AKADEMİK ACİL TIP DERGİSİ

Case report
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Non-comatous Myxedema Attack in an Elderly which Precipitated by Acute Coronary Syndrome and Propranolol Usage. A Case Report and Review of the Literature

Yaşlı Bir Hastada Akut Koroner Sendrom ve Propranolol Kullanımının Tetiklediği Non-komatöz Miksödem Atağı. Bir Olgu Sunumu ve Literatürün Gözden Geçirilmesi

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ABSTRACT

OBJECTIVE: Myxedema coma is a rare, but severe reason of altered mental status with high mortality up to 80% in endocrine emergencies, also in non-comatose patients. The purpose of this presentation is to summarize existing patient's data, and to discuss emergency management of to be a rare reason of noncomatous myxedema attack, which precipitated with acute coronary syndrome and β blocker usage.

METHOD: In this case report, 64 year-old male patient who presented to emergency department with mental change which beginning with cold and tremor in day was reported.

RESULTS: The authors suspected hypothyroid and learned Captopril and Propranolol usage for acute coronary syndrome and hypertension in his past medical history. Also non ST elevation myocardial infarction was detected in emergency management. Patient treated successfully and discharged to home.

CONCLUSION: Prompt recognition and emergency medical treatment are essential for a successful outcome. Also peroral L-thyroxine sodium measure is a safety choice in non-comatous patients.

Key Words: Acute coronary syndrome, Beta blockers, Elderly, Emergency department, Myxedema

ÖZET

GİRİŞ VE AMAÇ: Endokrin aciller içerisinde %80'in üzerinde mortalitesi ile miksödem koması uzamış bilinç değişikliği durumunun nadir ama ciddi bir sebebidir. Bu sunumun amacı hasta bilgilerini özetlemek ve nadir bir sebep olan, akut koroner sendrom ve β bloker kullanımının tetiklediği, komatöz olmayan miksödem atağının acil tedavisini tartışmaktır.

METOD: Bu olgu sunumunda 64 yaşında acil servise gün içinde üşüme ve bilinç değişikliği ile başvuran bir erkek hasta sunulmuştur.

BULGULAR: Hastanın tıbbi öyküsünden akut koroner sendrom ve hipertansiyon nedeniyle Kaptopril ve Propranolol kullanıldığı öğrenilmiş ve hipotiroididen şüphelenilmiştir. Aynı zamanda acil serviste ST elevasyonu olmayan miyokard enfarktüsü tanısı konmuştur. Hasta başarı ile tedavi edilip evine taburcu edilmiştir.

SONUÇ: Başarılı bir gidişat için acil tanı ve tedavi esastır. Komatöz olmayan hastalarda peroral L-thyroxine sodyum tedavisi güvenli bir tercihtir.

Anahtar Kelimeler: Akut koroner sendrom, Acil servis, Beta blokerler, Miksödem, Yaşlı hasta

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INTRODUCTION

Myxedema coma is a rare but severe life threatening clinical state of hypothyroidism with high mortality also in non-comatose patients. [1,2] Symptoms are very often masked because of concurrent illnesses. The age of the patient, stage of the disease, and other illnesses or conditions such as pregnancy or acute coronary syndromes can change the clinical presentation. [1,3]

The purpose of this report is to summarize existing patient's data, and to discuss emergency management, to be a rare reason of noncomatous myxedema attack, which precipitated with acute coronary syndrome and β blocker usage.

CASE REPORT

Sixty-four years old male patient was presented to emergency department (ED) with cold, tremor and weakness complaints which suddenly onset in the morning additionally has slowing in speech, impaired memory, and changes in mental condition for a while. Initially vital signs were revealed as arterial blood pressure: 170/90 mmHg, pulse rate: 82 beats/min, respiratory rate: 20 breaths/min, body temperature: 36.0 ºC, pulse O_2%: 96% in the room weather.

In past medical history; he has no known allergy. He has hypertension, myocardial infarction and dislipidemia history for 9 years. Also he has smoking (1 packet/day) for 40 years and taking alcohol (30cc/day) for 34 years. There has no any guatrogenic disease or surgical intervention history. He was taking peroral Propranolol (50 mg/day), Captopril (25 mg/day) and Simvastatine (20 mg/day) tablets.

