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CASE REPORT
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Two Deadly Complications of Untreated Hypothyroidism: Sudden Cardiac Arrest and Acute Coronary Syndrome

ABSTRACT

Myxedema coma is a rare but life-threatening endocrinological emergency condition that may present with serious conditions such as sudden cardiac arrest or acute coronary syndrome. In this context, 2 cases are presented in this case report as examples of how deadly complications of myxedema coma can be prevented with rapid diagnosis and intervention. A 58-year-old female patient was admitted to the emergency service with complaints of altered consciousness and speech and balance disorders. She was hypothermic at admission. Her electrocardiogram was compatible with complete atrioventricular block. The patient who developed cardiac arrest during the follow-up was intubated, and spontaneous circulation was restored after 28 minutes of cardiopulmonary resuscitation. The patient's thyroid function tests were compatible with hypothyroidism. The patient was diagnosed with myxedema coma, and treatment for myxedema coma was started. The patient was discharged after 40 days. A 55-year-old male patient presented to the emergency department with chest pain. His electrocardiogram was compatible with first-degree atrioventricular block. There was ST segment elevation in D2, D3, and aVF derivations. The patient's thyroid function tests were compatible with hypothyroidism. The patient was diagnosed with myxedema coma and was immediately started treatment. The patient was discharged after 18 days. Myxedema coma is rarely seen due to the easy accessibility and feasibility of hypothyroidism treatment, however, in cases when it is seen it may present with mortal manifestations. Hence, it is of utmost importance that clinicians take this serious condition into consideration and initiate treatment without delay.

Keywords: Acute coronary syndrome, myxedema coma, sudden cardiac arrest

Introduction

Hypothyroidism is highly prevalent but can easily be treated. However, if not noticed or treated, it can turn into a rare but life-threatening condition known as myxedema coma over time. There are also cases where myxedema coma is the first sign of hypothyroidism.[1] Myxedema coma is an endocrinological emergency condition caused by low thyroid hormone levels. In the vast majority of cases, the underlying cause of hypothyroidism is Hashimoto's thyroiditis.[2] Early diagnosis and treatment are critical in patients experiencing this condition.

In fact, myxedema coma is characterized by the exacerbation of the symptoms and signs of hypothyroidism. However, in myxedema coma, symptoms such as hypothermia, impaired mental status, and general edema also accompany the general symptoms and signs of hypothyroidism.[2] Myxedema coma patients may present to hospitals with cardiac and mortal features such as bradycardia, acute coronary syndrome, and sudden cardiac arrest. Acute coronary syndrome, infections, and cold weather are among the precipitating factors.[1] High suspicion is very important for the diagnosis of myxedema coma.

The objective of this case report is to discuss a female case with myxedema coma who developed cardiac arrest and underwent cardiopulmonary resuscitation and a male case with myxedema coma who was admitted to the emergency room with acute coronary syndrome. Although rare and relatively easy to treat, due care should be taken in relation to myxedema coma, especially since delays in its diagnosis can cause morbid complications.

Case Presentations

Case 1

A 58-year-old female patient was admitted to the emergency service with complaints of altered consciousness and speech and balance disorders. She was hypothermic at

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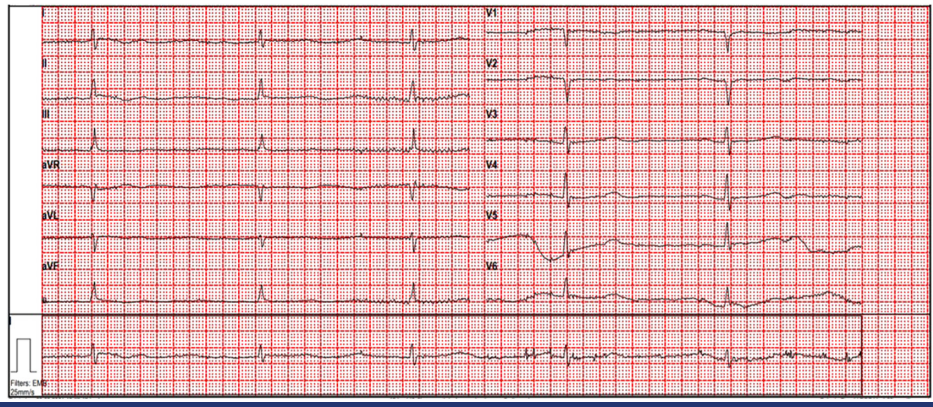

