

Triad of palpitation, angina, and murmur in a non-cardiac patient

Kanupriya Arora, Prasan K. Panda

Department of Medicine, All India Institute of Medical Sciences (AIIMS), Rishikesh, Uttarakhand, India

ABSTRACT

The triad of palpitation, angina, and murmur is a classical feature of cardiac pathology. However, their presence sometimes uncovers a thyroid etiology. Identification well in time decreases out-of-pocket expenditures on illness and suffering. We report a case of a 40-year-old woman who presented with fever with chills, vomiting, palpitations, and shortness of breath for the past month. Also, she described chest pain as typical of angina. Multiple diagnoses were made elsewhere, but none of the treatments resulted in the resolution of symptoms. ST changes were suggestive of ischemic pathology, cardiac MRI done showed up hypertrophied myocardium. After a negative blood culture for infective endocarditis and serology sought for fever work-up, suspicious cardiac examination with a murmur, and an abnormal thyroid profile with a thyroid scan, led to a diagnosis of Graves' disease. This case defines the triad in a noncardiac patient and emphasizes what a thyroid disease does to the heart.

Keywords: Chest pain, fever, Graves' disease, subclinical hyperthyroidism

Introduction

Hyperthyroidism is a disease with multisystemic side effects. Elevated body temperature is a misleading presentation and directs the physician to an infective etiology. The embryological relation of the heart and thyroid, explains a variety of cardiovascular changes ranging from hyperdynamic flow mechanics to rhythm abnormalities and angina could also be a feature.^[1] Heart is an organ which is highly susceptible to thyroid hormones and therefore cardiac manifestations are observed even in subclinical cases of hyperthyroidism. Though there is a small percentage of those with cardiac pathology who develop overt hyperthyroidism.^[2] Thyroid hormones could develop a *de novo* cardiac condition or could uncover

an underlying cardiac pathology. Palpitations comprise 85% of cardiovascular symptoms, dyspnea on exertion and fatigue occurs in 50% of patients. Angina pectoris is uncommon among them. Such a presentation could simulate ischemic pathology, an underneath coronary disease, which is more common and should always be ruled out. The most common cardiovascular finding on examination is tachycardia, with 90% of them experiencing it. Bounding peripheral pulses, a wide pulse pressure, an active precordium, an increase in the intensity of heart sounds, are common findings, with systolic ejection murmur in up to 50% of cases.^[3] These findings hold importance in being common but a differential should always be thought of, as systolic murmur is now also being related to mitral valve prolapse in thyroid disease. Palpitation, angina, and murmur together in a patient with no underlying cardiac pathology may hint at a thyroid etiology.

Thereby, we report a middle-aged lady who wasted 1 month with detailed fever work-up and cardiac evaluations for her clinical presentations but later confirmed to have Graves.

Address for correspondence: Dr. Prasan K. Panda, Department of Medicine, Sixth Floor, College Block, All India Institute of Medical Sciences (AIIMS), Rishikesh, Uttarakhand - 249 203, India.
E-mail: motherprasanna@rediffmail.com

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Case Report

A 40-year-old housewife presented with fever associated with multiple episodes of vomiting for the past month. She had palpitations, chest pain, and shortness of breath for the same duration. Fever was gradual in onset and remained throughout the day with associated chills vomiting was nonprojectile and nonbilious in nature with intolerance to any intake of food. Palpitations were intermittent, exertional, regular type, associated with episodes of exertional chest pain more in the middle part along with radiation to her left hand which resolved at rest. Her shortness of breath was progressive in nature ultimately limiting her daily activities since last week and mild nonproductive cough. She visited multiple hospitals where she was given a provisional diagnosis of dengue fever, malarial fever, and typhoid fever at different times for which she was treated accordingly with no significant relief. She had no other manifestations or co-morbidities or any history of substance abuse.

As trans-thoracic echocardiography was normal, she was referred to our tertiary care hospital for cardiac-consultation along with angiography to manage angina, for trans-esophageal echocardiography to rule out subtle rheumatic heart disease or infective endocarditis (IE), and even for starting the prolonged empirical antibiotic course to treat IE.

On examination, she had tachycardia and was tachypneic with normal oxygen saturation, having a blood pressure of 150/90 mm Hg but afebrile on presentation. Cardiovascular examination revealed a mid-systolic murmur in the suprasternal region, radiating to the neck, with normal S1 S2. No abnormality was detected in other systems.

