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Impact of untreated hypothyroidism on the cardiac conduction system: a case report and review of pathophysiology

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ABSTRACT

Background. *Third-degree atrioventricular (AV) block, also referred as complete heart block, results from the complete disruption of impulse transmission between the atria and ventricles, leading to desynchronized electrical activity. Among the numerous causes involved in the development of an AV block, severe hypothyroidism is one of the rarest.*

Case Report. *We documented the case of a 77-year-old female patient diagnosed with severe hypothyroidism alongside a complete atrioventricular (AV) block.*

Conclusions. *Evaluating thyroid function is essential whenever a patient is diagnosed with a high-degree AV block, as severe hypothyroidism could potentially be the underlying factor.*

Keywords: hypothyroidism, myxedema, atrioventricular block, pacing

INTRODUCTION

In a healthy heart, electronically charged impulse are generated in the sinoatrial node, and then conducted along a channeled pathway from the atria to the ventricles, resulting in synchronized contractions in the myocardium [1]. Disruption of the conduction pathways in the heart can result in delays or complete blocks in signal transmission, causing various degrees of atrioventricular (AV) block.

Idiopathic fibrosis and sclerosis within the conduction system is the main cause of atrioventricular (AV) block. Other factors such as ischemic cardiac disease or pharmacological agents might be involved [2].

Hypothyroidism can be primary (due to thyroid gland dysfunction) and secondary or tertiary (due to pituitary or hypothalamic dysfunction). The assessment of a patient suspected of having hypothyroidism should aim to confirm the presence of hormone deficiency and determine its underlying cause.

Hypothyroidism has been identified as a potential underlying factor contributing to complete atrioventricular (AV) block and ventricular tachycardia [3]

We present the case of a 77-year-old woman diagnosed on admission with complete atrioventricular (AV) block and an underlying severe hypothyroidism.

CASE REPORT

A 77-year-old woman was transferred to our hospital with persisting fatigue and dizziness. Over the course of the preceding two weeks, the patient had been experiencing worsening dizziness and fatigue, associated with lower limb edema. Her medical history revealed hypertension under treatment with calcium channel blockers, diabetes mellitus on premixed regimen and recurrent strokes. Moreover, she confirmed she has been diagnosed with hypothyroidism but could not recall the exact date, nor did she have any relevant medi-

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cal files. She admits non-compliance regarding treatment with Levothyroxine. No allergies to either food or medication were reported and she did not smoke.

On physical examination, the patient was conscious; she had periorbital and peripheral edema with an overall puffy aspect and dry, pale skin. The thyroid gland was non-palpable, and there were no visible surgical scars in the neck region. Heart sound was normal, without murmur and bruits, she presented with high blood pressure 175/70 mmHg and a heart rate of 35 beats/min. Initial electrocardiogram (ECG) showed a complete AV block with an infranodal alternative escape rhythm and a heart rate of around 40 bpm (Figure 1).

The chest X-ray revealed no active pulmonary lesions and cardiomegaly. Transthoracic echocardiography showed normal left ventricular systolic function, mild mitral and tricuspid regurgitation and moderate pericardial effusion.

Laboratory findings revealed severe hypothyroidism with a thyroid-stimulating hormone (TSH) level >100 pmol/l (normal range 0.27-4.20), a free T4 of 0.95 pmol/l (normal range 2-22) and positive TPO antibodies. Basal cortisol level was within normal limits. Additional observations disclosed uncontrolled diabetes with a fasting blood glucose value of 317 mg/dL and A1C 9.5%, as well as elevated kidney and liver enzymes (AST 41 IU/L, ALT 45 IU/L, Creatinine 3.5 mg/dL, BUN 71 mg/dL).

After diagnosis, treatment with Levothyroxine was reinitiated with a progressive increase in dosage.

A permanent dual chamber cardiac pacemaker was implanted through the left axillary vein. Both leads (RA and RV) with active fixation were connected to the pulse generator located in a left subclavian pocket. The RV lead was placed at the upper part of the interventricular septum with His bundle capture. The detection and stimulation parameters had normal values (RA = 0,75 V/0,4 ms, RV = 0,5 V/0,4 ms) and also normal impedance values. The pacemaker was programmed in a DDDR mode with a lower rate of 60 beats /minute. No other complications were observed.

