วารสารวัณโรค โรคทรวงอก และเวชบำบัดวิกฤต
Thai Journal of Tuberculosis Chest Diseases and Critical Care

รายงานผู้ป่วย
Case Report

Myxedema Coma with Possible Obesity Hypoventilation Syndrome: A Case Report

Nattapong Boonrod*

Nitipatana Chierakul**

Nopparat Sakonsontisate**

** Department of Medicine, Trat Hospital, Trat, 23000*

*** Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand*

Abstract: The association between hypothyroidism and breathing disorders has been well recognized. In Thailand, a document case of myxedema coma with obesity hypoventilation syndrome (OHS) has never been reported. A 47-year-old woman was admitted with progressive dyspnea suspected of congestive heart failure. Her weight was 120 kg with the height of 1.67 m and body mass index of 43 kg/m^2. She had hypothermia, bradycardia, loss of the outer third of the eyebrows, and slow relaxation of deep tendon reflexes. The serum T3 was 0.587 ng/mL (0.87-1.78), FT4 0.163 ng/dL (0.58-1.64), and TSH 45.440 mIU/mL (0.64-5.60). Unfortunately, she developed coma and respiratory failure within 24 hours of admission. After gradually step-up dose of oral thyroid hormone ɩreplacement and respiratory support, her symptoms were gradually improved and successfully liberated from mechanical ventilation to spontaneous breathing with non-invasive ventilation. Arterial blood gas while breathing room-air demonstrated moderate hypoxemia and chronic respiratory acidosis. Further investigation for concomitant obesity hypoventilation syndrome is in process.

Introduction

Myxedema coma is a medical emergency that requires immediate treatment due to life-threatening condition and the need for prompt and appropriate management, especially in patients with a history of untreated or inadequately managed thyroid disease. Almost 80% of myxedema coma cases typically occur in women.[1] The diagnosis is based on clinical of altered mental status and hypothermia after precipitating events such as infection, burn, trauma, surgery, drugs, hypercapnia, and hypoxemia etc.[2] Obesity hypoventilation syndrome (OHS) is defined as a combination of obesity (body mass index ≥ 30 kg/m^2), daytime hypercapnia (arterial carbon dioxide tension ≥ 45 mmHg) and sleep-disordered breathing, after ruling out other disorders that may cause alveolar hypoventilation.[3] In real-world clinical practice, the co-existence of myxedema coma and exacerbation of OHS is not easy to differentiate.

Case report

A 47-year-old woman, working as a net maker from Trat Province, was admitted to Trat Hospital because of dyspnea on exertion over the past month.

รับไว้ตีพิมพ์เมื่อวันที่ 3 ตุลาคม 2567

During the past 10 years, she has gradually gained 25 kilograms of body weight. In the recent years, habitual loud snoring, frequent awakenings with gasping for breath at night, and excessive daytime sleepiness were noted. Subsequently, she has had experienced progressive dyspnea on exertion during the past year, along with orthopnea and paroxysmal nocturnal dyspnea. Neither chest pain nor fever was noticed. During the past 2 weeks, the aforementioned symptoms became worsening. Her past medical history includes hypothyroidism due to post iodine-ablation for thyrotoxicosis last 11 years ago. During the COVID pandemic, she lost to follow-up and had discontinued thyroid hormone supplement. She used to smoke socially but had quit for the past 3 years. No history of alcohol drinking or drug abuse is established.

Initial physical examination revealed a conscious obese woman in acute distress, her height was 1.67 m. with body weight of 120 kg and BMI of 43 kg/m^2, her neck circumference was 47 cm. The body temperature was 37.4^{o}C, blood pressure 140/80 mmHg, heart rate 100 beats/min, respiratory rate 30 breaths/min, and room air pulse oxygen saturation of 88 %. Pitting pedal edema and fine crackles in both lungs were noted. Admission laboratory studies disclosed: hemoglobin 11.2 g/dL, hematocrit 35.2 % with normal red blood cell morphology, WBC 7,200/μL with normal differential count, HbA1C 6.5%, cholesterol 295.7 mg/dL, triglycerides 166.6 mg/dL, HDL-cholesterol 66.8 mg/dL, and LDL-cholesterol of 196 mg/dL. Serum bicarbonate was 41.2 mmol/L but other electrolyte levels wee within normal limit. Chest radiography demonstrated markedly increased cardiac silhouette with perihilar reticular opacities (Figure 1). Electrocardiogram showed sinus rhythm with generalized low voltage without specific ST-T changes.

