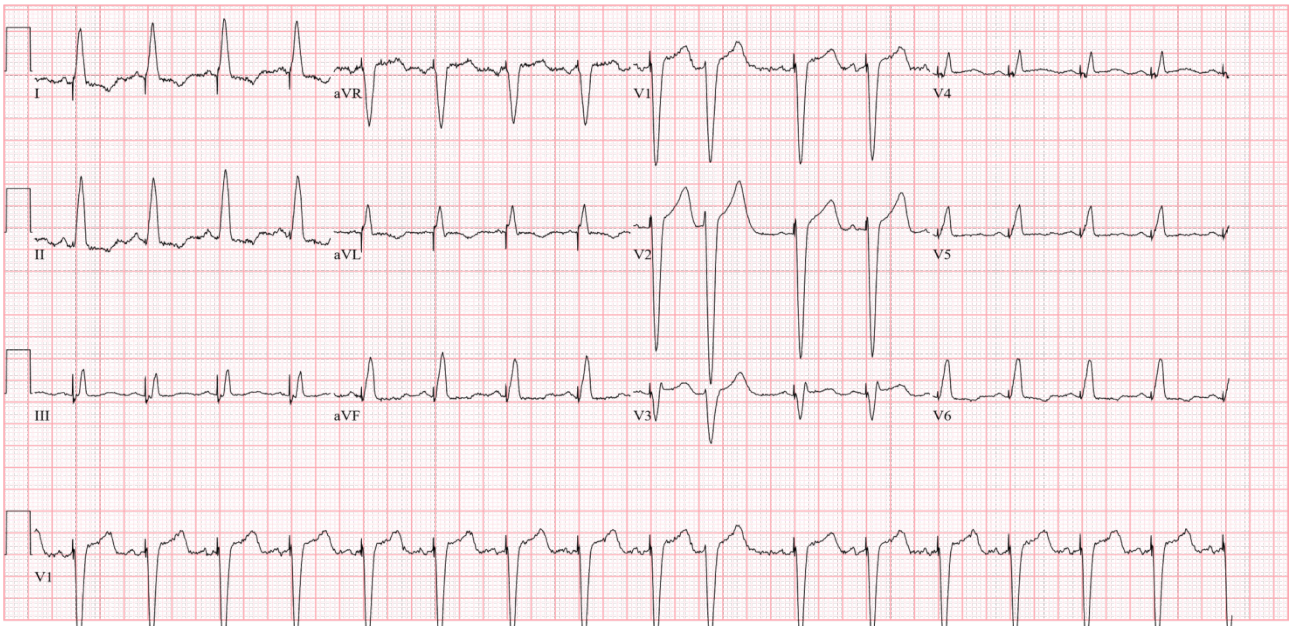

Figure 1. Initial ECG showing atrial-sensed ventricular-paced rhythm with occasional premature ventricular contractions (PVCs). No specific ST-segment changes

Electrocardiography (ECG) showed atrial-sensed ventricular-paced rhythm at 100 beats per minute with occasional premature ventricular complexes, unchanged from baseline (Figure 1). Computed tomographic angiography (CTA) of the chest was negative for pulmonary embolism (PE). Transthoracic echocardiography (TTE) showed ejection fraction (EF) from 35 to 40% with hypokinesis of the anteroseptal wall with normal left ventricular wall thickness. In the emergency department, the patient was adequately resuscitated with IV fluids and was given morphine, sublingual nitroglycerin, antiplatelet therapy and started on a heparin drip. Cardiology was consulted and the patient was admitted to the cardiac intensive care unit (CICU) for further workup for a primary diagnosis of acute coronary syndrome.

Coronary catheterization was performed, clearly demonstrating triple-vessel with two eccentric calcified stenotic lesions in both the distal left main and proximal right coronary arteries (65% and 60%, respectively and 40% occlusion of the distal right coronary artery (RCA). Compared to the prior catheterization report one year earlier, there was no clinical change seen, indicating no intervention at this time (Figure 2).

