A forgotten life-threatening medical emergency: myxedema coma

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Abstract

Nowadays myxedema coma is a rare medical emergency but, sometimes, it still remains a fatal condition even if appropriate therapy is soon administered. Although physical presentation is very non-specific and diversified, physicians should pay attention when patients present with low body temperature and alteration of neurological status; the presence of precipitating events in past medical history can help in making a diagnosis. Here we discuss one such case: an 83-year-old female presented with abdominal pain since few days. Laboratory tests and abdomen computed tomography scan demonstrated alithiasic chole cystitis; she was treated but, during the Emergency Department stay she experienced a cardiac arrest. Physicians immediately started advanced cardiovascular life support algorithm and she survived. Later on, she was admitted to the Intensive Care Unit where doctors discovered she was affected by severe hypothyroidism. Straightway they started the right therapy but, unfortunately, the patient died in a few hours.

Introduction

Myxedema coma is an uncommon life-threatening endocrinological emergency: it can occur in patients with a poorly longstanding hypothyroidism or, very rarely, it can represent the first clinical manifestation of an unknown hypothyroidism. Patients affected by hypothyroidism develop many physiological strategies to compensate thyroid hormone lack; when these homeostatic mechanisms fail, patients may move towards myxedematous state. The physical presentation is non-specific and diversified: diagnosis is easier if a thyroid disease is already known, but it could be a challenge in case of unknown disease. Mortality rate ranges from 30 to 60% even in case of early detection and appropriate therapy administration.

Case Report

An 83-year-old woman came to our observation in Santa Croce and Carle Emergency Department (Cuneo, Italy) complaining of abdominal pain since few days, which was getting worse in the last four hours. She lived alone and she was in good general conditions: she was affected by artherosclerosis and primary hypertension treated with celecoxib (cyclooxygenase-2 inhibitor) and lercanidipine (calcium channel blocker) respectively. She did not report any other medical disease or medications. At the first clinical examination her vital signs were normal and the electrocardiogram proved atrial fibrillation. She was alert but objectively suffering, with dry, pale, cold and speckled skin. She referred abdominal pain mostly in the right side without signs of peritoneal irritation; ultrasound examination (exploring lungs, aorta, inferior cava vein, abdomen and deep veins) was immediately performed and it did not show any sonographic abnormalities. Laboratory tests demonstrated mildly elevated white blood cells with neutrophilic leukocytosis, normocytic non-morocchomria anaemia, hepatic dysfunction with slight elevation of cytolysis and cholestasis indexes, a probable acute kidney failure, mild hypernatrema and hyperkalemia, minimum PT-INR elongation, elevated creatine kinase (CPK) values, high glucose detection and very high c-reactive protein (CRP) levels. Cardiomegalia with minimal pleural effusion and some intestinal fluid levels were respectively detected at chest and abdomen radiographies; the abdomen CT scan showed alithiasic chole cystitis. Endovenous rehydration, antibiotic therapy (ceftriaxone and metronidazole) and analgesic treatment with morphine were started. Blood pressure decreased in a few minutes and the patient became drowsy: suspicing incipient septic shock, norepinephrine was started. Despite this, the patient lost consciousness developing cardiac arrest; physicians started cardiopulmonary resuscitation and declared Return of Spontaneous Circulation (ROSC) after 10 min. Given the previous detection of acute cholecystitis, patient immediately underwent a diagnostic laparoscopy; surprisingly, the gallbladder walls resulted edematous without any sign of acute cholecystitis. Moreover, no sign of intestinal ischemia were excluded on ECG, echocardiography and CT scans respectively. Once admitted to ICU, she presented hypothermic, with low blood pressure and very low heart rate; invasive mechanical ventilation, saline solution (2000 mL/die) and norepinephrine (0.10-0.15 mcg/kg/min) administration were continued, passive external warming measures and endovenous hydrocortisone (100 mg tid) were started, but clinical conditions worsened. Blood exams showed increasing hyperkalemia and renal impairment persistence. On past laboratory test revision, a severe hypothyroidism was discovered, probably caused by an immunogenetic mechanism [thyroid stimulating hormone (TSH) 93.4 μU/mL, n. 0.35-4.7 μU/mL, free thyroxine (FT4 3.5 pg/mL, n. 8-17.6 pg/mL, thyroid peroxidase antibodies 930 U/mL, n. <60 U/mL]. This clinical situation was unknown to our patient since laboratory tests had just been made the day before ED admission. A diagnosis of myxedema coma was formulated. The endocrinologist suggested immediate thyroxine endovenous administration (thyroxine 100 mcg) and the nephrologist indicated a continuous veno-venous hemodialysis (CVVHD). Unfortunately, after few hours, the patient developed another cardiac arrest and died. Her niece confirmed us the patient complained fatigue since few days so that her family doctor had prescribed blood test to evaluate thyroid status.