Figure 1. Electrocardiogram of the patient at admission to the emergency room.

admission and her tympanic temperature was 35˚C. Her blood pressure, oxygen saturation at room air, and heart rate were measured as 130/75 mm Hg, 96%, and 40 beats per minute (bpm), respectively. Her electrocardiogram (ECG) was compatible with complete atrioventricular (AV) block (Figure 1). Her skin was dry and her face was edematous (Figure 2). At initial assessment, it was thought that complete AV block might have developed due to the risperidone she was using, taking into consideration her history of psychotic disorder and hypothyroidism. Her ECG revealed a moderate pericardial effusion but no major valve pathology. The results of her biochemical tests did not indicate any electrolyte disorder. Cranial computed tomography (CT) revealed an ischemic infarct area that may pertain to the subacute-chronic stage in the area corresponding to the left posterior cortical watershed area, but no intracranial hemorrhage. Her neurological examination did not indicate anything abnormal and thus neurological etiologies were ruled out.

Temporary pacemaker was implanted in the patient whose ECG was compatible with AV block. The patient was intubated while she was under observation in the emergency room since she developed cardiac arrest. Cardiopulmonary resuscitation was performed for 28 minutes and spontaneous circulation was restored. She was planning to have thyroid function tests since her clinical findings and history of hypothyroidism raised suspicion for myxedema coma. The results of her thyroid function tests were as follows: thyroid-stimulating hormone (TSH): 60 mU/L (normal range: 0.27-4.2 mU/L), free thyroxine (T4): <0.1 ng/dL (normal range: 0.89-1.76 ng/dL), free triiodothyronine (T3): 0.99 ng/L (normal range: 2-4.4 ng/dL), anti-thyroid peroxidase (TPO) antibody: 484 IU/mL (normal range: <34 IU/mL), and anti-thyroglobulin (TG) antibody: 543 IU/mL (normal range: <115 IU/mL).

MAIN POINTS

- Myxedema coma is a rare but life-threatening endocrinological emergency.
- Patients with myxedema coma may have cardiac symptoms on their first admission to the hospital.
- It is important to diagnose myxedema coma without delay based on clinical findings, including physical examination and laboratory parameters. Clinicians should keep this rare condition in mind.

It was learned that she had not used medication for hypothyroidism in the past 1 year. Given her clinical features and laboratory findings, myxedema coma diagnosis was made. She was inserted a nasogastric tube and started on 500 µg/day levothyroxine treatment in tablet form. Parenteral levothyroxine preparation is not available in Turkey. Concurrently, she was started on 200 mg/day hydrocortisone and 50 µg/day liothyronine treatments and hydration therapy was planned. The patient was transferred to the intensive care unit. Inotropic therapy was initiated since she was hypotensive. No scar was observed on her neck which would be indicative of any thyroid surgery during her questioning regarding the etiology of hypothyroidism. The patient's state of consciousness responded to the myxedema coma treatment. The patient was put on mechanical ventilation and followed up in an intubated manner for 19 days. Temporary pacemaker was removed since her heart rate was stable around 70 bpm without a pacemaker. No loss of consciousness or bradycardia-related condition was observed in the patient after the removal of the temporary pacemaker. After having been treated for 24 days in the intensive care unit, the patient was transferred to the endocrinology ward to regulate her treatment. The dosages of the liothyronine and hydrocortisone treatments were gradually reduced. Ultimately, the liothyronine and hydrocortisone treatments were discontinued, whereas the dosage of the levothyroxine treatment was adjusted based on her needs. At the final assessment before she was discharged, the edema