Electrocardiogram (EKG) revealed sinus tachycardia with left ventricular (LV) hypertrophy and inferior wall ischemia changes. Transthoracic echocardiography confirmed the same. Routine hemogram, liver, and kidney function tests were normal. Three blood culture samples in view of infective endocarditis, from different sites, reported sterile. Infective work-ups for dengue, scrub typhus, malaria, hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), and enteric fever came negative. Her initial thyroid profile showed features of hyperthyroidism {TSH - 0.037 m IU/L (low), FT4-22.0 (high), FT3-49.9 (high)}. An ophthalmology consultation was taken to rule out Graves ophthalmopathy but came to be insignificant. Anti-TPO was normal, ultrasonography neck suggested features of thyroiditis. A thyroid scan was performed that reported Graves disease and at the same time, a cardiac MRI was also done that reported mild concentric left ventricular hypertrophy.

Tab. propranolol 40 mg twice daily and Tab. neomarcazole 10 mg thrice daily were started immediately as thyroid profile revealed hyperthyroidism. During the hospital stay, propranolol was increased to 40 mg PO thrice daily. Gradually, she improved with other supportive treatments (clonazepam and pantoprazole). She developed mild hypokalemia that was corrected with oral potassium supplementation.

Her majority of symptoms resolved. Heart rate and blood pressure normalized. She was discharged with medications and advised to remain in follow-up in Medicine and Nuclear Medicine for radioiodine therapy. On her last follow-up at 1-month, she is living a normal life, and repeat thyroid function tests were within a normal range.

Discussion

The key approach, in this case, is a triad of angina, palpitation, and murmur along with hyperdynamic circulation in a middle-aged woman prompts thyroid profile to rule out hyperthyroidism. Fever is not rare in thyrotoxicosis, if present with other findings like the above triad. Thyroid disease should be suspected first and ruled out before going for extensive evaluations and treatment.

EKG showing ST-segment changes with a history of typical angina, an ischemic cardiac pathology was thought of. It is no wonder to have an ischemic finding in a hyperthyroid, as literature mentions angina although uncommon, as a result of mismatch or could be due to vasospasm, usually, an obstructive coronary artery disease is the one to be thought of first.^[3] Mismatch in blood supply and demand is a result of hypertrophied myocardium. Thyroid hormones target myosin heavy chain-alpha, sarcoplasmic reticulum calcium-ATPase, Na K-ATPase, beta-1 adrenergic receptor, cardiac troponin-I, and atrial natriuretic peptide, activating these and repressing MHC-beta.^[4-8] Differential activation of MHC-alpha and repression of MHC-beta, causes a shift in isoform expression, increasing V1, and decreasing V3. Higher ATPase enzymatic activity of V1 leads to an increase in muscle fibre velocity and subsequent shortening.^[9-11] This increases myocardial contractility, left ventricle mass, and an increase in heart rate. Thereby, angina, not a common attribute to hyperthyroid, if present with other findings like palpitation and murmur, thyroid disease should always be suspected.

Palpitation due to tachycardia being the most common cardiovascular finding due to hyperthyroidism. Rhythm defects are not uncommon in the pathology discussed, out of which atrial fibrillation is most prevalent, and negligible association with VT, SVT. Atrial fibrillation may present with subclinical hyperthyroidism as the heart responds to minimal changes in serum thyroid, even in T3, T4 normal, and suppression of TSH.^[12] There is evidence of conduction defects at the atrioventricular junction – shortened PR interval being most common followed by intra-atrial conduction abnormalities – increase in the duration or notching of the P wave and delayed in intraventricular conduction with a right bundle-branch block.^[13]

Hyperdynamic flow due to high cardiac output state, due to increased cardiac muscle strength is a direct effect of thyroid hormones, or indirectly due to increase in basal metabolic rate. As a result, systolic ejection murmur is found in 50% of cases. In our case, a mid-systolic murmur was heard radiating to the suprasternal region with normal heart sounds. The intensity of heart sounds may increase.^[3] Researchers also described a

systolic scratchy sound as rubbing of hyperdynamic pericardium against pleura and named it Means Lerman scratch.^[14] Bounding peripheral pulses and wide pulse pressure, are other vascular manifestations due to hyperdynamic flow, which could even cause mitral valve prolapse, or it may have a genetic role.^[15,16]

Hyperthyroidism can complicate pre-existing cardiac disease or may cause cardiac complications such as heart failure. A case series on cardiac findings in a hyperthyroid could be more supportive of the triad and suggest varied other findings. Angina, palpitation, and murmur defining clinical cardiac features of a hyperthyroid, is what was observed in a previously misdiagnosed case of Graves'. This triad could make an easy catch to go for thyroid profile and help early detection as the heart gets affected even in subclinical hyperthyroidism.

Conclusions

Triad of angina, palpitation, and murmur, sum ups the cardiac manifestation in hyperthyroid. The systemic examination is of immense importance like auscultation finding, in this case, had a leading role in putting symptoms together and heading towards thyroid workup. Cardiac changes may come early in course of hyperthyroidism.

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Conflicts of interest

There are no conflicts of interest.

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