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Case Report

A Rare Case of Severely Symptomatic and Reversible 2:1 Atrioventricular Block Associated with Subclinical Hypothyroidism: Case Report

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Abstract

Background: It has long been recognized that hypothyroidism, leads to sinus bradycardia, low amplitude P and T waves with low voltage QRS complexes and lengthening of the corrected QT interval on the surface electrocardiogram. However, the degree by which the heart rate slows down is often modest and disturbances in atrioventricular conduction seem to be rare. It is unknown whether patients with AV block are expected to have a benign course after the initiation of appropriate thyroid hormone replacement therapy, the time course between the initial therapy and recovery of AV block is not clear and it is challenging for clinicians to manage patients with AV block in association with hypothyroidism. The question "Does the thyroid hormone replacement therapy improve both the AV conduction and hypothyroidism?" remains controversial. We are reporting a case of complete resolution of 2:1 AV block associated with subclinical hypothyroidism in an elderly woman under thyroid hormone replacement therapy.

Case Presentation: A 68 year old woman, not receiving any AV node blocking agent, presenting with recurrent lipothymia without symptoms or signs of hypothyroidism. Physical examination at admission at the Intensive Cardiology Care Unit finds a regular heart rhythm, pulse: 37 bpm with no other signs. 12-lead electrocardiogram on admission finds a regular rhythm, heart rate: 37 bpm, 2:1 AV block. A temporary transvenous pacing using a percutaneous approach of the right femoral vein guided by ultrasound was performed. Demand temporary pacemaker was set to 70/min. Transthoracic echocardiogram was normal. Coronary angiography showed normal coronary arteries, no atheroma and no stenoses. Thyroid function testings: TSH: 12 (normal range: 0.4 - 4 mUI/l), serum free T3: 0.1 (0.2 - 0.5 ng/dl), serum free T4: 0.8 (0.8 - 2.8 ng/dl). Thyroid investigations have confirmed Hashimoto thyroiditis. L-thyroxine was prescribed. We could withdraw temporary pacing at 5 days of thyroid hormone replacement therapy after checking the spontaneous underlying rhythm: regression of 2:1 AV block, regular sinus rhythm at 50 bpm. 24 Holter monitoring showed no episodes of AV block. At 8 days, the patient was discharged with a cardiology and endocrinology follow-up. At 5 months follow-up, the patient was asymptomatic, taking a 75 mcg dose of L-thyroxine daily, normal TSH, free T3 and T4 levels with a 12-lead ECG showing a regular sinus rhythm at 70 bpm and no AV block on 24 hours Holter monitoring.

Conclusion: High degree AV block can be explained by hypothyroidism and thyroid hormone replacement therapy could improve both AV block and hypothyroidism avoiding unnecessary pacemaker implantation.

Keyword: *Subclinical Hypothyroidism; 2:1 Atrioventricular Block; Thyroid Hormone Replacement Therapy; Pacemaker*

Abbreviations

AV: Atrioventricular; TSH: Thyroid Stimulating Hormone; ECG: Electrocardiogram

Introduction

The heart is a major target organ for thyroid hormone action. Hypothyroidism is well known to be related to cardiac diseases. It can result in diastolic hypertension, atherosclerotic cardiovascular disease [1], lowered cardiac output, impaired left ventricular contractility, diastolic relaxation and congestive heart failure [2]. Pericardial effusion and modest bradycardia can also be associated [3,4]. It has long been recognized that hypothyroidism, leads to sinus bradycardia, low amplitude P and T waves with low voltage QRS complexes and lengthening of the corrected QT (QTc) interval on the surface electrocardiogram [5,6]. However, the degree by which the heart rate slows down is often modest and disturbances in atrioventricular conduction seem to be rare and hypothyroidism is thought to be a reversible cause of atrioventricular (AV) block [5].

It is unknown whether patients with AV block are expected to have a benign course after the initiation of appropriate therapy for thyroid dysfunction and the time course between the initial therapy for thyroid dysfunction and recovery of AV block is not clear. Since, there is no obvious study to confirm a levothyroxine as the drug of hypothyroidism-related AV block, it is challenging for clinicians to manage patients with AV block in association with hypothyroidism. The question "Does thyroid hormone replacement therapy improve both the AV conduction and hypothyroidism?" remains controversial.

We are reporting a case of complete resolution of 2:1 AV block associated with subclinical hypothyroidism in an elderly woman under thyroid hormone replacement therapy.

