JOURNAL OF COMMUNITY HOSPITAL INTERNAL MEDICINE PERSPECTIVES
2018, VOL. 8, NO. 5, 292–295
https://doi.org/10.1080/20009666.2018.1514934

Taylor & Francis
Taylor & Francis Group

CASE REPORT

OPEN ACCESS Check for updates

De novo coronary artery disease in graves' disease. coincidence?

Dariush Shahsavari MD [a] and Bryan Zoll BA[b]

[a]Section of Hospital Medicine, Department of Medicine, Lewis Katz School of Medicineat Temple University, Philadelphia, PA, USA; [b]Lewis Katz School of Medicine at Temple University, Philadelphia, PA, USA

ABSTRACT

Hyperthyroidism is associated with increased risk of cardiovascular conditions. We report a case of a 50-year-old woman with no prior cardiac history who presented to the emergency department with shortness of breath, chest pain, lower extremity swelling, and generalized fatigue. She was found to have Graves' Disease (GD) and extensive coronary artery disease (CAD), suggesting the possibility of increased risk of de novo CAD in patients with GD in the absence of other risk factors.

ARTICLE HISTORY
Received 30 June 2018
Accepted 17 August 2018

KEYWORDS
Graves' disease; hyperthyroidism; coronary artery disease; CAD; goiter; de novo

1. Case report

A 50-year-old woman with past medical history of sciatica and seasonal allergies who presented to the emergency department with shortness of breath, chest pain, lower extremity swelling, and generalized fatigue.

Two weeks prior to this presentation, she noticed bilateral ankle swelling after a 2-hour road trip. Over the course of the following days, the swelling worsened and continued to ascend up her legs. A week after the onset leg swelling, she developed a non-radiating midsternal chest tightness and shortness of breath which was resolved with resting. The symptoms were associated with mild nausea but no vomiting. She presented to another hospital for workup including serial troponins, EKG and lower extremity doppler studies, all of which were unremarkable. Transthorathic echocardiogram (TTE) was performed which showed an Ejection Fraction (EF) of 65% with no significant valvular abnormalities or regional wall motion variations. She was discharged on oral furosemide to follow up with her primary care physician.

She visited her primary doctor a few days later and he continued her furosemide with the addition of metoprolol. Over the subsequent (10 days) her symptoms did not improve which prompted her to present to our hospital. During that time, she had also developed a non-productive cough for 2 days. She denied any other symptoms including trouble swallowing, fever, chills, cold symptoms, congestion, nausea, vomiting, diarrhea, constipation, abdominal pain. Upon further questioning, she recalled feeling fatigued for the past five months but denied weight loss, hyperactivity, nervousness, irritability, insomnia, impaired concentration, or tremor. Family history is significant for diabetes in her mother and high blood pressure in her father. There was no family history of heart disease or sudden death in her family.

Her vital signs on arrival showed regular tachycardia (heart rate of 123 beats/minute), temperature of 97.0 degrees of Fahrenheit, blood pressure of 124/70, respiratory rate of 18/minute and Oxygen saturation of 92% on room air. On physical exam, she was well-nourished and did not appear to be in distress. Head and neck were unremarkable. No evidence of exophthalmia was present. Thyroid exam revealed a normal size with no palpable nodules, bruits, or tenderness. Lung exam was remarkable for decreased breath sounds at the bases with fine crackles at the lower and middle lobes on both sides. A regular tachycardic rate was auscultated with no murmurs or gallops. Abdomen was soft with mild suprapubic tenderness. Bowel sounds were within normal limits in all quadrants. Lower extremity exam showed a 2 + bilateral pitting edema which was not tender to touch. Skin exam was normal with no rash or lesions. Neurological exam did not reveal hyperreflexia, muscle wasting, or myopathy.

EKG showed sinus tachycardia. Chest Xray showed diffuse bilateral bronchial wall thickening, pulmonary vascular congestion, and trace pleural effusions on both sides.