The post-implantation ECG showed atrial stimulation and a non-selective His bundle pacing with a narrow QRS complex, an early QRS transition in V2, an initial QRS slur (pseudo-delta wave) in left ventricular leads, a small initial "r" wave in V1, R-wave peak time (RWPT) in V6 of 90 ms and secondary ST-T changes. (Figure 2) The non-selective His diagnosis was based on electrophysiological criteria, such as differentiated pacing and ECG appearance.

Even though her severe hypothyroidism might have been a potentially reversible cause of the AV block, due to the potential life-threatening complications, in parallel with the high risk of being lost to follow-up, the implantation of the permanent pacemaker was decided. The patient was instructed to seek further medical care in an Endocrinology department in her region in order to optimize the treatment protocol.

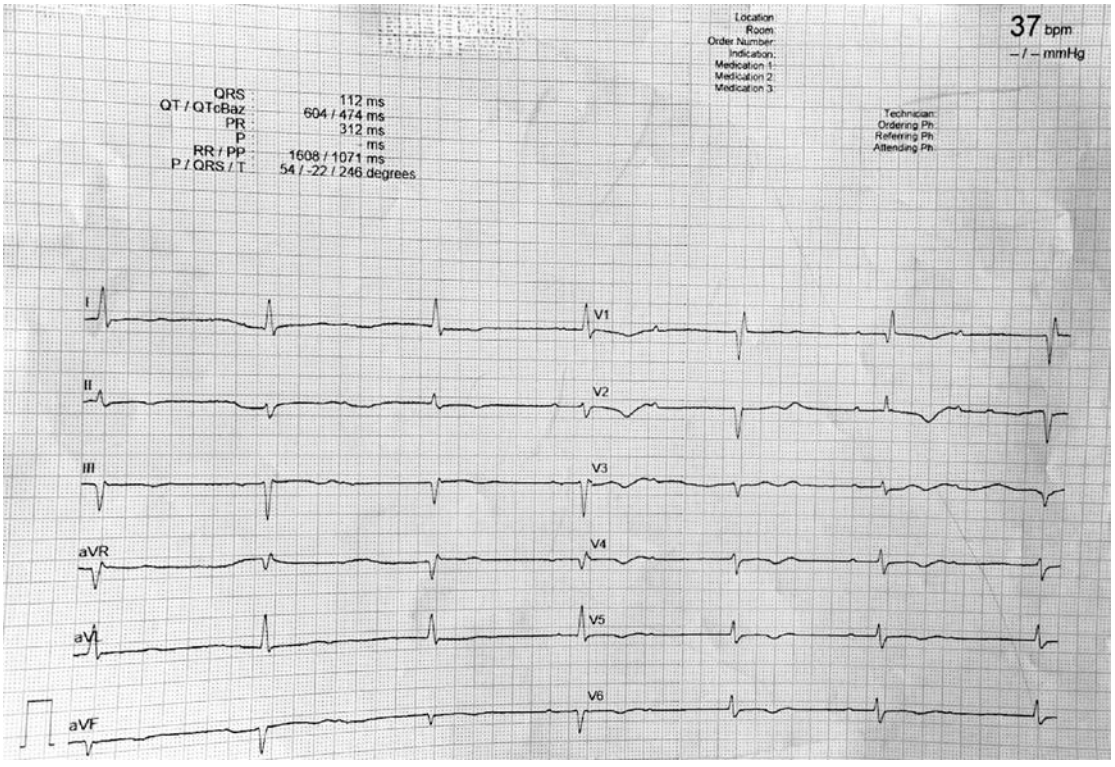

FIGURE 1. *Initial ECG showing sinus rhythm with 3rd degree AV block with an infranodal alternative escape rhythm (heart rate = 40 bpm)*

