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Hyperthyroidism and Cardiac Arrhythmia: Symptoms Necessitate Screening

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PERMISSION

Title: Hyperthyroidism and Cardiac Arrhythmia: Symptoms Necessitate Screening

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Abstract

The United States Preventative Services Task Force, the American Thyroid Association and the American Association of Clinical Endocrinologists offer no screening guidelines for cardiac arrhythmia in patients with hyperthyroidism. Signs and symptoms of hyperthyroidism are often nonspecific or even non-existent, especially in elderly patients. Reports indicate that 20 percent of patients with hyperthyroidism also have the cardiac arrhythmia atrial fibrillation. Consequences of atrial fibrillation can be serious and are very important to avoid. If hyperthyroidism and atrial fibrillation are occurring concomitantly, the treatment of the hyperthyroidism leads to conversion to normal sinus rhythm in many patients. Therefore, providers must detect and treat these conditions but the guidelines are unclear about when to screen.

A case studying hyperthyroidism which was discovered in a 65 year old male who presented with subtle symptoms is detailed. His hyperthyroidism places him at risk for atrial fibrillation. In the clinic office his electrocardiogram was normal but he did reveal symptoms of intermittent arrhythmia on review of systems. Therefore, further testing with Holter monitoring was ordered to rule out the dangerous condition of atrial fibrillation which often occurs in patients with hyperthyroidism.

This case study highlights the importance of a thorough history and physical to identify hyperthyroidism, atrial fibrillation or both. It is recommended that guidelines not dictate screening for cardiac arrhythmias in patients found to have hyperthyroidism, but that diligent health care providers trust their interviewing and assessment skills to determine when to screen.

Hyperthyroidism and Cardiac Arrhythmia: Symptoms Necessitate Screening

The United States Preventative Services Task Force (USPSTF) states that there is insufficient evidence to routinely screen for thyroid dysfunction in adults who are asymptomatic (Agency for Healthcare Research and Quality, 2011). Selmer et al. (2013) report that 20 percent of patients with hyperthyroidism also have the cardiac arrhythmia atrial fibrillation. Tachycardia, premature atrial contractions and premature ventricular contractions are also commonly seen in patients with hyperthyroidism (Buscemi et al., 2007). USPSTF, the American Thyroid Association and the American Association of Clinical Endocrinologists offer no screening guidelines for cardiac arrhythmia in patients with hyperthyroidism (Agency for Healthcare Research and Quality, 2011; Bahn et al., 2011).

This paper presents a case of endogenous hyperthyroidism detected in a primary care clinic in rural North Dakota. The patient's chief complaint was night time awakening and inability to return to sleep. Only after further investigation and review of systems by the clinician does the patient report occasional vague cardiac symptomology. The subtlety of presentation may cause a well-meaning provider to miss the diagnosis and leave a patient untreated and potentially to suffer the cardiac sequela of hyperthyroidism.

Thyroid dysfunction can lead to other medical problems. Hyperthyroidism is a modifiable risk factor for the development of atrial fibrillation and heart failure (Biondi, 2012). The purpose of this report is to address the evidence that hyperthyroidism and atrial fibrillation are often seen together in the same patient and that clinicians must be keenly aware of symptoms of either condition that may necessitate screening.

Case Report

The subject was a 65 year old man who came into his family practice clinic in rural North Dakota with a chief complaint of being unable to sleep resulting in feeling tired during the daytime. His own past medical history is unremarkable with the exception of benign positional vertigo, which he had not experienced in quite some time. He took multivitamins and a calcium supplement daily. He was retired, lived with his wife and was a life-long non-smoker. He walked daily with his wife and enjoyed hobbies such as woodworking. His family history was significant for diabetes in his father, Alzheimer disease and "heart problems" in his mother.