Case Presentation

Clinical history: A 68 year old woman treated for a type 2 diabetes mellitus, not receiving any AV node blocking agent, presenting with recurrent lipothymia for 7 days without symptoms or signs of hypothyroidism. Physical examination at admission at the Intensive Cardiology Care Unit finds a regular heart rhythm, pulse: 37 bpm, blood Pressure: 130/70 mmHg, percentage oxygen saturation was 96% on room air, without rales, heart murmur or carotid bruit, without goiter at thyroid gland palpation. The rest of physical examination was normal.

12-lead electrocardiogram on admission: Regular rhythm, heart rate: 37 bpm, 2:1 AV block, normal P wave (80 ms duration and 0.1 mV amplitude), normal QRS morphology and duration (80 ms), isoelectric ST segment, normal T waves and normal corrected QT interval using Bazett formula (408 ms) (Figure 1).

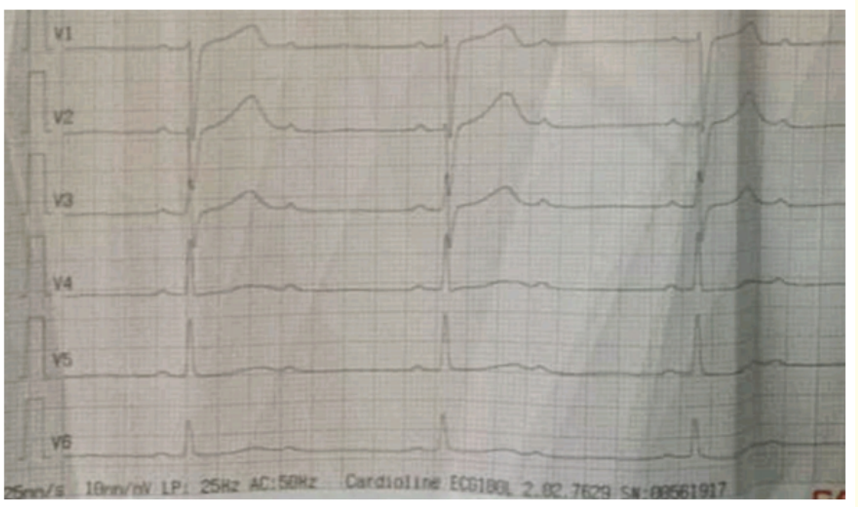

Figure 1: *Precordial leads of an ECG on admission: 2:1 AV block, HR: 37 bpm, QT interval: 520ms, cQT interval: 408 ms, QRS duration: 80 ms.*

Atropine was tested at admission. HR increased temporary to 50 bpm and the 2:1 AV block was persistent.

A temporary transvenous pacing using a percutaneous approach of the right femoral vein guided by ultrasound was performed. Demand temporary pacemaker was set to 70/min, pulses of 1.4V and sensitivity to maximum.

Transthoracic echocardiogram: Normal LV and RV dimensions and functions, LVEF: 65%, normal LV filling pressures, normal atrial dimensions (LA area: 16 cm^2, RA area: 14 cm^2), a trace mitral, aortic and tricuspid regurgitations, no pulmonary hypertension and no pericardial effusion.

Coronary angiography was performed. It showed normal coronary arteries, no atheroma and no stenoses. The indication was only the arrhythmia. AngioCT could have been performed but it is not available in our hospital.

Laboratory tests: Haemoglobin: 10.4 (N: 12 - 16 g/dl), Platelets: 154.000 (N: 150.000 - 400.000 elements/mm^3, PTT: 34 (N: 25 - 35 sec), PT: 132 (70 - 140%), fibrinogen: 3.4 (N: 2 - 4 g/l), WBC: 5.300 (N: 4.000 - 11.000 elements/mm_3, C-reactive protein: 2.2 (N: < 3 mg/L), kaliemia: 4.5 (N: 3.5 - 5 mmol/l), calcemia: 91 (N: 85 - 103 mg/l), magnesium: 17 (N: 17 - 22 mg/l), BUN: 0.26 (N: 0.05 - 0.25 g/l), plasma creatinine: 6.5 (N: 6 - 11 mg/l) estimating a GFR by simplified MDRD formula at 96 ml/min/1.73m^2 BSA, glycemia: 210 mg/dl, triglycerides: 130 mg/dl (N < 150 mg/dl), total cholesterol: 120 mg/dl (N < 200 mg/dl), HbA1C: 7.5% (N < 7%), LDL cholesterol: 90 mg/dl (N < 100 mg/dl), HDL cholesterol: 50 mg/dl (N > 45 mg/dl). US troponin Ic level: 26 (N < 35 ng/l). Thyroid function testings: TSH: 12 (N: 0.4 - 4 mUI/l), serum free T3: 0.1 (N: 0.2 - 0.5 ng/dl), serum free T4: 0.8 (N: 0.8 - 2.8 ng/dl). The presence of TPO (thyroid peroxidase) antibodies have confirmed Hashimoto thyroiditis.

