Myxedema Coma After Surgical Procedures: Case Report

Cerrahi Girişimler Sonrası Gelişen Miksödem Koması

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ABSTRACT Myxedema coma is an emergency condition caused by severe hypothroidism. This case report illustrates the difficulties in treating patients with untreated hypothyroidism following emergency surgery. Two patients with myxedema coma, one after appendectomy and the other after carotid endarterectomy are presented in this case report. In the differential diagnosis, Addison crisis, prolongation of duration of muscle relaxant or an intracranial event should be considered. Rapid response to levothyroxine makes diagnosis clear when clinical and laboratory assessments support myxedema coma. It is strongly recommended for the physicians to measure the thyroid hormone levels in patients with risk factors. If myxedema occurs, immediate use of intravenous levothyroxine is effective for this lethal complication.

Key Words: Myxedema; coma; anesthesia, general

ÖZET Miksödem koması ağır hipotiroidinin neden olduğu acil bir durumdur. Bu sunuda uygun tedavi edilmemiş olan hipotiroidi olgularında acil operasyonlardan sonra yaşanabilecek zorluklar vurgulamaktadır. Olguların biri apendektomi diğeri karotid endarterektomidir. Ayırıcı tanıda Addison krizi, kas gevşeticinin etki süresinde uzama ve intrakraniyal bir olay da göz önünde bulundurulmalıdır. Klinik ve laboratuvar bulgular miksödem komasını destekliyorsa, levotiroksine hızlı cevap ile tanı netleşir. Doktorlar risk faktörleri olan hastalarda tiroid hormon seviyelerini mutlaka kontrol etmelidir. Miksödem geliştiğinde hızlı levotiroksin tedavisi bu letal komplikasyonu önlemede etkindir.

Anahtar Kelimeler: Miksödem; koma; anestezi, genel

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Hyperthyroidism crisis has been widely regarded as a severe complication for patients with hyperthyroidism undergoing surgical s attention[1] Hypothyroidism is the most common pathological hormone deficiency.[2] Myxedema coma caused by severe hypothyroidism has a very low incidence, but it is a medical emergency with a high mortality characterized by severe lack of thyroid hormones, unconsciousness and serious disturbance of the vital functions. The mortality rate ranges between 50 and 80%.[1-3] In patients with inapparent hypothyroidism, myxedema coma occasionally follows acute stress events such as infection, cold exposure, a major operation or medications. If the history and signs and symptoms suggest pituitary insufficiency, one has to measure pituitary hormone levels including thyroid stimulant hormone and thyroid hormones (TSH,

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$_fT_3$, $_fT_4$). When the levels of thyroid hormones get very low, the symptoms get worse and can result in a serious condition called myxedema coma. People with hypothyroidism who are in or near a coma should be taken into an emergency department immediately. Infections, heart failure, stroke, trauma, surgery, drugs such as phenothiazines, amiodarone, lithium and tranquilizers, prolonged iodide use as well as not taking prescribed thyroid medications can contribute to myxedema coma. Blood tests are performed to check the blood cell count, electrolytes, blood glucose and thyroid hormone levels. Tests are also performed to evaluate how the liver and adrenal glands are functioning. Blood gases are evaluated to check the oxygen and carbon dioxide levels.[2-7]

Sheehan's syndrome is a condition affecting women who experience life-threatening blood loss during or after childbirth. Severe blood loss deprives the oxygen and can seriously damage vital tissues and organs. In Sheehan's syndrome, the damage occurs to the pituitary gland. The result is the permanent underproduction of essential pituitary hormones (hypopituitarism). It can lead to an adrenal crisis-a life-threatening shortage of the hormone cortisol. Treatment of Sheehan's syndrome involves hormone replacement therapy. Because pituitary hormones control so many aspects of the metabolism, Sheehan's syndrome can cause a number of problems, including acute adrenal crisis, a sudden, life-threatening state that can lead to extremely low blood pressure, shock, coma and death.[2,4,7]

There have been a few cases reported previously about myxedema coma after surgery.[1,3,4,8]

The informed consents of the patients were obtained for these case reports.