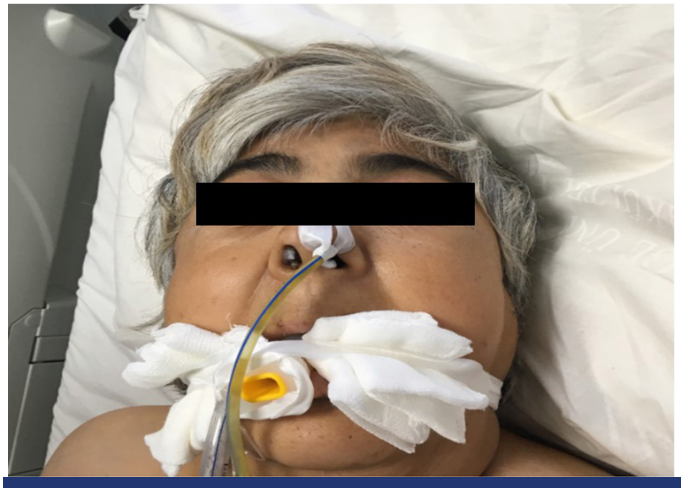

Figure 2. The first photograph of the patient at admission.

Figure 3. Photograph of the patient at discharge.

on her face disappeared (Figure 3). The patient was discharged from the hospital to be followed up as an outpatient.

Case 2

A 55-year-old male patient presented to the emergency department with constipation for 10 days and severe chest pain that developed immediately before admission. The patient had no known chronic disease and was not on any medication. At admission, his blood pressure, tympanic temperature, oxygen saturation at room air, and heart rate were measured as 130/70 mmHg, 35.9˚C, 96%, and 57 bpm, respectively. His physical evaluation indicated that he had periorbital edema and that his skin was very dry (Figure 4A-C). His ECG was compatible with first-degree AV block. There was ST segment elevation in D2, D3, and aVF derivations (Figure 5). His troponin T level was measured as 34 ng/L (normal: <14 ng/L). The patient was diagnosed with inferior myocardial infarction (MI). His troponin T level had elevated to Troponin T: 1389 ng/L at the sixth hour control examination. Angiography was performed on the patient. Angiography revealed 60% stenosis in the proximal left anterior descending artery (LAD), 80% stenosis in the distal LAD artery, 80% stenosis in the first obtuse marginal artery of the circumflex (Cx) artery (OM1), and 80% and 99% stenosis in the right coronary artery (RCA) in the proximal and before crux, respectively (Figure 6A-C). Coronary artery bypass grafting surgery was planned for the patient who was determined to have multiple vascular occlusions. The results of the patient's thyroid function tests, on the other hand, were as follows: TSH: 54.5 mU/L (normal range: 0.274.2 mU/L), free T4: <0.1 ng/dL (normal range: 0.89-1.76 ng/dL), free T3: <0.97 ng/dL (normal range: 2-4.4 ng/dL), anti-TPO antibody: 484 IU/mL (normal range: <34 IU/mL), and anti-TG antibody: >4000 IU/mL (normal range: <115 IU/mL). In addition, the results of the lipid panel revealed that his low-density lipoprotein (LDL) was 314 mg/dL (normal range <130 mg/dL). No scar was observed on his neck which would be indicative of any thyroid operation. Myxedema coma diagnosis was made based on his clinical findings and the results of the thyroid function tests, and it was thought that myxedema coma might have had triggered acute coronary syndrome. The patient was transferred to endocrinology service and started on 50 mg/day hydrocortisone, 400 µg/day levothyroxine, and 50 µg/day liothyronine. Thyroid Doppler ultrasonography revealed a heterogeneous appearance and a reduction in the echo of the thyroid gland parenchyma, which were considered to be indicative of chronic thyroiditis. The dosages of the liothyronine and hydrocortisone treatments were gradually reduced based on his clinical status and laboratory findings while in the endocrinology service. Ultimately, the liothyronine and hydrocortisone treatments were discontinued, whereas the dosage of the levothyroxine treatment was adjusted based on his needs. Coronary artery bypass grafting surgery, which was planned for the patient given the multiple occlusions, could not be performed since he refused to have the operation. The patient, whose general condition improved was discharged to be followed up as an outpatient.