Initial Troponin was 0.078 ng/ml and D-dimer at 1,709 ng/ml. Hemoglobin was 9.9 mg/dL with an MCV of 90.3. Triglycerides were 41 mg/dL and total cholesterol was 118 mg/dL with HDL of 97 mg/dL and LDL of 13 mg/dL. The rest of her labs were within normal limits. Due to elevated D-dimer, a CT angiogram of chest was obtained which did not

CONTACT Dariush Shahsavari, MD Dariush.shahsavari@tuhs.temple.edu

show any pulmonary embolism but showed diffuse smooth thickening of the pulmonary interlobular septa suggesting interstitial edema with small bilateral (right greater than left) pleural effusions with adjacent atelectasis. CT also showed evidence of pulmonary hypertension and enlarged heterogeneous, nodular thyroid gland.

Thyroid function test were subsequently ordered which showed TSH (Thyroid Stimulating Hormone) of < 0.00 m[iU]/mL, total T4 of 23.4 ug/dL, and free T4 of 4.69 ng/dL. Total T3 was 433 ng/dL and free T3 was 1,556 pg/dL. TSI (Thyroid Stimulating Immunoglobulin) was 610%. Thyroid ultrasound showed diffuse increased vascularity throughout the heterogenous thyroid gland (Figures 1 & 2). She was started on propranolol 20 mg 3 times a day and methimazole 5 mg 3 times a day and her symptoms as well her heart rate improved.

Overnight, subsequent serial troponins continued to increase to 0.397 ng/ml and then to 2.810 ng/ml, from which point it trended down. She did not have any more chest pain and there were no remarkable changes on repeat serial EKGs except for improving heart rate. A repeat TTE was obtained which demonstrated a moderately reduced systolic function with an estimated EF of 35%. There was severe hypokinesis of the apical wall(s) with milder diffuse hypokinesis of remaining segments. Patient was started on heparin drip and cardiology service was consulted. Patient subsequently underwent a cardiac catheterization which showed a discrete 70% stenosis in the left main coronary vessel with minor luminal irregularities in other areas. She was ultimately taken to the operating room for a LIMA (Left Internal Mammary Artery) to LAD (Left Anterior Descending) artery bypass surgery. She was stable postoperatively and was discharged home after 5 days. She is currently in good health; her symptoms have significantly improved and is being closely followed up by endocrinology and cardiology specialists.

2. Discussion

Hyperthyroidism is defined as an excessive concentration of thyroid hormones from increased synthesis, excessive release, or an extrathyroid source [1]. In the USA, the overall prevalence of hyperthyroidism is 1.2%[2]. Worldwide, hyperthyroidism is known to affect as many as 0.4/1000 women and 0.1/1000 men [3]. Graves disease is the most common pathophysiological process known to drive hyperthyroidism, with toxic nodular goiter second [4]. Other causes include iodine or drug induced, factitious ingestion, and thyroiditis.

Classic symptoms of overt hyperthyroidism include heat intolerance, palpitations, weight loss, dyspnea, tremor, anxiety, fatigue, and irregular menses in women. Stare and lid lag are also known to occur in hyperthyroidism, possibly mediated by increased alpha-adrenergic receptors in peri-ocular tissue [5]. Subclinical hyperthyroidism presents much more vaguely with nonspecific complaints, if