An initial diagnosis of congestive heart failure was made and intravenous furosemide along with oxygen supplement were given. Her subsequent urine output was 3,500 mL in 16 hours, however, her consciousness was deteriorated. The body temperature became 36.0^{o}C, blood pressure 120/74 mmHg, regular heart rate of 40 beats/min, respiratory rate of 18 breaths/min, and pulse oxygen saturation of 90% while breathing high-flow oxygen cannula of 60 LPM and FiO_2 1.0. Thorough physical examination revealed a comatose woman with dry and coarse skin. Loss of the outer one-third of her eyebrows, macroglossia, acanthosis nigricans, and slow relaxing deep-tendon reflexes were noted. Cardiovascular examination demonstrated apical impulse at 6th intercostal space 2-cm lateral to mid-clavicular line with LV heave. Chest auscultation revealed fine crackles in both lower lung zones. Her thyroid gland was not enlarged and other physical examinations were unremarkable.

Myxedema coma was diagnosed based on altered mental status, hypothermia, bradycardia, and precipitating events such as carbon dioxide retention, hypoxemia, congestive heart failure, and the use of furosemide. The subsequent thyroid function tests (TFT) showed triiodothyronine (T3) 0.587 ng/mL, free thyroxine (FT4) 0.163 ng/dL, and thyroid stimulating hormone (TSH) 45.440 mIU/mL. Other blood chemistry results were within normal limit. Initial treatment composed of oral thyroxine at 500 μg stat and then 200 μg/day (1.6 μg/kg/day) with close clinical follow-up for cardiovascular complications. At the same time, an endotracheal tube was inserted and the patient was connected to mechanical ventilation, and intravenous hydrocortisone was started at 100 mg stat and then 200 mg/day. Initial arterial blood gas results were pH 7.474,

pO_2 54.3 mmHg, pCO_2 45.8 mmHg, and bicarbonate 35.5 mmol/L. Echocardiography showed no pericardial effusion and good left ventricular ejection fraction. Her symptoms were gradually improved within few days and she became alert and responsive following commands. Her pulse rate increased from 40 to 60 beats/min, and her body temperature also returned to normal. Due to the intensive care unit (ICU) bed was not available, her medical care was conducted in general ward under close monitoring. Liberation from mechanical ventilation was successful at 8 days later and replaced by non-invasive ventilation (NIV) with bi-level continuous positive pressure (BiPAP) without oxygen supplement. Duration of spontaneous ventilation without BiPAP was gradually increased (Figure 2). The serum cortisol level measured before administering hydrocortisone was 32.700 µg/dL, so the steroid was tapered off. Because of the high clinical likelihood of obstructive sleep apnea (OSA) with the STOPBANG score of 5 from the total of 8 points, we plan to send her for polysomnography at Siriraj Hospital for establishing the diagnosis of OSA and OHS in conjunction with additional bariatric surgery. Before discharge, her serum FT4 was increased to 0.46 ng/dL and TSH was decreased to 14.20 mIU/L Additionally, enalapril was administered to treat hypertension. At the 2-week follow-up visit after discharge, her physical activity was improved without symptoms of heart failure and she can tolerate only nocturnal BiPAP quite well. Her body weight was 115 kg, and the TFT showed serum FT4 increasing to 1.070 ng/dL and TSH lowering to 7. 202 mIU/L with oral thyroxine 200 µg/day (1.6 µg/kg/day).

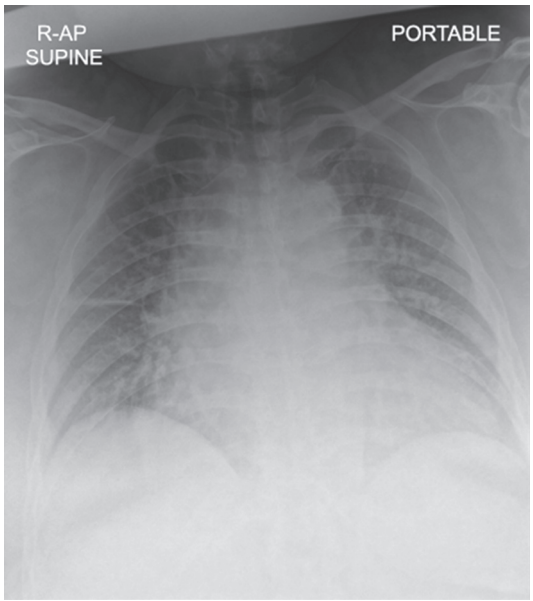

Figure 1. Initial portable chest radiograph demonstrates cardiomegaly with perihilar interstitial opacities.