Discussion

Myxedema coma is rarely seen due to the easy accessibility and feasibility of hypothyroidism treatment, however in cases when it is seen it may present with emergent manifestations. The 2 cases presented here show that hypothyroidism, which is easy to treat and accessible, may present with cardiac features such as acute coronary syndrome and cardiac arrest if left untreated. A literature review revealed only a few cases of cardiac arrest requiring emergency hospitalization for this rare condition, and only a few cases of myxedema coma presenting with acute MI.[3-6]

Figure 4. (A-C): Photograph of the patient at the time of diagnosis.

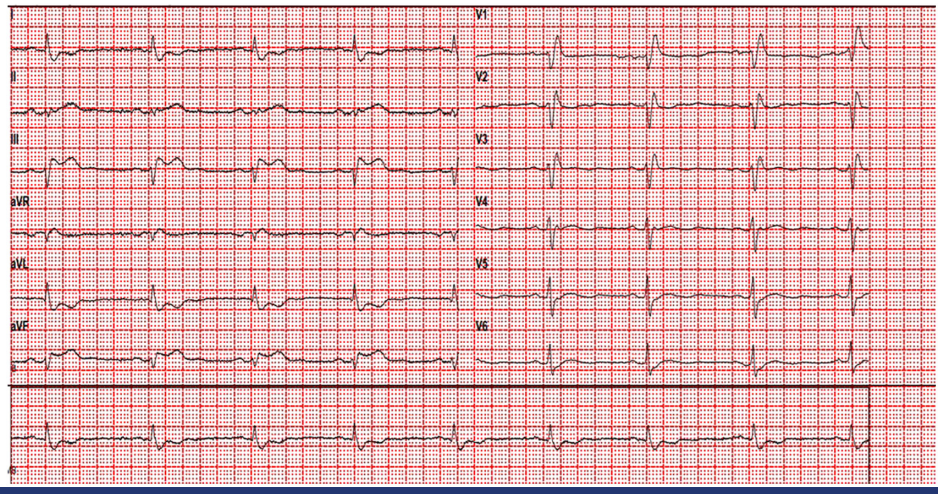

Figure 5. The first electrocardiogram of the patient at admission to the hospital.

As for the 2 cases presented herein, cardiac arrest with complete AV block and bradycardia developed in the first case, and inferior MI developed in the second case, both in the context of myxedema coma. Acute MI may be a trigger for myxedema coma, or it may be the result of an advanced myxedema coma. In this context, it may not always be clear which is cause or effect.

Thyroid hormone has an important regulatory role in cardiac gene expression, and many of the cardiac manifestations of thyroid dysfunction are associated with changes in T3-mediated gene expression. Cardiac pacemaker activity is present in specialized myocytes that generate action potentials. Thyroid hormone regulates the duration of action potential and repolarization currents in cardiac myocytes through both genomic and non-genomic mechanisms. Furthermore, thyroid hormones have an important role in maintaining the cardiovascular hemodynamics by decreasing systemic vascular resistance in the heart and peripheral vascular tissue and by increasing heart rate, left ventricular contractility, and blood pressure.