Treatment: L-thyroxine, starting dose of 12.5 mcg daily with daily checking of spontaneous heart rhythm, TSH measurement and L-thyroxine dose adjustments every 2 - 4 weeks.

Evolution: We could withdraw temporary pacing at 5 days of thyroid hormone replacement therapy after checking the spontaneous underlying rhythm: regression of 2:1 AV block, regular sinus rhythm at 50 bpm, normal P waves (0.15 mV amplitude and 80 ms duration), normal PR interval (200 ms, upper normal of limit), normal QRS morphology and duration (80 ms duration), isoelectric ST segment, normal T waves and normal corrected QT interval (438 ms) (Figure 2). 24 Holter monitoring showed no episodes of AV block. At 8 days, the patient was discharged with a cardiology and endocrinology follow-up. At 5 months follow-up, the patient was asymptomatic, taking a 75 mcg dose of L-thyroxine daily, TSH level was stable at 3 mUI/l, free T3 at 0.3 ng/dl and free T4 at 1.7 ng/dl with a 12-lead ECG showing a regular sinus rhythm at 70 bpm and no AV block on 24 hours Holter monitoring.

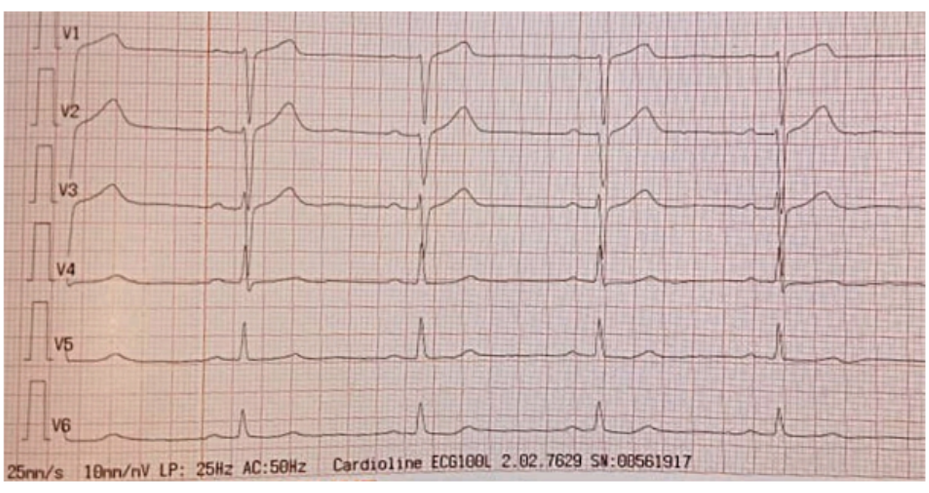

Figure 2: *Precordial leads of an ECG at five days of thyroid hormone replacement therapy: HR: 50 bpm, PR interval: 200 ms, QT interval: 480 ms, cQT interval: 438 ms, QRS duration: 80 ms.*

Discussion

This case report is showing a rare case of symptomatic 2:1 AV block complicating subclinical hypothyroidism, requiring intensive cardiology care unit admission and temporary pacing and reversible after 5 days of initiation of thyroid hormone replacement therapy.

Thyroid hormone is essential for life and has a major influence on the cardiovascular system by a number of direct and indirect mechanisms [7]. It exerts its cardiovascular effects by binding to intracellular thyroid receptors which, in turn, bind to thyroid hormone response elements on various genes and can affect gene transcription and, subsequently, protein translation. The thyroid hormone increases the basal metabolic rate in almost every tissue and organ system in the body by regulating gene expression, and the increased metabolic demands lead to changes in cardiac output, systemic vascular resistance and blood pressure. Cardiac dysrhythmias have been reported with hyper as well as hypothyroidism. Bradyarrhythmias can be associated with hypothyroidism [8].