In physical examination, apathy in mental status, dryness and desquamation on skin with pale edematous face, swollen eye lids and slurred speech with hoarseness were observed. He has not palpable nodule on the thyroid loge and shortness of breath. In chest and heart examination, inspiratory and expiratory rales in lower zones and decrease in heart sounds were revealed. There was not murmur. Abdomen was distended but painless. There were not any pretibial edema or motor dysfunction in extremities but, dorsums of the hands were a little swollen. Glasgow Coma Score was 15 ($E_4M_6V_5$) and deep tendon reflexes were accepted normal.

In diagnostic laboratory tests, elevated cardiac biomarkers, Thyroid Stimulating Hormone (TSH) levels and decreased free thyroxin (fT_4) level were detected (Table 1). Electrocardiogram (ECG) showed normal sinus rhythm with decrease ST elevation in DI, aVL and V_5, V_6. Also, PA chest X-Ray (CXR) revealed heterogenic right lower lobe infiltration, enlarged cardiac index and minimal right pleural effusion with significant right horizontal fissure sign in right hemi thorax suspected signs of early pulmonary edema. Computed cranial tomography was normal.

Otherwise, there was not further drug usage, trauma, surgery or any medical therapy history. Patient admitted to emergency observation unit and 1 mg/kg intravenous metylprednisolone, 0.025 mg peroral L-thyroxine sodium tablet were ordered, additionally to serum physiologic resuscitation and acute coronary syndrome treatment. Patient was referred to intensive care unit bed. He discharged to be healthy 10 days later.

Table 1. Laboratory feature of the patient

Laboratory parameters	Results and Normal Ranges
Serum glucose	211 mg/dl (70-110)
Serum Glutamate Pyruvate Tranaminase	20 U/L (<45)
Serum Glutamate Oxaloacetate transaminase	69 U/L (<35)
Serume Creatinin	1.01 mg/dl (0.7-1)
Blood Urea Nitrogen	49 mg/dl (25-50)
Sodium (Na)	138 mg/dl (136-145)
Potassium (K)	3.4 mg/dl (3.5-5)
Free triiodothreonine (fT3)	1.33 pg/ml (2.4-2.7)
Free Thyroxin (fT4)	0,09 pg/ml (7-18)
Thyroid Stimulating Hormone	>100 pg/ml (0.2-4.2)
Creatine Kinase	3288 U/L (41-171)
Creatine Kinase-MB mass	62 U/L (<25)
Troponin T	0.05 ng/ml (<0.03),
Myoglobulin	161.8 ng/ml (25-58)
Hemoglobin	11,6 gm/dl (Male: 13-18, Female: 12-16)
White Blood Cell	7.75x103/mm3 (4.3-10.8)
Platelet	207 x103/mm3 (150-350)
Red Blood Cell	3.47x106/mm3 (4.2-6.9)
Mean Corpuscular Volume	101.2 fL (80-96.1)
Mean Corpuscular Hemoglobin	33.4 pg (27.5-33.2)
Mean Corpuscular Hemoglobin Concentration	33 g/dl (33.4-35.5)

Table 2. Common complaints and physical findings of myxedema

Common complaints	Physical findings
Arthralgias and myalgias	Dry hair and skin, pallor
Weigh gain	Classic myxedema face (generalize puffiness, macroglossia, ptosis, periorbital edema, coarse, sparse hair)
Generalize weakness	Pseudomyotonic reflexes
Slow speech	Abdominal distention
Constipation	Nonpitting waxy dry edema
Blurred in vision	Hypothermia
Emotional liability and headache	Altered mental condition and lethargy
Cold intolerance	Bradicardia and hypotension
	Coarsening of voice

DISCUSSION

Epidemiology

The most common etiology of hypothyroidism worldwide is iodine deficiency typically associated with endemic goiter. Primary hypothyroidism (dysfunction of the thyroid gland) accounts for up to 90-95% of cases. [2,4]

The syndrome occurs almost exclusively in older patients. More than 90% of cases occur in females (female-to-male ratio 5-10:1) during the winter months. [1,2,4] The prevalence of hypothyroidism ranges from 0.5% to 18%, depending on the study population.[5,6]

Myxedema coma occurs rarely, appearing in 0.1% of all cases of hypothyroidism. Mortality rate in myxedema coma has historically been as high as 80% but, aggressive management and early recognition have improved the mortality rate to 15-20%. [2,4,5] In the majority of patients, myxedema coma was the 1st manifestation of thyroid disease. [1]

Emergency Diagnosis and Laboratory Features
Clinic

A common misconception is that a patient must be comatose to be diagnosed with myxedema coma. However, myxedema coma is a misnomer because most patients exhibit neither the non-pitting edema known as myxedema nor coma. Instead, the major manifestation of myxedema coma is a deterioration of the patient's mental status. [7] Presented patient was one to one matched to this description.