Serial electrocardiograms (EKG) were performed and serial cardiac troponins were obtained every six hours. The patient continued to have atypical chest pain, along with a continual rise of the cardiac biomarker and a persistently elevated heart rate of greater than 110 bpm despite administering propranolol and holding levothyroxine. A decision was made to start the patient on an esmolol drip with a heart rate goal of 60-70 bpm.

Twenty-four hours later, the patient's heart rate remained stable in the 80’s and the troponins started to down-trend. Complete cardiac workup was completed and the esmolol drip was stopped. All known reversible causes of sinus tachycardia had been ruled out, making inadvertent overdose of levothyroxine an attractive diagnostic entity that is likely the cause of ACS in this patient.

Patient showed improvement and stabilized upon medication adjustments and was discharged home with endocrinology follow-up to restart levothyroxine at an appropriate dose.

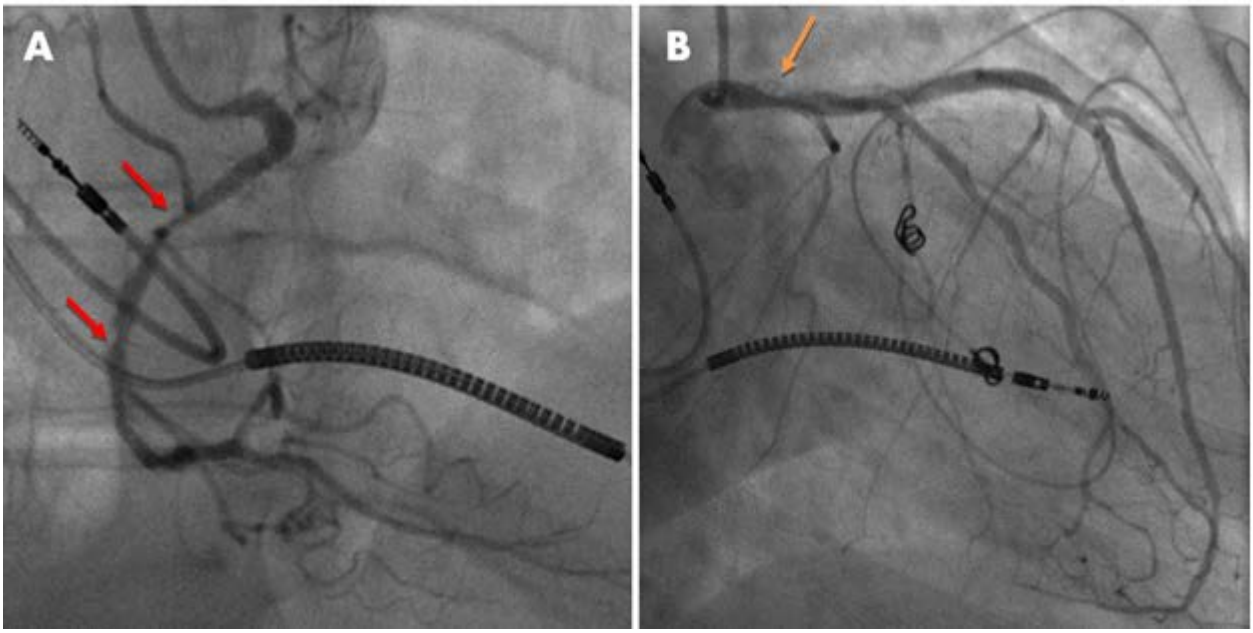

Figure 2. Coronary angiography demonstrating two lesions (proximal / distal) of the right coronary artery (A, red arrows) and one eccentric calcified stenotic lesion in the distal left main coronary artery (B, yellow arrow)