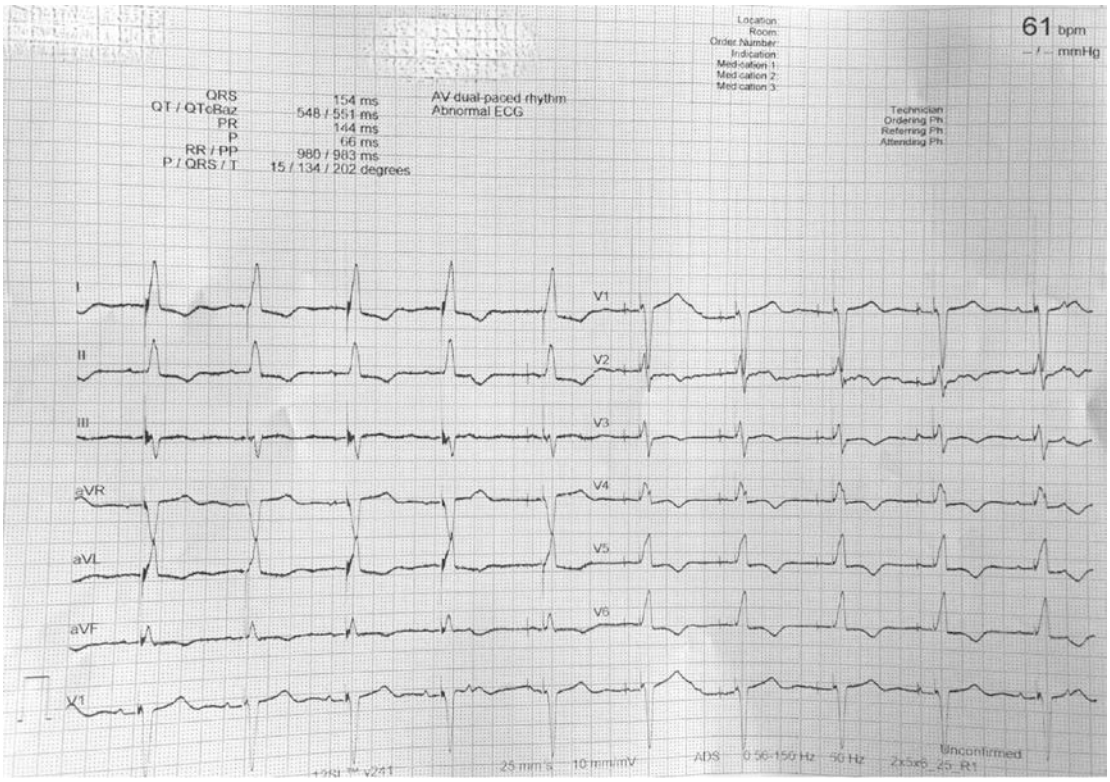

FIGURE 2. *The post-implantation ECG showed a non-selective His bundle pacing with a narrow QRS complex, an early QRS transition in V2, an initial QRS slur (pseudo-delta wave) in left ventricular leads, a small initial "r" wave in V1, R-wave peak time (RWPT) in V6 of 90 ms and secondary ST-T changes*

DISCUSSION

An Overview of Atrioventricular Block

The main types of atrioventricular block are classified as:

- First-degree AV block: characterized by a prolonged PR interval on ECG
- Second-degree AV block: subdivided into Mobitz type I, II, 2:1 and high-degree. On the ECG, Mobitz type I is characterized by a progressive prolongation of the PR interval, followed by a missed beat, whereas in Mobitz type II the PR interval anticipating the missed beat is constant. A 2:1 AV block means that there is a regular PP interval and every other P wave is conducted to the ventricle. In the case of a high-degree AV block, the P waves are constant, but they do not conduct.
- Third-degree AV block (complete AV block): where impulse conduction from the atria to the ventricles is completely desynchronized. On the ECG you could find regular PP and RR intervals, but irregular PR intervals [4].

A range of physiological and pathophysiological factors contribute to an atrioventricular (AV) block. Factors such as increased vagal tone, which is common in athletes or during painful conditions, carotid sinus massage, or hypersensitive sinus syndrome, can lead to AV block by slowing the sinus rate or disrupting conduction [5]. Fibrosis and sclerosis within the conduction system is responsible for almost half of AV block cases, while conditions like progressive cardiac conduction defect (Lenegre's or Lev's disease), ischemic heart disease, cardiomyopathies, myocarditis, and congenital complete heart block are stated as additional causes [6]. It also exist a familial form of AV block, inherited as an autosomal dominant trait, which manifests as a progressive conduction abnormality [7].

In the elderly, age-related physiological changes such as reduced maximal heart rate, diminished heart rate variability, prolonged AV node conduction time, and attenuated baroreflex function, as well as a heightened parasympathetic sensitivity represent common findings. While sinus bradycardia can be asymptomatic in the geriatric patients and typically requires no intervention, conditions such as sinus node dysfunction, carotid hypersensitivity, sinoatrial exit block, AV block, hypokalemia, hypothyroidism, and drug-induced toxicity may require specific medical care [8,9].