CASE REPORTS

CASE 1

A 43-year-old female who had a 13-year history of Sheehan's syndrome was presented with acute appendicitis. The results of thyroid function tests were in the normal ranges three monts previously and the levels were stable for 8 years according to the patient's history. The patient was taking levothyroxine 1+1/3 per oral daily and methyl prednisolon 5 mg per oral/daily regularly until the day of surgery. Thyroid functions could not be tested due to the urgency of the operation. There were no abnormalities on physical examination, lung auscultation or the electrocardiogram. Other laboratory tests, including the complete blood count (Hb: 12.7 g/dl), blood coagulation tests revealed normal results. The patient's blood chemistry results were as follows: blood glucose: 79 mg/dL, ALT: 20 IU/L, AST: 50 IU/L (high), Na: 132 mEq/dL (low), therefore no contraindications were identified for the urgent surgery. Because of the risk of Addison crisis (loss of salt, hypotension, shock) the Addison protocol (100 mg IV methyl prednisolon right before the operation and then 300 mg IV infusion/24 hour during operation, saline infusion 2-3 L/day in postoperative period by checking serum electrolyte concentrations and urine output) was applied during operation as recommended by the endocrinology clinic. After informed consent was obtained, ASA II E patient was brought to the operating room without any premedication, and routine monitoring was established including noninvasive blood pressure (NIBP), peripheral oxygen saturation (SpO_2), end-tidal carbon dioxide ($ETCO_2$ and heart rate. All vital signs were in normal ranges. Preoxygenation with 100% O_2 via a face mask was followed by induction of anesthesia with propofol 2 mg/kg, vecuronium 0.1 mg/kg. The maintenance of anesthesia was achieved by end-tidal sevoflurane 2% in O_2/N_2O: 1/1. Surgery lasted for approximately 60 minutes; 30 minutes after beginning the operation mild hypotension (mean: 55-60 mmHg), bradycardia (50 beat/min), hypotermia (35.8 °C, rectal) occurred. Adrenaline was given 50 μg four times until the end of the operation since bradicardia got deeper (lower than 45 beat/min) and hypotention (mean: lower than 50 mmHg), but no response to therapy could be obtained.

At the end of the surgery, although hypotonic, the patient was awake and the tidal volume was about 400-450 mL. neuromuscular block was antagonized (atropine 0.5 mg, neostigmine 1 mg IV) and then patient was extubated. Although SpO_2 was 95-96% at first, 10 minutes after the extubation

SpO_2 decreased to 85% with O_2 given through the mask. The patient regained consciousness, hypotonicity in muscles, somnolence, dyspnea, periorbital edema, abdominal distention and SpO_2 decreased gradually to 60% in room air. The blood gas analysis revealed PO_2: 50 mmHg, PCO_2: 45 mmHg and pH: 7.22 in the room air. Body temperature was 34.4°C (rectal). Lung auscultation was normal. Although nasogastric catheter has been applied and gastric ingredients were drained out, abdominal distention continued. After urinary catheter insertion, furosemide 20 mg IV was given. Diuresis was normal. A neurologist examined the patient in the operating room. Dry mucous membranes, and delayed deep tendon reflexes confirmed hypothyroidism. The patient was not neurologically normal since she had somnolence- stupor. Passive rewarming was initiated. As hypoxemia gradually deepened, the patient was re-entubated easily despite significant posterior pharyngeal edema obscuring direct visualization of the vocal cords, we administered propofol 50 mg IV without any muscle relaxant and then we initiated mechanical ventilator-assisted ventilation by transporting her into the intensive care unit. The patient remained unconscious, and respiratory functions stayed unstable for the next 8 hours. A chest X-ray showed no signs of respiratory infection, atelectasis, pleural effusion, or pneumo. The possibility of thyroid function abnormality after the stress of the operation was considered as the patient had a history of hypothyroidism. Blood thyroid hormone levels were tested before hormone replacement. The test results indicating myxedema coma were as follows:

${}_fT_3$: 0.38 pmol/L (0.6-1.95), ${}_fT_4$: 3.9 pmol/L (5-11.5), TSH: 0.729 mU/L (0.3-4), sodium: 130 mEq/dL.