History of Present Illness

In addressing more deeply his chief complaint it was found that he had been able to fall asleep easily but he awakened "a few hours later" and was unable to return to sleep. The onset of this pattern was about 6 weeks ago. On the day of the office visit he reported that it had been happening every night. He had not tried sleeping medication. He had decreased his daytime caffeine intake. He followed appropriate sleep hygiene and used a routine for retiring to bed that had not changed from what had been successful in the past. He was unable to identify the stimulant of his awakenings and he denied culprits such as pain, need to urinate or restless legs. He did not snore nor did he describe symptoms of sleep apnea. He had not been under additional stress nor had he been feeling more anxious than usual during the last 6 weeks since his chief complaint began.

Review of Systems

A review of systems revealed that he was also feeling forgetful occasionally. He also reported a weight loss of about 10 pounds over the last 6 weeks, which was unintentional. He described feeling unable to "stay on task" and having a "shorter temper than usual." He had

been attributing these changes to his lack of sleep. Also, once per day, the subject reported feeling a "flutter" in his chest which he did not experience prior to the onset of his sleeping trouble. He denied chest pain or pressure at any time. He also denied orthopnea, dizziness, numbness, or tingling. He felt that his activity tolerance may have been slightly decreased and he had been attributing this to his feeling tired during the day. He denied shortness of breath, coughing and nasal congestion. He did not experience painful joints, his bowel and bladder habits had not changed. He denied nocturia. He denied polyuria and polydipsia.

Physical Examination

His vital signs revealed a heart rate of 96 beats per minute, blood pressure of 124/84 and temperature of 99.4 degrees F taken orally. These are all very slightly on the higher end of normal. His respiratory rate was 12 breaths per minute. His weight was 136 pounds, a 10 pound decrease from 6 weeks ago. He was a pleasantly conversant, alert, oriented, and well-groomed man who appeared in no acute distress. He was dressed appropriately for a winter day in North Dakota. Neck revealed a slightly enlarged thyroid gland with no palpable nodules. The neck was also supple, non-tender and without palpable lymph nodes. Chest was clear to auscultation throughout all lung fields. Regular heart rate and rhythm was appreciated on exam. S1 and S2 heart sounds with no murmurs, clicks or gallops were noted. There was no peripheral edema and no carotid bruit. Dorsalis pedis and posterior tibial pulses were easily palpable bilaterally. He exhibited a normal monofilament exam on both feet. His abdomen was soft and non-tender with present bowel sounds in all four quadrants. Skin was intact and without abnormality. There were no tremors. Fine and gross motor skills were appropriate and reflexes were normal.

Lab values. On the day of this visit serum TSH, free T4, hemoglobin A1C and basic metabolic panel were drawn and evaluated. His TSH resulted slightly on the low side at 0.23

mIU/L, with normal range considered to be 0.45-4.5 mIU/L. The free T4 resulted within the normal limits at 0.93 ng/dL with the normal value range considered to be 0.8-2.4 ng/dL. His hemoglobin A1C was normal as were all of his electrolytes.

Electrocardiogram. An electrocardiogram was performed in light of the cardiac rhythm irregularities he described feeling daily. The results represented normal sinus rhythm with a rate of 96 beats per minute. There were no ectopic beats on this sample and each QRS complex was preceded by a P wave indicative of a normal electrocardiogram while in the clinic office.

Thyroid imaging. A thyroid ultrasound was performed and revealed a slightly enlarged thyroid gland with no nodules.

Differential Diagnosis

Initial differential diagnoses were hyperthyroidism, atrial fibrillation, other cardiac arrhythmia or diabetes mellitus. Electrocardiogram ruled out current or sustained atrial fibrillation or other cardiac arrhythmia. Electrolytes within normal limits were reassuring in this area as well. Hemoglobin A1C below 5.7% ruled out diabetes.

His lab work points the provider toward the diagnosis of hyperthyroidism and the symptoms of sleeplessness, unintended weight loss, inattention, slightly elevated heart rate and temperature support that diagnosis. Transient or intermittent cardiac rhythmatic abnormalities are not able to be ruled out.