Discussion

Myxedema coma is defined as severe
hypothyroidism leading to slowing of function in multiple organs. Case series and case reports from western world showed that the incidence of myxedema coma is 0.22 million per year; in another study including 200 cases between 1953 and 1996, Werner and colleagues demonstrated that when only comatose patients are considered myxedema coma is outermost rare. Even if diagnosis is now easier, as a result of the widespread availability of TSH assays, mortality rate remains very high (from 30 to 60 percent) despite the best possible treatment. Hypothyroidism is four time more common in women than in men; myxedema coma occurs quite exclusively in over 60 years people and it typically occurs during winter months. Myxedema can result from any of the usual causes of hypothyroidism: primary hypothyroidism due to chronic autoimmune thyroiditis (which can remain latent) and, rarely, due to chronic autoimmune hypothyroidism due to long-standing disease. 

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Myxedema coma is a medical emergency: in case of high suspicion, physicians should not hesitate in starting replacement therapy while waiting for laboratory tests. The patient should be admitted to the intensive care unit in order to start ventilator support, central venous pressure monitoring, appropriate fluid administration, and aggressive management of precipitating factors. The cornermost of treatment remains thyroid hormone replacement and steroid supplementation in case of coexisting adrenal insufficiency. The optimal treatment still remains controversial because of the very low occurrence of the disease and the absence of RCT’s or clinical trials that compare different therapies. 

High thyroid hormone doses can bring to precipitating fatal tachycardia or myocardial infarction, while, on the other hand, low doses may be inadequate to improve clinical status. Treatment with T4 provides a slow and steady onset of the action with relatively low adverse reactions, but it may results less effective because of the impaired hormone conversion from the precursor T4 into the active T3. The use of T3 includes quickly shows clinical benefits, especially on neuropsychiatric symptoms, but it exposes tissues to higher thyroid hormone concentrations with more frequent side effects. Furthermore, high T3 plasma values during treatment have been correlated with high mortality rate. Treatment should be initiated intravenously because of possible gastrointestinal absorption impairment; it should be continued orally as soon as possible. Typically, T4 is administered in a loading dose of 200 to 400 mcg to saturate the body pool followed by a daily dose of 1.6 mcg/kg thereafter. If the clinical status does not improve within 24 hours, addition of T3 is recommended. Another therapy scheme consists in dispensing T3 in a dose of 5 to 20 mcg, followed by 2.5 to 10 mcg every eight hours, depending upon patient’s age and the presence of cardiovascular risk factors. T3 is then discontinued when patient improves and reaches clinical stability, while daily oral T4 is maintained. Assuming a coexisting hypopituitarism and adrenal insufficiency, empiric intravenous glucocorticoid coverage should be employed (stress dose of hydrocortisone 100 mg tid). 

Plasma cortisol levels should be drawn in case of normal or low TSH and low free T4 plasma levels. Physicians should not be surprised in case of normal or low TSH and low free T4: they may be facing secondary hypothyroidism (pituitary dysfunction), tertiary hypothyroidism (hypothalamic disorder) or low T4/low T3 syndrome (euthyroid sick syndrome: thyroid function test are altered as a result of illness unrelated to thyroid). 

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Conclusions

Myxedema coma is a potentially lethal condition. During last years, diagnosis became easier with TSH blood test availability, but it often remains unrecognized because it is a rare disease. Physicians have to maintain a high index of suspicion when facing the three following clinical conditions: altered mental status, persistent hypothermia and the presence of potential precipitating events. Unfortunately, mortality rate remains high despite early diagnosis and immediate administration of the proper therapy.

References