

Isolated right ventricular failure in hyperthyroidism: a clinical dilemma

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Abstract

We present a unique case of a 42-year-old gentleman with newly diagnosed Graves' disease and isolated right ventricular failure. Extensive evaluation to include echocardiogram and cardiac catheterization were negative for significant pulmonary hypertension or coronary artery disease as potential etiologies. Hyperthyroid induced vasospasm is a rare but reported clinical entity that serves to be a clinical and diagnostic dilemma.

Case Report

We report the case of a 42-year old man with a history of pernicious anemia and Graves' disease, without any previous cardiac history, who presented to the emergency department with pleuritic chest discomfort. Three days

before the patient had been diagnosed with Graves' disease manifesting as palpitations, increased night sweats, 20 lb. weight loss over the previous three months, chronic headaches, and thyroid enlargement. On admission, the patient was taking propranolol 60mg twice daily with a planned future radioiodine uptake scan and subsequent ablation on an outpatient basis. Physical examination was significant only for tachycardia and an enlarged thyroid. There was no friction rub, murmurs, or appreciable gallops. Chest X-ray showed marked enlarged cardiac silhouette with pulmonary vascular prominence, right pulmonary artery with pulmonary pruning indicative of history of pulmonary hypertension, and hazy opacities suggestive of heart failure with pulmonary edema (Figure 1). Electrocardiogram showed evidence of right bundle branch block with no ST segment shifts (Figure 2). Three sets of serial cardiac enzymes were negative with a TSH level less than 0.005IU/mL, Free T4 = 7.7ng/dL. The patient was in thyroid storm (Burch-Wartofsky score 40) secondary to his recently diagnosed Graves' disease and treatment was started with methimazole 20 mg daily and prednisone 40mg daily. Dosage of propranolol was increased to 80 mg twice daily. Further cardiac evaluation with a transthoracic echocardiogram showed normal left ventricular size and function with an ejection fraction estimated to be 55-65%. The right ventricle (RV) was severely dilated and hypokinetic with flattening of the interventricular septum during diastole consistent with isolated volume overload (Figure 3). Pulmonary artery peak systolic pressure was estimated to be 40 mmHg with a right atrial pressure of 10 mmHg. There was no evidence of pericardial effusion. A bubble study to evaluate intra-cardiac shunt was negative for evidence of right-to-left or left-to-right shunt. There was no previous echocardiogram available for comparison. On day 2 of hospitalization the patient developed transient ST elevation in the inferior leads with associated chest discomfort which differed from his pleuritic chest pain. Since the patient was allergic to aspirin, administration of clopidogril was started to cover possible acute coronary syndrome; amlodipine 2.5 mg daily was started for possible coronary spasm. Troponin

T rose from negative (<0.01 ng/mL) to indeterminate (0.03 ng/mL) 12 h after the onset of symptoms and serial electrocardiograms (ECG) showed diffuse ST elevations with PR depression consistent with pericarditis and not ST elevation myocardial infarction. The patient was then switched to colchicines 0.6mg twice daily. NSAIDs were contraindicated given his known history of angioedema related to their administration. To complete evaluation, an ECG gated 64-slice CT was performed to evaluate his coronary anatomy and rule out pulmonary embolism (PE) as a potential cause of his right ventricular failure and pulmonary hypertension. This showed a severely enlarged right ventricle, no PE, normal coronary artery origins and normal coronary calcium score. In addition, on some images the proximal right coronary artery (RCA) appeared to be possibly compressed against the chest wall during the diastolic phases (Figure 4).

The patient was then scheduled for a left and right heart catheterization with plans to evaluate further the right coronary artery for possible compression or spasm and to determine the severity of the pulmonary hypertension observed on echocardiography. Coronary angiography did not show any evidence of RCA compression or spasm (Figure 5). Right heart catheterization demonstrated mildly elevated pulmonary artery systolic pressure of 43 mmHg systolic; mean 27 mmHg. Pulmonary capillary wedge pressure was 15. The patient had normal cardiac output of 7.2 L/min by Fick. No shunt was identified on screening venous oxygen concentration measurements. The patient was discharged on colchicine for acute pericarditis, as well as amlodipine for possible coronary spasm.

The patient's echocardiogram was consistent more with a picture of volume overload than with pressure overload, as supported by the patient's only mildly elevated pulmonary pressures on both invasive and non-invasive measurements. In addition, the D-shaped deformity only occurred during diastole and not systole. It was felt that the patient suffered transient coronary spasm which was the cause of his chest discomfort and ECG changes with recurrent inflammation resulting in acute pericarditis.

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Key words: coronary artery, vasospasm, hyperthyroidism, ventricular failure.

The opinions or assertions contained herein are the private views of the authors and are not to be construed as reflecting the Department of the Army or the Department of Defense.

Received for publication: 24 May 2011.
Revision received: 5 August 2011.
Accepted for publication: 5 August 2011.

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Licensee PAGEPress, Italy
Heart International 2011; 6:e11
doi:10.4081/hi.2011.e11

Discussion

Coronary vasospasm is an atypical etiology of myocardial infarction which has only recently been characterized. While there have been numerous case reports in the past of patients presenting with typical signs and symptoms of myocardial infarction in the absence of angiographic evidence of obstructive coronary artery disease, it was not until the Coronary Artery Spasm in Patients With Acute Coronary Syndrome study (CASPAR), published in 2008, that the incidence of coronary artery vasospasm was formally characterized.¹⁻⁴ In



Figure 1. Portable chest X-ray showed engorged pulmonary vasculature and enlarged cardiac silhouette.