Treatment Plan and Follow Up

It was planned for the patient to visit with an endocrinologist. On the day of the primary care visit he was prescribed Atenolol 25-50 mg nightly for symptom management. He was also sent home with a Holter monitor for 48 hours with the goal of catching a view of the "flutter" he described feeling in his chest. It was recommended that he return to the primary care provider

after completing the Holter monitor testing and again after seeing the endocrinologist for follow up and discussion of the plan moving forward.

Literature Review

Hyperthyroidism is a form of thyrotoxicosis and is a result of excessive synthesis and secretion of thyroid hormone by the thyroid gland (Bahn et al., 2011). Hyperthyroidism, both overt and subclinical, can be the result of endogenous or exogenous factors. Endogenous hyperthyroidism is found in 1.2% of the population (Bahn et al., 2011; Poola, Mathiason, & Caplan, 2011). Subclinical hyperthyroidism is characterized by a low serum thyroid stimulating hormone (TSH) level while the free thyroxine (free T4) and total or free triiodothyronine (T3) levels are still within normal limits. Subclinical hyperthyroidism is further divided into two classifications; low but detectable TSH levels between 0.1 to 0.4 mIU/L and suppressed TSH levels of below 0.1 mIU/L (Bahn et al., 2011; Collet et al., 2012; Donangelo & Braunstein, 2011; Ertek & Cicero, 2013). Causes of endogenous hyperthyroidism include Grave's disease, thyroid hormone producing thyroid adenoma or toxic multi-nodular goiter.

Exogenous hyperthyroidism may be related to treatment of hypothyroidism with excessive thyroid hormone replacement (Donangelo & Braunstein, 2011; Canaris, Manowitz, Mayor, & Ridgway, 2000). It is cited by Canaris, Manowitz, Mayor, and Ridgway (2000) that as many as 20 percent of those treated for hypothyroidism fall in to this exogenous hyperthyroid state because of over treatment of the poorly functioning thyroid gland seen in their original thyroid disorder.

The case study subject would fall into the low but detectable TSH category of subclinical hyperthyroidism with his low TSH of 0.23 mIU/L and his free T4 of 0.93 ng/dL being within normal range. His condition is endogenous. The term subclinical implies asymptomatic but it is

important to remember that the subject did present with symptoms, although vague at first. This patient was appropriately screened for hyperthyroidism considering his symptomatology.

Expected subjective signs of hyperthyroidism include palpitations, tachycardia, fatigue, and temperature increase with heat intolerance and weight loss (Seidel et al., 2011). It is important to note that signs and symptoms of hyperthyroidism, both overt and subclinical, are often nonspecific or even non-existent especially in elderly patients (Palacios, Pascual-Corrales, & Galofre, 2012). Thus an extensive probe of the patient's history of present illness may be necessary for detection. Older adults with untreated overt or subclinical hyperthyroidism may experience such cardiac complications as atrial fibrillation, embolic events, and heart failure (Biondi, 2012; Palacios, Pascual-Corrales, & Galofre, 2012; Selmer et al., 2013). It is important for providers to identify symptoms of hyperthyroidism, cardiac arrhythmias or both so that patients can be appropriately screened and treated if need be.

While the most obvious thyroid related cardiac complications are seen in overt hyperthyroidism, it has also been proven that subclinical hyperthyroidism is associated with problematic cardiac function (Cappola et al., 2006; Collet et al., 2012; Donangelo & Braunstein, 2011; Ertek & Cicero, 2013; Sawin, Geller, & Wolf, 1994). The provider in this case study considered that intermittent atrial fibrillation or another cardiac arrhythmia could have been responsible for the "flutter" he reported feeling in his chest daily. In a large cohort study, Sawin, Geller, and Wolf (1994) found that the presence of subclinical hyperthyroidism tripled the risk of atrial fibrillation in patients over 60 years of age. Cappola et al. (2006) concluded that subclinical hyperthyroidism is independently associated with the development of atrial fibrillation in the 13 year follow up period used in their large cohort study of men and women over 65 years of age in the United States. Atrial fibrillation is a cardiac arrhythmia in which the