The patient's vital signs monitored in intensive care unit were stable during the postoperative first day. Levothyroxine (300 μg per oral) was immediately administered and maintained in a dose of 60 μg daily. Her clinical condition gradually improved. Concentrations of thyroid hormones on postoperative second day were still low (Normal ranges were given different as tests were performed in two different laboratories):

${}_fT_3$: 2.45 pmol/L (2.5-3.9), and ${}_fT_4$: 0.38 pmol/L (0.61-1.2). TSH: 0.68 mU/L (0.3-4).

One month later: TSH: 0.069 mU/L (0.3-4), ${}_fT_4$: 1.38 pmol/L (0.61-1.2).

The patient was discharged from intensive care unit two days later. There were no post-extubation airway difficulties or complications, and amnesia resolvedcompletely. The patient's condition remained stable except incisional pain. Other supportive measures were applied to maintain the electrolyte and acid-base balance. The patient was able to take a semi-liquid diet on the 8th day of the hospitalization and discharged home on day 10 uneventfully with daily levothyroxine.

CASE 2

A 55-year-old woman presented with a 2-month history of right ear pain. The patient was diagnosed with glomus caroticum and planned to undergo endarterectomy. The patient had thyroidectomy operation two years ago and was taking per oral levothyroxine irregularly. Thyroid hormone levels were not obtained, the electrocardiogram showed sinus bradycardia (45 beat/min), other laboratory tests including the complete blood count, blood coagulation tests and blood chemistry revealed normal results. No contraindications wee identified for the procedure. After the procedure, the patient was unconscious and disorientated, had a tendency for stupor, had hypotermia (35°C), bradycardia (43 beat/min), hypotension (70/40 mmHg), hyponatremia (128 mEq/L) and hypoglycemia (68 mg/dL). Control cranial tomography and cranial angiography showed no signs of subarachnoid bleeding or an intracranial event. The possibility of thyroid function abnormality after the stress of the operation was considered as the patient had history of hypothyroidism. The blood was drawn for thyroid hormone analysis one day after the operation. The test results were as follows:

${}_fT_3$: 2.16 pmol/L (2.5-3.9), ${}_fT_4$: <0.25 pmol/L (0.6-1.2), TSH: 38.28 mU/L (0.34-4.25).

Levothyroxine (300 μg per oral) was immediately administered and maintained in a dose of 60 μg daily. The patient's clinical condition improved

gradually. The patient was discharged on postoperative 5th day. Ten days after the operation, TSH level was 1.2 mU/L (0.34-4.25).

DISCUSSION

After an emergency procedure, a hypothyroid patient may appear with myxedema coma. In the differential diagnosis, Addison crisis, prolongation of duration of muscle relaxant or an intracranial event should be considered. Attention should be paid for the risk of cardiac complications and the body temperature. In our cases, Addison crisis was not considered because of corticosteroid replacement during surgery. There was no possibility of prolongation of the muscle relaxant effect since its effect was reversed. Therefore there was no objection for extubation, but the patient could not tolerate extubation and re-entubated. Clinical and laboratory assessments of the patient supported myxedema coma (weakness, confusion, feeling cold, low body temperature, edema of the body, dyspnea, abnormal blood gases, low thyroid fonction test values). Rapid response to levothyroxine made the diagnosis clear (Oral form of levothyroxine was given due to absence of the intravenous form).

Clinical manifestations of myxedema coma may vary in patients, but the presentation usually includes decreased mental status, hypothermia, hypotension, bradycardia, hyponatremia, hypoglycemia and hypoventilation. Laboratory findings can show distinctive thyroid stimulating hormone, free triiodothyronine, and free thyroxine changes. Early diagnosis and treatment are crucial for a successful rescue.[2,4-9] All signs were present in our patients.