In ED, a good medical history and physical examination can uncover signs and symptoms that may help confirm the diagnosis of hypothyroidism. The signs and symptoms characteristic of hypothyroidism are numerous yet often vague and subtle especially in early stages of the disease. [2] The more common complaints and physical findings encountered by emergency physicians were reported as in Table 2. However, elderly patients with hypothyroidism often have atypically presentations, such as decreased mobility. [2,4,7]

Laboratory Studies

Abnormal thyroid function tests are common for older adults. Measurement of serum TSH concentration comes closest to such an ideal test. The second key test is the measurement of serum fT_4, especially in exhibiting evidence of secondary hypothyroidism and those recently treated for thyroid disorders. TSH is elevated in primary hypothyroidism, but it may be normal or low in secondary causes of hypothyroidism. Free T_4 levels are low. Serum triiodothreonine (T_3) level is seen often low in ill elderly patients. [2,4,8]

Candidates for thyroid function testing clearly include patients with presentations consistent with thyroid storm or myxedema coma in the ED. Other patients with milder signs or symptoms consistent with thyroid dysfunction may also benefit from thyroid function testing. Routinely screening ED patients for thyroid disease is not indicated. [8]

Ancillary Laboratory Testing

Hyponatremia is common secondary to extracellular volume expansion produced by elevated antidiuretic hormone. Also, blood glucose level can range from normal to low secondary to decreased gluconeogenesis and reduced insulin clearance. Creatin Phosphokinase, Aspartate Aminotransferase (AST or SGOT), and Lactate Dehydrogenase levels may be elevated in myxedema coma due to increased muscle membrane permeability. Creatin Kinase M Band levels are typically normal. Furthermore, hypoventilation commonly results in hypercapnia and hypoxia in patients with myxedema coma. Additionally, urine analyze should be evaluate for source of infection. Also complete blood counts should be done because of hematological risk as a result of hypothyroidism. Lumbar puncture may be indicated to rule out meningitis. [2,4]

Imaging studies

Chest X-Ray may reveal an enlarged cardiac silhouette as a reflection of pericardial effusion. However, CXR is reported to have a 30% false-negative rate in detecting pericardial effusions due to hypothyroid. Also, it can help detect pulmonary infections often associated with myxedema coma. [2] In patients with altered mental status, the computerized cranial scan may be helpful in ruling out other etiologies such as intracerebral hemorrhage. ECG may present bradycardia, low voltage, prolonged PR interval, T wave abnormalities, and electrical alternans (suggestive of effusion), so an ECG must be done. [2,4] Furthermore, echocardiography can perform if pericardial effusion is suspected. [2]

Differential Diagnose

The hallmarks of myxedema coma are deterioration of the patient's mental status (manifesting as confusion, psychosis, apathy and, rarely coma) and hypothermia. The degree of hypothermia is directly related to mortality. [4,8] If the patient is comatose, other causes of coma must be considered. [4,8]

Myxedema coma is particularly developed during the course of chronic autoimmune thyroiditis (especially in Hashimato's throiditis). It can also occur in patients with secondary hypothyroidism (especially in pituitary radiation as iatrogenic). There are many reports of its occurrence in patients with iodide and iodine-containing drugs induced hypothyroidism because of inhibition in thyroid hormone synthesis such as in lithium, amiodarone or iodinated radiographic contrast agents. [4,7,8]

Myxedema coma also can be precipitated by an acute event such as a septic event, particularly pneumonia and urinary tract infection, as well as a myocardial infarction, or exposure to cold temperatures. [2,4-7] A few reports indicate that myxedema coma can be precipitated by metabolic disorders (such as poorly controlled diabetes mellitus, hepatic disease, renal failure) [7], malignancy, malnutrition, major surgery (e.g. coronary artery by pass surgery), burns, gastrointestinal and heavy menstrual bleeding [4,7] or by drugs (diuretics, salicylates, β blockers, clestipol, ferrous sulfate and sucralfate) especially narcotics and antiepileptics (valproat, carbamazepin, fenitoin, levo-sulpiride). [2,4-7]

As we understand from presented patient's history, he has hypothyroidism clinic for along time. Hypertension, dislipidemia, cardiac enlargement and ischemic heart disease may be the consequences of hypothyroidism in this

patient. This is similar as in *Li TM (2002)* and *Sundaram V et al. (1997)* reports. Physical and laboratory examinations revealed CHF in presented patient but, we do not need to perform echocardiography in ED conditions because of mild clinic of him.