atria quiver instead of having organized contractions. As a result of the incoordination of the atria, cardiac output may be decreased by up to 20% (National Collaborating Centre for Chronic Conditions, 2006 (NCCCC). Complications associated with atrial fibrillation come with significant morbidity and mortality such as heart failure, embolic stroke or pulmonary embolism. According to Greener (2010) having atrial fibrillation increases the chance of stroke by four to five times, the risk of dementia is doubled and the chance of developing heart failure triples. Correction of thyroid hormone levels leads two thirds of patients with hyperthyroidism and atrial fibrillation to convert to normal sinus rhythm thus decreasing the risks associated with either condition (Bielecka-Dabrowa, Mikhailidis, Rysz & Banach, 2009).

A large cohort study conducted by Selmer et al. (2013) in Denmark lead to the surveillance of 145,623 people with new-onset atrial fibrillation. The researchers studied the new-onset atrial fibrillation patients to determine how many would develop hyperthyroidism within the follow up period compared to the general population. This research uncovered that one out of every twenty five participants with new-onset atrial fibrillation who were euthyroid at time of that diagnosis went on to develop hyperthyroidism that necessitated intervention. The risk of hyperthyroidism was doubled in the presence of atrial fibrillation and that risk increased by three fold for middle-aged men when compared to the general population of Denmark (Selmer et al., 2013). It is hypothesized by Selmer et al. (2013) that minute fluctuations in thyroid function such as a small decrease in TSH and/or slight increase in free T4 levels could instigate the onset of atrial fibrillation. These fluctuations could even remain within the normal laboratory reference ranges, as seen in the laboratory findings of subclinical hyperthyroidism, but deviate from the range which is normally functional to the specific patient. In such a situation, the diagnosis of hyperthyroidism might not be made until after the diagnosis of atrial fibrillation

(Selmer et al., 2013). It is beneficial to uncover and treat thyroid dysfunction in patients who have concomitant atrial fibrillation, especially those over 60 years old. Once a euthyroid state is re-established in this population, 60 percent will convert back to normal sinus rhythm within four months (Bielecka-Dabrowa, Mikhailidis, Rysz, & Banach, 2009).

Atrial fibrillation tops the list of causes for hospital admissions related to cardiac arrhythmias (Kang, 2006). Gutierrez and Blanchard (2011) cite that the financial cost of caring for patients with atrial fibrillation is five times higher than caring for patients in more stable cardiac rhythms. Kang (2006) conducted a small cohort study using personal interviews of patients who were newly diagnosed with atrial fibrillation and found that quality of life and personal health perceptions were negatively impacted by atrial fibrillation. This suggests the cost is even deeper than financial. Therefore, it is important to diagnose atrial fibrillation and treat it if possible. The American College of Cardiology, American Heart Association and the European Society of Cardiology (ACC/AHA/ESC) have come together to formulate extensive guidelines for the detection and treatment of atrial fibrillation (Fuster et al., 2006). This expert panel names hyperthyroidism as a reversible cause of atrial fibrillation and with treatment for the endocrine abnormality the atrial fibrillation is often eliminated as well (Fuster et al., 2006). ACC/AHA/ESC report that the clinical manifestations of atrial fibrillation may be paroxysmal or even non-existent, particularly in the elderly population. When symptoms are present, most patients exhibit dyspnea, fatigue, dizziness, chest pain, or palpitations; these may manifest so gradually that patients may unknowingly accommodate making them unaware that the symptoms are occurring (Fuster et al., 2006). Significantly, the symptoms listed for atrial fibrillation are many of the same which are seen in patients with hyperthyroidism in any form.

As mentioned, hyperthyroidism is detected serologically. There is no lab test for atrial fibrillation. Fuster et al. (2006) and the ACC/AHA/ESC suggest that it requires electrocardiogram, bedside telemetry or Holter monitoring for diagnosis. Included in the list of laboratory tests recommended once atrial fibrillation is detected is thyroid function.