In the medical treatment, usually thyroid hormones are administered (intravenously) to correct the low thyroid hormone levels quickly (Oral form of thyroid hormones are usually not used for treatment of severe myxedema coma, because it may take days or weeks to obtain the proper blood level). Endocrinologists strongly recommend that physicians should measure the thyroid hormone levels in patients with risk factors. If myxedema coma occurs, immediate use of intravenous levothyroxine is an effective in treatment for this lethal complication.[1-3,6]

In the treatment, fluid resuscitation is commonly required even in the absence of associated hypotension since intravascular volume depletion is common. Exacerbation of underlying congestive heart failure and hyponatremia must weigh against the benefits of fluid resuscitation.[7]

Comprehensive supportive therapy, including mechanical ventilation if necessary, rewarming the body temperature, and treatment of the hypotension, bradycardia, and hyponatremia is essential for this life-threatening condition. More importantly, intravenous thyroid hormone replacement therapy should be started immediately. Myxedema coma can result in cardiovascular collapse; prompt recognition and treatment can be life saving. Patients presenting with possible myxedema coma should be treated with levothyroxine 100-500 μg intravenously.[10] According to the literature, there is not a consensus concerning the emergent perioperative management of myxedema coma.[1,9] Some endocrinologists prefer ${}_fT_3$ (10-25 μg intravenously every 8 h) as it has grater biological activity and ${}_fT_4$ to ${}_fT_3$ conversion is impaired in hypothyroidism. However if excess ${}_fT_3$ is given, mortality may increase. Alternatively, many prefer 200-500 μg ${}_fT_4$ intravenously or via nasogastric tube as the first dose, followed by 50-100 μg/day using smaller doses in the elderly. Others advise giving a combination of ${}_fT_3$ and ${}_fT_4$. The medication is levothyroxine initially administered at a dose of 200-500 μg IV, followed by 50-100 μg/day. These patients were successfully rescued with 300 μg of levothyroxine, followed by 60 μg/day.[2,5,7-12] By the way, attention should be paid for the risk of cardiac complications and the body temperature. The core temperature must be checked using a low-reading thermometer, as the mortality of this condition is related to the severity of the hypothermia. Hypotermia is due to decreased metabolism resulting in reduced heat generation.[9]

Acute severe stress of appendectomy caused myxedema coma, so that the need for thyroid hormone replacement increased dramatically after the operation. Thus, the compensation of the thyroid gland was not sufficient to meet this increasing metabolic requirement in a relatively short period, and as a result, the patient presented with severe hypothyroidism manifesting as myxedema coma.

In summary, it is strongly recommended that physicians should test the thyroid hormone levels especially in patients with thyroid gland diseases. If myxedema coma occurs, immediate intravenous thyroid hormone replacement ($_fT_4$ and/or $_fT_3$) is effective for this lethal complication.

REFERENCES

1. Yuan Y, Hu Y, Xie T, Zhao Y. Myxedema coma after esophagectomy. Ann Thorac Surg 2010;90(1):295-7.
2. Roberts CG, Ladenson PW. Hypothyroidism. Lancet 2004;363(9411):793-803.
3. Yamamoto T, Fukuyama J, Fujiyoshi A. Factors associated with mortality of myxedema coma: report of eight cases and literature survey. Thyroid 1999;9(12):1167-74.
4. Pimentel L, Hansen KN. Thyroid disease in the emergency department: a clinical and laboratory review. J Emerg Med 2005;28(2):201-9.
5. Utiger RD. Altered thyroid function in nonthyroidal illness and surgery. To treat or not to treat? N Engl J Med 1995;333(23):1562-3.
6. Bailes BK. Hypothyroidism in elderly patients. AORN Journal 1999;69(5):1026-30.
7. Tews MC, Shah SM, Gossain VV. Hypothyroidism: mimicker of common complaints. Emerg Med Clin North Am 2005;23(3):649-67, vii.
8. Ragaller M, Quintel M, Bender HJ, Albrecht DM. [Myxedema coma as a rare postoperative complication]. Anaesthesist 1993;42(3):179-83.
9. Wall CR. Myxedema coma: diagnosis and treatment. Am Fam Physician 2000;62(11):2485-90.
10. Barbetakis N, Asteriou C, Tsilikas C. Treatment of myxedema coma after major thoracic surgery. Ann Thorac Surg 2011;91(4):1310; author reply 1310-1.
11. Kearney T, Dang C. Diabetic and endocrine emergencies. Postgrad Med J 2007;83(976):79-86.
12. Fritsch N, Tran-Van D, Dardare E, Gentile A, Deroudilhe G, Fontaine B. [The myxoedema coma exists, we met it]. Ann Fr Anesth Reanim 2007;26(9):795-8.