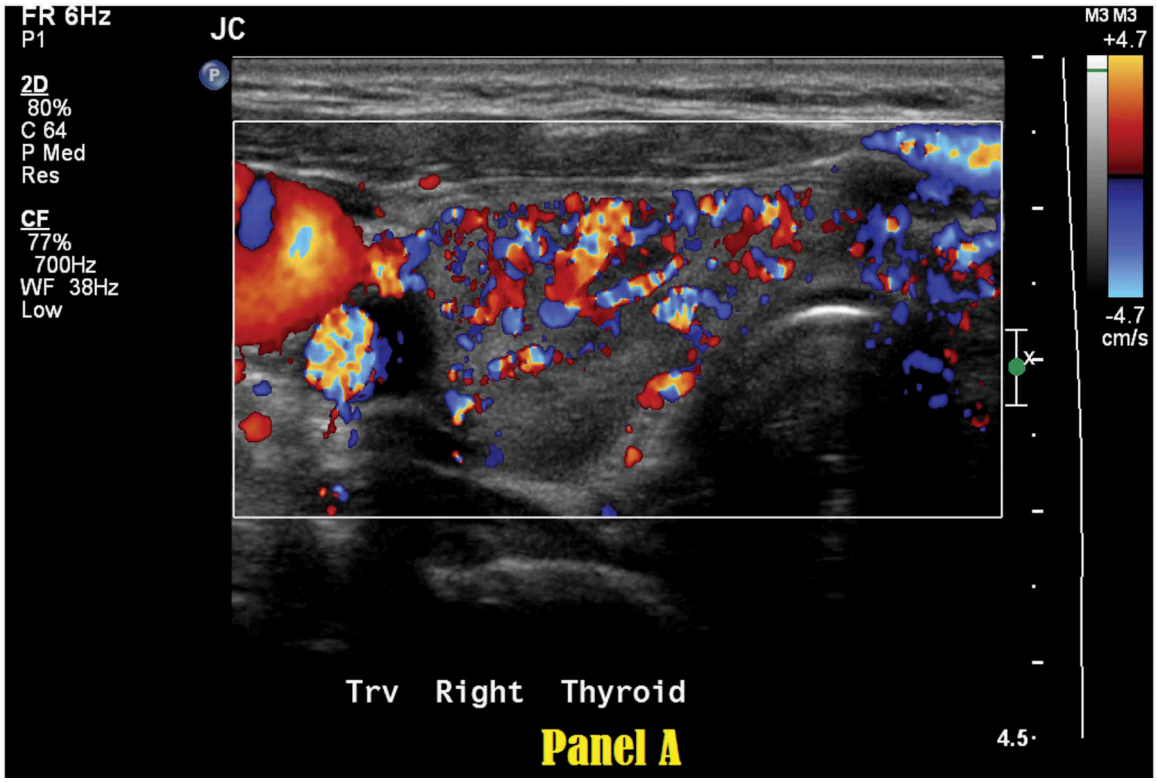

Figure 1. Diffuse thyroid hypervascularity.