In the case of hypothyroidism, cardiac functions are adversely affected and cardiac output is reduced by 30%-50%.[7] In the event of myxedema coma, which is a severe state of hypothyroidism with manifestations of exacerbated hypothyroidism signs and symptoms, uncontrolled hypothyroidism causes a decrease in T3 expression in heart cells, thereby leading to strain on the heart muscle, decrease in heart rate, and slowing down of the conduction of electrical impulses in the heart muscle, giving rise to bradycardia.[7] Myxedema coma patients may experience life-threatening cardiac arrhythmias such as sinus bradyarrhythmia, heart block, and torsade de pointes.[8] The first case presented herein was a hypothyroidism patient who did not have any treatment for hypothyroidism for 1 year. The above-mentioned mechanism may explain the reason why complete AV block and ensuingly sudden cardiac arrest were developed in the patient.

Hypothyroidism may cause hyperlipidemia characterized by increased LDL and apolipoprotein B levels.[7] In addition to decreased receptor activity, the leading mechanism reported for the development of hyperlipidemia in the context of hypothyroidism is decreased fractional clearance of LDL by a decreased number of LDL receptors in the liver.[9] Moreover, hypothyroidism leads to increased systemic vascular resistance by impairing endothelial dysfunction and relaxation of vascular smooth muscle cells. These effects give rise to diastolic hypertension in approximately 30% of the hypothyroidism patients.[7] Hypothyroidism, which can cause hyperlipidemia and hypertension, may contribute to accelerated atherosclerosis and coronary artery disease. The cardiovascular system is a major target of thyroid hormone action and the 2 systems are closely interlinked. As a matter of fact, the second case presented herein had multiple vessel occlusions as indicated by the coronary angiogram, and it is possible that myxedema coma had triggered inferior MI by causing acute coronary spasm in RCA. On the contrary, acute MI, which developed due to multiple vascular occlusions detected in the patient, may have triggered myxedema coma by disturbing the balance of the patient who was already hypothyroid.

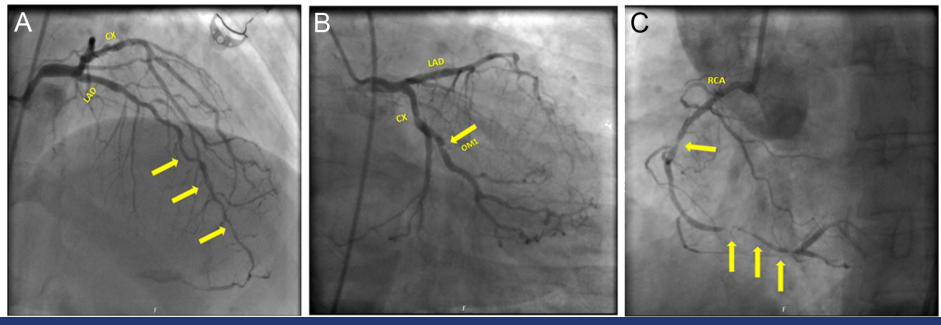

Figure 6. (A-C): Coronary angiography images of the patient.

Given that myxedema coma is a rare condition, there is no standard protocol for thyroid hormone replacement as a treatment strategy. Patients with myxedema coma are usually treated with either levothyroxine or liothyronine-levothyroxine combination therapy.[1] Especially in hypothyroidism due to autoimmune etiologies, coincidental adrenal insufficiency may be found, and accelerated metabolism of cortisol following levothyroxine treatment may lead to the development of functional acute adrenal insufficiency. In addition, subnormal cortisol response to stress may develop as a result of severe hypothyroidism reducing pituitary adrenocorticotropic hormone secretion. Therefore, it is important to add a stress dose of glucocorticoid to the treatment until the suspicion of adrenal insufficiency is eliminated. Cardiac effects can be corrected with timely and adequate treatment of hypothyroidism, and patients can go on with their lives without experiencing life-threatening conditions.

Conclusion

In conclusion, it is of utmost importance that clinicians take the differential diagnosis of myxedema coma into consideration on the basis of physical examination, ECG, and laboratory findings and initiate treatment without delay before any complications occur. Myxedema coma, which can be morbid and mortal, should definitely be kept in mind for critically ill patients presenting to the emergency department.

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