3. Discussion

Thyroid hormones greatly impact energy homeostasis in the heart. The thyroid gland produces two hormones, thyroxine (T4) and triiodothyronine (T3), which have a significant effect on cardiac function and structure. Excess thyroid hormone results in increased numbers and increased sensitivity of adrenergic receptors on the myocardium and on the coronary arteries. For this reason, cardiovascular hemodynamics are altered resulting in tachycardia, hyperdynamic precordium, diastolic relaxation, increased cardiac output, widened pulse pressure, myocardial oxygen consumption and a hypermetabolic state. [3,4]

Molecular mechanisms of thyroid hormones action on the heart have been clearly defined. An uncontrolled hyperthyroid state has been shown to have deleterious repercussions on the hemodynamics of the heart via increased catecholamines and an overactive renin angiotensin aldosterone system.

Characterized by increases in resting heart rate, blood volume, stroke volume, myocardial contractility, ejection fraction and peripheral vasodilation. The reduction in systemic vascular resistance results in decreased renal perfusion pressure and activation of the renin-angiotensin-aldosterone system (RAAS).

The presence of thyroid dysfunction significantly influences the emergence and development of acute coronary syndromes [5]. Our patient presented with ACS secondary to overt hypothyroidism. She had inadvertently taken a higher dosage of her levothyroxine than recommended. Levothyroxine has a narrow therapeutic index, and errors in levothyroxine dosage are known to result in cardiovascular side effects. Althought less common than the typical risk factors for coronary artery disease such as age, sex, presence of smoking, diabetes,

hypertension, dyslipidemia, obesity, psychosocial factors, family history and prior MI, hyperthyroidism has been reported in many cases to be an independent risk factor as well. [3]

Hyperthyroidism of any cause is related to an increased risk of a hypercoagulable state and a mild decrease of coronary reserve. Increased thyroid hormone predisposes to ischemia is by raising the concentrations of von Willebrand Factor, Factor 8, and Factor 9; increase platelet plug formation and levels of plasma fibrinogen and plasminogen activator inhibitor; and decrease levels of tissue plasminogen activator. [3]

The cause of ischemia and infarction in thyrotoxic patients with normal coronary arteries is unclear. It may be due to in situ coronary thrombosis or to a direct metabolic effect of thyroid hormone on the myocardium or be secondary to supraventricular tachycardia or atrial fibrillation. [6] Angina and acute myocardial infarction may occur due to the increased sympathetic activity, causing a catecholamine-induced increased myocardial oxygen demand, inducing coronary vasospasm in patients with underlying coronary artery disease. [6]

Coronary spasm is typically reversible which responds well to nitroglycerin, calcium channel blockers, and decrease in exertion. This was seen in our patient who had chest pain improvement with sublingual nitroglycerin. The pathophysiology of ACS in our patient is likely due to diffuse coronary vasospasm with potentiation of ischemia of diseased territory. Cardiac catheterization performed during admission supports this theory as it showed 65% stenosis of the distal left main, 30% stenosis of the proximal LAD, 40% stenosis of the circumflex and 60% stenosis of the proximal RCA.

4. Conclusion

Thyroid hormone has an essential role in cardiovascular homeostasis, having both direct and indirect actions on the cardiovascular system. Patients with thyroid disease, especially those with hyperthyroidism, often have symptoms and signs indicating changes in cardiovascular hemodynamics. [7]

Mild hormone disorders, even small variations of the thyroid hormone within the physiological range have been linked to adverse cardiovascular prognosis. Thus, clinicians have to consider thyroid function test abnormalities as the case with traditional coronary risk factors that include hypertension, diabetes and dyslipidemia during CCU hospitalization for ACS. Given the literature, we conclude that overt hyperthyroidism of any etiology should be considered as a cause of life-threatening myocardial ischemia, particularly in patients with known atherosclerotic disease.

Acknowledgements

This work is supported, in part, by the efforts of Dr. Moro O. Salifu MD, MPH, MBA, MACP, Professor and Chairman of Medicine through NIMHD Grant number S21MD012474.

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