Cardiac implications of hypothyroidism: impact on heart function and structure

Thyroid hormones play a crucial role in cardiac function by regulating gene expression, metabolism, and ion channel activity in cardiomyocytes [10]. In hypothyroidism, there is a decrease in circulating levels of thyroid hormones, triiodothyronine (T3) and thyroxine

(T4). This hormonal deficiency significantly affects the heart, primarily manifesting as bradycardia due to reduced sympathetic responsiveness. Moreover, diastolic dysfunction occurs, impairing myocardial relaxation and filling dynamics. These alterations lead to clinical symptoms such as fatigue, dyspnea, and reduced exercise tolerance. In severe cases, hypothyroidism can cause pericardial effusion, worsening cardiac function [11].

Hypothyroidism is often associated with a higher incidence of atrioventricular block (AVB) compared to other thyroid conditions. Thyroid hormones exert hypermetabolic effects on the heart. Therefore, the hormone insufficiency affects energy homeostasis in the heart, leading to reduced contractility and an increased risk of heart failure [12]. Certain researchers propose that this mechanism could potentially play a role in the development of bradycardia and subsequently atrioventricular block (AVB) in individuals with hypothyroidism [13]. Alternatively, another hypothesis suggests that dysfunction within the autonomic nervous system and changes in the structure of the sinoatrial node in hypothyroid patients might also contribute to the occurrence of bradycardia and AV block [14].

Molecular mechanisms of thyroid hormone action in the myocardium

Thyroid hormones regulate the expression of genes encoding proteins involved in myocardial contractility, including myosin heavy chain isoforms and sarcoplasmic reticulum calcium ATPase (SERCA), as well as for cardiac hypertrophy, remodeling, and metabolism. Additionally, thyroid hormones affect the sensitivity and responsiveness of adrenergic receptors in the myocardium, enhancing the inotropic and chronotropic effects of catecholamines [10].

Furthermore, thyroid hormones exert non-genomic actions within the myocardium, including the activation of signaling pathways such as protein kinase cascades, phosphatidylinositol-3 kinase (PI3K)/Akt pathway, and nitric oxide (NO) pathway. These pathways modulate ion channel activity, calcium handling, and myocardial contractility through rapid, non-transcriptional mechanisms [15].

When diagnosing a case of hypothyroidism, medical history is crucial, as it may uncover factors such as past treatments for hyperthyroidism with radioactive iodine or thyroidectomy, the use of medications impacting thyroid hormone production, or previous cranial irradiation, which could indicate a central cause. Moreover, physical examination could reveal thyroid enlargement or the presence of a scar from a prior thyroidectomy. To confirm the diagnosis of hypothyroidism, laboratory tests typically involve measuring serum levels of thyroid-stimulating hormone (TSH) and free thyroxine (T4) [16].

Overt hypothyroidism has been associated with an increased risk of cardiovascular events, such as coronary artery disease, heart failure or cardiac arrhythmias [11]. Syncope has been recognized as a potential initial manifestation of AV block in patients with thyroid dysfunction [17].

In the elderly population, hypothyroidism is frequently overlooked due to its symptoms, such as fatigue, dry skin, constipation or oedema that can mimic those commonly associated with aging. The assessment of serum thyroid-stimulating hormone (TSH) levels should be integrated into the biochemical evaluation among elderly individuals [18].

Despite ongoing advancements, significant gaps persist in understanding true prevalence, natural history, optimal therapeutic strategies, and prognostic implications associated with AV block among patients diagnosed with severe hypothyroidism. Furthermore, there is a lack of consensus regarding the need for permanent pacemaker implantation in such cases, given the potential reversibility of atrioventricular block with optimal Levothyroxine therapy. While some studies propose conservative approaches, alternative recommendations advocate for the implantation of a permanent pacemaker [19].

CONCLUSION

Evaluating thyroid function is essential whenever a patient is diagnosed with a high-degree AV block, as severe hypothyroidism could potentially be the underlying factor. It is important to note that the manifestation of hypothyroidism in elderly patients can be subtle and lacking in specificity.

The necessity of pacing versus the adequacy of antithyroid treatment alone to resolve atrioventricular block (AVB) remains an unsettled topic and requires further studies. Present evidence suggests a careful and individualized approach to decision making.

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Conceptualization, I.A.P. and M.L.P.; methodology, I.A.P.; software, M.L.P.; validation, A.I.U., I.A.P., M.L.P.; formal analysis, A.I.U.; investigation, M.L.P.; resources, X.X.; data curation, X.X.; writing—original draft preparation, I.A.P.; writing—review and editing, I.A.P.; visualization, I.A.P.; supervision, A.I.U.
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