Conduction block from the atrium to the ventricle may occur because of various reasons in a number of clinical situations. The etiologies may be classified as functional or structural. Those that are functional (metabolic disorders including hypothyroidism) are stated to be reversible in textbooks of internal medicine and hypothyroidism is one of the rare problems which can recover pharmacologically, but clinical practice is much more challenging [9].

Disturbances of AV conduction in hypothyroidism are rare [10,11]. Not only overt hypothyroidism but also subclinical hypothyroidism is reported to be a possible cause of reversible AV block. It is unknown whether patients with AV block and hypothyroidism are expected to have a good outcome. Moreover, the time course between initiation of thyroid hormone replacement therapy and AV block recovery in unclear. Therefore, managing hypothyroidism related- AV block is challenging for physicians. The mechanism of conduction disturbance in the heart remains unknown. Histopathologic finding of myocardium in myxedema heart is varied. There may be interstitial edema compressing the AV node, myocardial fibrosis and mucinous vacuolization [12,13]. Levothyroxine is thought to have an indirect effect on improving AV conduction by resolving edema. Although, it can be irreversible with extensive fibrotic change in myocardium [14].

There are only few cases reported in the literature. There are some case reports of complete reversal of AV block with the normalization of TSH level after treatment of hypothyroidism [15-20]. Nakayama., *et al*. reported a middle-aged man with transient 2:1 AV block and subclinical hypothyroidism and conduction disturbance was improved completely after two weeks of thyroid hormone replacement therapy [21]. Schoenmakers., *et al*. reported an elderly woman with complete AV block due to severe hypothyroidism which was resolved after thyroid hormone replacement therapy [22]. However, in one study from Lardoux., *et al*. 14 of 42 non-treated hypothyroidic patients had conduction disturbances on routine ECG evaluation, and there was no evident effect of hormone therapy on conduction disturbances [23]. Also, in a research study by Kazim., *et al*. [24], the resolution of AV block occurred in only 24% of hypothyroidic patients despite the treatment with levothyroxine and normalization of TSH. These findings are distinct and controversial to the general belief that "AV block in association with hypothyroidism is reversible".

It is recommended that all patients with AV block of unknown origin receive a careful evaluation of thyroid function, especially in elderly patients before inserting a permanent pacemaker. We should replace thyroxine if hypothyroidism is diagnosed. American College of Cardiology Foundation/American Heart Association/Heart Rhythm Society (ACC/AHA/HRS) 2018 guidelines for device-based therapy of cardiac rhythm abnormalities recommend permanent pacemaker implantation in patients with advanced second-degree and third-degree AV blocks who have symptoms (Class I recommendation, level of evidence C). However, the guidelines also give a Class III recommendation in favor of deferring pacemaker placement in patients who are asymptomatic and have a benign reversible cause of AV blocks such as Lyme disease, drug toxicity, or transient increases in vagal tone (level of evidence: B). There are no clear guidelines regarding how to manage patients with high degree AV blocks with severe hypothyroidism, and there is controversy in the literature. The decision to place a permanent pacemaker in patients with hypothyroidism should be individualized based on symptoms, comorbid conditions, and response to thyroxine replacement. A temporary pacemaker can be placed in selected cases that require cardiac pacing due to the sever-

ity of symptoms or hemodynamic compromise, while awaiting restoration of normal sinus rhythm with thyroid hormone replacement therapy. If AV block is not improved by the treatment of thyroid dysfunction, there are two possibilities; no relation to thyroid dysfunction or irreversible damage induced by the disease. However, defining the exact cause of irreversible AV block is not of clinical importance because a pacemaker should be placed in both situations.

Our patient had a symptomatic 2:1 AV block with a slow ventricular response requiring temporary endovenous pacing and thyroid hormone replacement therapy with complete resolution at 5 days. At 5 months follow-up, there was no AV block on Holter monitoring and therefore no need for a permanent pacemaker.

Conclusion

Our case study demonstrates that thyroid function abnormalities should always be tested when patients present with syncope due to AV conduction block, since the AV block may be caused by hypothyroidism.

High degree AV block can be explained by hypothyroidism and thyroid hormone replacement therapy could improve both AV block and hypothyroidism and avoiding unnecessary pacemaker implantation. In some cases, AV block is irreversible and pacemaker placement is necessary. Therefore, the therapeutic decision should be individualized and further studies are needed in order to make specific guidelines to the management of such patients.

Conflict of Interest

No conflict of interest to declare.

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