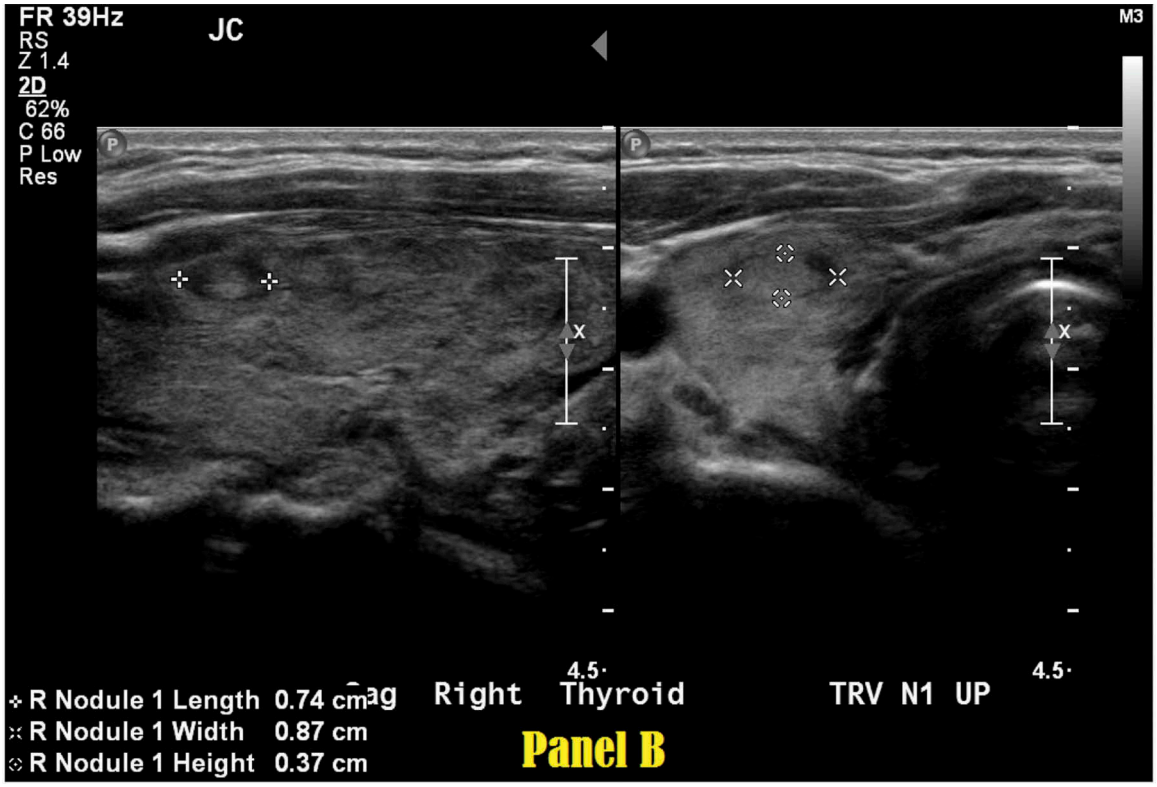

Figure 2. Multiple nodules shown by 'x'.

any at all. Symptoms are more prevalent in younger populations, with a paucity of clinical symptomatology making diagnosis challenging in the elderly [6].

The diagnosis of thyroid disease is confirmed by laboratory evaluation in concert with clinical picture. In patients with clinical symptomatology of hyperthyroidism, the TSH is the best first test. If a low TSH is obtained, a free T3 and T4 is warranted. Other metabolic labs can be abnormal further highlighting a diagnosis of hyperthyroidism. Low serum total HDL, low total cholesterol/HDL ratio, hyperglycemia, and low cortisol have all been reported in hyperthyroid patients [7–9]. Once hyperthyroidism has been established, the cause can be further investigated with thyrotropin receptor antibody testing and radioactive iodine uptake scans.

Treatment is based on a combination of symptomatic and pathologic control. Beta blockers are usually started first for symptom management, helping to improve the adrenergic driven palpitations, tachycardia, anxiety and temperature dysregulation. Thionamides are first line medications to achieve euthyroidism; methimazole and propylthiouracil remain as the most popular choices in this class. Of note, methimazole is teratogenic and as such, PTU should be used exclusively in the first trimester of pregnancy. Failure of medical therapy warrants escalation to radioiodine ablation, and as a last resort, surgical thyroidectomy.

Clinically, hyperthyroidism is associated with increased cardiovascular risk, with up to a 65% increased risk of cardiovascular events [10]. In a study by Dekkers et al, atrial fibrillation (HR 7.32), arterial embolism (HR 6.08) were both dramatically increased in hyperthyroid patients [11]. Isolated right heart failure has also been seen in hyperthyroid patients, likely resulting from the increased circulatory dynamics adding functional stress on the tricuspid valve [12].

Molecular mechanisms drive the cardiovascular risk in hyperthyroidism. Upregulation of alpha myosin heavy chains and inhibition of SERCA can lead to increased myocardial contraction [13]. Prolongation of sodium channel activation, decreased L-type Calcium channels, and upregulation of beta-adrenergic receptors can also influence myocardial contraction [14]. The results of these molecular changes lead to increased stroke volume (from increased preload) and increased heart rate due to increased sympathetic tone. Altogether, these molecular processes can lead to cardiovascular compromise, including sinus tachycardia, atrial fibrillation, tachyarrhythmia, and thyrotoxic cardiomegaly [14].

The link between coronary artery disease and hyperthyroidism is underreported. A study in 2012 by Collet et al reports that subclinical hyperthyroidism was associated with increased CAD mortality (HR 1.29), CAD events (HR 1.21), with risks unaffected by age, sex or preexisting cardiovascular disease [15]. The mechanism behind this increased risk may be increased factor X activity [16]. Additionally, a study by Beyer et al demonstrated increased high

grade and overall stenosis in patients with hyperthyroidism and subclinical hyperthyroidism [17]. In concert with increased coronary calcium score, patients also demonstrated increased non-calcified and lipid rich plaques [17].