We speculate that non ST elevation myocardial infarction additionally suspected mild congestive heart failure together with pulmonary edema and β blocker usage, as already reported by others as precipitating factors [5,6], were played an important role in further impairing thyroid function leading to non-comatous myxedema attack in presented patient. Also, these were masking the typical clinical and laboratory features of severe hypothyroidism. This was the first hypothyroidism attack of him.

Emergency Management

Patients with myxedema coma may present to ED in extreme conditions; implement initial resuscitative measures, including intravenous access and fluid resuscitation in the absence of associated hypotension, cardiac monitoring, and oxygen therapy, as indicated. Mechanical ventilation may be necessary for patients with diminished respiratory drive in response to hypercapnia and hypoxia resulting in a worsening respiratory acidosis. Stabilizing acute life-threatening conditions and initiate supportive therapy are also essential in prehospital care. [2,4]

ED management rarely requires distinguishing between primary and secondary origins. Clinical significance of abnormal test results and the need for treatment vary but, overt hypothyroidism and myxedema coma always require treatment. However, subclinical hypothyroidism treatment is not as clear. [2]

High dose (potentially toxic) thyroid hormone replacement has been recommended for treatment of myxedema coma while questions of safety of the therapy and of efficacy of low dose thyroid hormone replacement have not been systematically addressed. [2,3] Many of report suggested that most of author recommend use of intravenous L-thyroxine alone. Current recommendations on initial L-thyroxine treatment dose are changing 0.1-0.6 mg intravenously. The maintenance dose is reported as 0.05-0.1 mg daily until the patient is able to take oral replacement. [4,7] Corticosteroids (iv hydrocortisone 100 mg/tid/day) also reported as should be given before thyroxine administration until evidence of clinical improvement and stabilization has occurred or primary hypothyroidism and adrenal insufficiency has been ruled out. [4,7]

Additionally, any precipitating factor or associated problem, as claim by many authors above, should be addressed and treated appropriately.

Differentially, *Cappelli C et al.* (*2007)* was reported success with use of sublingual triiodothreonine (20 µg/tid/day for 3 days) and concomitant peroral L-thyroxine (25 mg/day) administration for treatment of severe hypothyroidism in their case report.

We used intravenous 70 mg/day methylprednisolone and peroral 25 µg/day L-thyroxine sodium tablet for treatment of myxedema attack, similarly in *Sheu CC et al.* (*2007)* case report which administered initially 50µg peroral L-thyroxine then 100µg/day for three days, followed by 150µg/day L-thyroxine plus 200mg/day corticosteroid in four divided doses in a myxedema coma patient.

We accepted presented patient as new diagnosed hypothyroid patient. We did not need to give intravenous L-thyroxine treatment because of patient can take orally and his clinic is mild and noncomatous.

CONCLUSION

Emergency physicians should be alert for myxedema coma. Prompt recognition and emergency medical treatment are essential for a successful outcome. Prevention requires screening of patients at risk for hypothyroidism and assuring thyroid hormone replacement, corticosteroid and appropriate supportive therapy additionally to treatment of precipitating factors. Also peroral levothyroxin sodium is a safety choice for noncomatous patients.

REFERENCES

1. Reinhardt W, Mann K. Incidence, clinical picture and treatment of hypothyroid coma. Med Klin (Munich). 1997 Sep 15; 92(9): 521-4.
2. Schraga ED. Hypothyroidism and Myxedema Coma. Available in: http://www.emedicine.com/emerg/topic280.htm. Article Last Updated in March 13, 2008. Accessed in May 18, 2008.
3. Yamamoto T, Fukuyama J, Fujiyoshi A. Factors associated with mortality of myxedema coma: report of eight cases and literature survey. Thyroid 1999 Dec; 9(12): 1167-74.
4. Tews MC, Shah SM, Gossain VV. Hypothyroidism: mimicker of common complaints. Emerg Med Clin North Am 2005; 23: 649-67.
5. Bailes BK. Hypothyroidism in elderly patients. AORN J 1999; 69: 1026-30.
6. Roberts C, Landeson PW. Hypothyroidism. Lancet 2004; 363: 793-803.
7. Wall CR. Myxedema coma: diagnosis and treatment. Am Fam Physician 2000; 1: 2485–2490.
8. Pimentel L, Hansen KN. Thyroid disease in the emergency department: a clinical and laboratory review. J Emerg Med 2005; 28: 201-9.