Hyperthyroidism may lead to other cardiac arrhythmias besides atrial fibrillation. Wustmann et al. (2008) investigated the occurrences of other cardiac arrhythmias before and after treatment for hyperthyroidism. It was discovered that the number of premature ventricular contractions and the episodes of supraventricular tachycardia decreased as serum T4 levels decreased (Wustmann et al., 2008). Buscemi et al. (2007) conducted a small prospective randomized control study which showed that patients experienced decreased blood pressure and significantly decreased number of premature ventricular contractions once euthyroid state was achieved using methimazole therapy for hyperthyroidism.

Treatment guidelines

There is agreement across the profession of endocrinology that treatment of overt and symptomatic hyperthyroidism should be recommended. Options for treatment include use of radioactive iodine, antithyroid pharmacotherapy and surgical removal of all or part of the thyroid gland (Bahn et al., 2011). These treatments should be initiated by an endocrinologist but patients who are undergoing, who have undergone these therapies or are in need of symptom management are well served in their primary health care needs by family practice providers. Recommendations by the American Thyroid Association and the American Association of Clinical Endocrinologists for symptomatic management of hyperthyroidism include prescribing beta-blocker therapy for elderly and for patients whose symptoms include a resting heart rate above 90 beats per minute or preexisting heart disease (Bahn et al., 2011). The beta blocker

atenolol was chosen for the patient in the case study because of its selective beta-1 blockade. Conveniently, beta blocker therapy may also be used in the rate control treatment of atrial fibrillation in the non-acute setting (Fuster et al., 2006).

The literature is unclear on the treatment of subclinical hyperthyroidism. The guidelines from the American Thyroid Association and the American Association of Clinical Endocrinologists recommends providers "strongly consider" initiation of treatment for thyroid dysfunction in individuals with TSH levels below normal limits when patients are over the age of 65, for those with cardiac risk factors and who are symptomatic with this level of subclinical hyperthyroidism (Bahn et al., 2011. p. 617). Ertek and Cicero (2013) cite that palpitations as well as activity intolerance, angina and congestive heart failure are cardiac symptoms of hyperthyroidism.

The endeavor of this project is to answer the question of the benefit to screening for cardiac arrhythmias in the presence of hyperthyroidism and vice versa. An affirmative answer is established if the patient has symptoms of either condition, or both.

Learning Points

- Providers must do a thorough history and physical.

Guidelines do not support screening asymptomatic patients for either hyperthyroidism or atrial fibrillation. The most important message for providers to receive from this project is that a very thorough history and review of systems must be completed on every patient. If this is well done, the provider and patient may uncover symptoms that necessitate screening for hyperthyroidism and/or cardiac arrhythmia regardless of guidelines.

- Let symptomatology guide screening for hyperthyroidism, atrial fibrillation or both

Patients with either atrial fibrillation or hyperthyroidism, especially subclinical, may be asymptomatic or experience vague symptoms which they themselves rationalize and may not bring to the provider's attention. The key to appropriateness of screening is the presence of symptoms. Symptoms that hyperthyroidism and atrial fibrillation share are palpitations, tachycardia, fatigue, and dyspnea. A thorough history and review of systems should reveal possible symptoms of atrial fibrillation, hyperthyroidism or both. Providers can use the symptoms they uncover to guide screening.

- Remember that hyperthyroidism and atrial fibrillation may occur together

A main point of advice beyond superb elicitation of patient history is for providers to keep the two conditions of hyperthyroidism and cardiac arrhythmia together as possible reasons for symptoms. A provider may find that a person is symptomatic for hyperthyroidism, then screen appropriately with lab studies and consequently diagnose the condition. Further examination for concomitant cardiac arrhythmias may be warranted by the same symptoms that lead to the hyperthyroid diagnosis and can be detected with the cardiac monitoring devices available. A provider will be more helpful to the patient by detecting and treating both hyperthyroidism and cardiac arrhythmia if present in the patient than finding one of those conditions and leaving the other undiagnosed and therefore untreated.

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