To our knowledge, we report the first case of an acute episode of coronary artery disease co-occurring with hyperthyroidism. Although the risks of such events are reported, no defining case has been established. Although our patient has limited historical context as to how long the coronary artery disease or the hyperthyroidism had been present; nonetheless, the co-occurrence of the two symptomatology is worth noting given the mechanistic and pathophysiologic ties. Given the acuity of our patient's presentation, we treated both the CAD (surgically) as well as the hyperthyroidism (medically). In cases where less invasive cardiac care is warranted, it is unclear whether treating the hyperthyroid state will reduce the cardiac pathologic burden. The European Thyroid Association guidelines assert a TSH level of < 0.10 mU/L in elderly patients as treatable to decrease cardiovascular risk; however, robust studies of such recommendations have yet to be completed [18]. Future studies about medical intervention of these two common overlapping clinical entities are merited to guide future care.

Disclosure statement

No potential conflict of interest was reported by the authors.

ORCID

Dariush Shahsavari MD http://orcid.org/0000-0002-4514-6973

References

[1] Kravets I. Hyperthyroidism: diagnosis and treatment. Am Fam Physician. 2016;93(5):3630370.
[2] Bahn Chair RS, Burch HB, Cooper DS, et al. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the american thyroid association and american association of clinical endocrinologists. Thyroid. 2011;21(6):593–646.
[3] Vanderpump M. The eipdemiology of thyroid disease. Br Med Bull. 2011;99(1):39–51.
[4] De Leo S, Lee S, Braverman L. Hyperthyroidism. The Lancet. 2016;388:906–918.
[5] Bilezikian JP, Loeb JN. The influence of hyperthyroidism and hypothyroidism on alpha- and beta-adrenergic receptor systems and adrenergic responsiveness. Endocr Rev. 1983;4(4):378–388.
[6] Trivalle C, Doucet J, Chassagne P, et al. Differences in the signs and symptoms of hyperthyroidism in older and younger patients. J Am Geriatr Soc. 1996;44(1):50–53.
[7] O'Brien T, Katz K, Hodge D, et al. The effect of the treatment of hypothyroidism and hyperthyroidism on plasma lipids and apolipoproteins AI, AII and E. Clin Endocrinol (Oxf). 1997;46(1):17–20.
[8] Mishra SK, Gupta N, Goswami R. Plasma adrenocorticotropin (ACTH) values and cortisol response to 250 and 1 microg ACTH stimulation in patients with hyperthyroidism before and after carbimazole therapy: case-control comparative study. J Clin Endocrinol Metab. J Clin Endocrinol Metab. 2007 ;92(5):1693–1696.
[9] Andersen OO, Fris T, Ottesen B. GLucose tolerance and insulin secretion in hyperthyroidism. Acta Endocrinol (Copenh). 1977;84(3):576–587.
[10] Brandt F, Thvilum M, Almind D, et al. Morbidity before and after the diagnosis of hyperthyroidism: a nationwide register-based study. PLoS One. 2013;8:6.
[11] Dekkers O, Horvath-Puho E, Cannegieter S, et al. Acute cardiovascular events and all-cause mortality in patients with hyperthyroidism: population-based cohort study. Eur J Endocrinol. 2017;176(1):1–9.
[12] Whitner TE, Hudson CJ, Smith TD, et al. Hyperthyroidism presenting as isolated tricuspid regurgitation and right heart failure. Tex Heart Inst J. 2005;32(2):244–245.
[13] Dillmann WH. Biochemical basis of thyroid hormone action in the heart. Am J Med. 1990;88(6):626–630.
[14] Ertek S, Cicero A. Hyperthyroidism and cardiovascular complications: a narrative review on the basis of pathophysiology. Arch Med Sci. 2013;9(5):944–952.
[15] Collet TH, Gussekloo J, Bauer DC, et al. Subclinical hyperthyroidism and the risk of coronary heart disease and mortality. Arch Intern Med. 2012;172(10):799–809.
[16] Erem C. Blood coagulation, fibrinolytic activity and lipid profile in subclinical thyroid disease: subclinical hyperthyroidism increases plasma factor X activity. Clin Endocrinol (Oxf). 2006;64(3):323–329.
[17] Beyer C, Plank F, Friedrick G, et al. Effects of hyperthyroidism on coronary artery disease: acomputed tomography angiography study. Can J Cardiol. 2017;33:1327–1334.
[18] Bondi B, Bartalena L, Cooper DS, et al. The 2015 european thyroid association guidelines on diagnosis and treatment of endogenous subclinical hyperthyroidism. Eur Thyroid J. 2015;4:149–163.