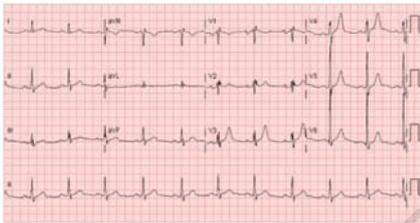


Figure 2. ECG showing left atrial abnormality, rSR', and left ventricular hypertrophy.



Figure 3. Enlarged right ventricle with D-shaped septum in diastole as expected in volume overload state.

this prospective study, patients who presented with acute coronary syndrome underwent elective coronary angiography. Those without evidence of a culprit coronary lesion underwent further testing with intracoronary provocation with acetylcholine to identify the presence of possible coronary artery vasospasm. Of the 28% of patients found to have no angiographic evidence of a culprit lesion, almost half tested positive for coronary artery vasospasm by acetylcholine provocation.⁴ Our institution does not routinely screen for vasospasm and our patient, therefore, did not undergo acetylcholine provocation. He had already received amlodipine which likely would have resulted in a potentially false negative result.

In conjunction with coronary artery vasospasm, hyperthyroidism has also been identified as a possible etiology of acute presentations of myocardial infarction. There have been previous case reports and series

establishing a relationship between hyperthyroidism and reversible pulmonary hypertension with resultant right-sided heart failure.⁵⁻⁸ While several theories have been proposed as to the pathophysiology behind this association, only recently has there been evidence to show the direct effects of thyroid hormone at the level of the endothelium.⁹

In 2001 Napoli *et al.* demonstrated that endothelium was a vascular target for thyroid hormone, and in patients who were hyperthyroid there was marked endothelial vasodilation at baseline due to excessive endothelial production of nitric oxide. In fact, there was an overall increase in the vascular reactivity of the endothelium such that an exaggerated response was seen to nitric oxide and norepinephrine. This abnormal vascular profile was reversed once a euthyroid state was maintained after medical treatment for hyperthyroidism.⁹ In patients presenting with acute coronary syndrome in the setting of reversible ventricular dysfunction and hyperthyroidism, perhaps coronary vasospasm induced by the direct effects of thyroid hormone at supraphysiological levels may be the unidentified culprit lesions in these cases.

In the case of our patient, his presentation of acute coronary syndrome could be explained by his hyperthyroid state with resultant exaggerated endothelial effects on the coronary artery vasculature and possible pressure and volume overload. Given the relative lack of significant obstructive coronary artery disease and normal coronary origins on coronary angiography, as well as by cardiac CT imaging, this remains a plausible explanation for his clinical presentation. What remains unexplained is the relative absence of left sided ventricular dysfunction despite his overall hyperthyroid state.

On echocardiographic testing, our patient's left ventricular function was preserved with an ejection fraction of 60-65%, without evidence of left ventricular hypertrophy, left-sided wall motion abnormalities, or significant diastolic dysfunction. In contrast, there was clear evidence of pure right ventricular dysfunction with a severely dilated right ventricle and atrium, as well as state of volume overload without significant pressure overload. As previously mentioned, there is a relationship between pulmonary hypertension and hyperthyroidism, especially in cases of right-sided heart failure. The level of pulmonary artery hypertension present in this particular patient was mild with a mean pulmonary catheter wedge pressure calculated to be approximately 15 mm Hg and a mean pulmonary arterial pressure of 27 mm Hg. Though not seriously elevated, our finding is consistent with previously published reports of thyrotoxicosis induced right ventricular failure.¹⁰ Isolated right ventricular failure has also been identified in the absence of ACS in



Figure 4. Right coronary artery as visualized on cardiac CT with possible compression in diastolic phase.

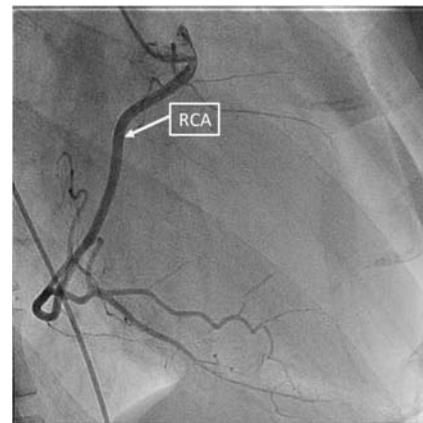


Figure 5. Right coronary artery with no evidence of compression in diastole during invasive angiography and no vasospasm on engagement. No acetylcholine challenge was performed.

patients with thyrotoxicosis. It is well documented that thyroid hormone has direct effects on the inotropic and chronotropic actions of the heart. It is felt that in patients with thyrotoxicosis, right ventricular failure is secondary pressure overload from induced pulmonary hypertension and volume overload from increased cardiac output.¹¹ Another proposed explanation for isolated right ventricular is a direct toxic effect of the thyroid hormone that results in a form of *stunned myocardium* that primarily affects the right ventricle. However, in the literature this is somewhat controversial. Given the dynamic ECG findings with associated chest pain, one has to consider the effects of the patient's hyperthyroid state and the likely coronary vasospasm response with associated volume and pressure overload as a multi-factorial etiology for his right-sided cardiac dysfunction. What makes this case so unique is the diagnostic dilemma which was presented. It is far more common to have both left and right ventricle involvement in hyperthyroid induced cardiomyopathy. Also, the patient's clinical presentation of chest pain with detectable troponins further complicated clinical management. The patient ultimately was treated for coronary vasospasm, pericardi-

tis, and Grave's disease. When he was discharged he was hemodynamically stable, pain free, and follow-up thyroid ablation was programmed. Follow-up transthoracic echocardiogram showed near resolution of the right ventricular dysfunction, chamber enlargement, and unchanged left ventricular ejection fraction of 65%.

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