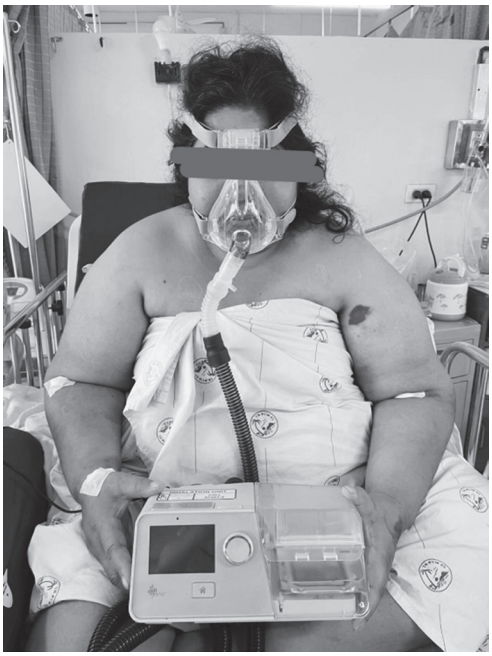

Figure 2. The patient is sitting in her bed with the support of her ventilation by BiPAP machine.

Discussion

Myxedema coma is a potentially fatal complication of hypothyroidism, and prompt diagnosis is an important factor in reducing morbidity and mortality. An appropriate response to treatment would be evidenced by improvement in mental status and stabilization of vital signs within hours to days. The monitoring of FT4 and TSH is an objective way to observe improvement in patients with myxedema coma. However, TSH levels may reflective of the thyroid status for the prior 6-8 weeks, therefore these levels may not be representative of response to current thyroid treatment. For this reason, clinical improvement and FT4 status may be superior in assessing response to therapy.[4]

Patients with OHS displayed some prevalence of hypothyroidism, particularly in women, the prevalence of clinical hypothyroidism was as high as 18.8% in one case series.[5] In certain definition of OHS, hypothyroidism and other causes of hypercapnia should be excluded before coming to the final diagnosis. However, concurrent hypothyroidism and OHS or severe hypothyroidism alone is quite difficult to differentiate. It has been previously proposed that hypothyroid status increases upper airway narrowing and suppresses hypoxic and hypercapnic ventilatory responses, which theoretically could increase the predisposition of patients to become obese and develop OSA which eventually may progress to OHS.[6-8] Deficiency of thyroid hormone also could promote mucopolysaccharides and proteins infiltrate the tongue producing enlargement of soft tissues in oropharynx and enhancing upper airway narrowing, resulted in anatomical upper airway obstruction during sleep.[9-11] On top of that, hypothyroidism may modify the myosin heavy chain profile, particularly in the genioglossus muscle, which causes dysfunction of the muscle.[12] Myopathy of the respiratory muscles related to the role of thyroid hormone in cellular metabolism and Na-K-ATPase activity may be contributed to progressive hypoventilation with subsequent hypercapnia. Impaired respiratory center function is another issue, the pathogenesis remains unclear but is thought to be an effect of thyroid hormone action.[6, 13] In one large cohort, almost 30% of patients with hypothyroidism have a reduced ventilatory response to hypoxia and hypercapnia.[14]

Female sex has been identified as a predictor of blunted ventilatory response in patients with hypothyroidism.[15] Studies of the effects of thyroid hormone replacement therapy on ventilatory response had reported conflicting results, some authors showed improvement in ventilatory response whereas others showed no improvement in respiratory parameters.[6, 14-16] Thyroid hormone replacement therapy in patients with myxedema or hypothyroidism caused no significant improvement in the hypercapnic responsiveness in either group.[6] In contrast, in a study of 38 patients with hypothyroidism who were assessed after 1 week of thyroid hormone therapy, most patients normalized their ventilatory responses after 1 week of treatment.[15] The discrepancy between these results reflecting complex interaction between thyroid hormone and ventilatory response. Other individual factors, including the severity and duration of the hypothyroidism, may contribute to the response of thyroid hormone replacement therapy.

Lastly, respiratory support and good respiratory care also play a pivotal role for patients presented with myxedema coma with or without OHS. With the advent of NIV either continuous positive airway pressure (CPAP) or BiPAP, caring of this kind of patient is more feasible even outside the ICU as in this case report. Initial CPAP may be considered in those with less severity, but for the complexity of myxedema and OHS and possible cardiomyopathy as in our patient, BiPAP is a suitable option.[17]

Summary

Myxedema coma is primarily diagnosed based on clinical findings accompany with biochemical results. Concomitant obesity hypoventilation syndrome should be considered in those with massive body mass index. With the careful titration of thyroid hormone replacement, along with appropriate supportive care especially for the respiratory and cardiovascular systems, uneventful hospital course is not inevitable.

References

1. Davis PJ, Davis FB. Hypothyroidism in the elderly. Compr Ther 1984; 10:17-23.
2. Jonklaas J, Bianco AC, Bauer AJ, *et al*. Guidelines for the treatment of hypothyroidism: prepared by the American Thyroid Association task force on thyroid hormone replacement. Thyroid 2014; 24:1670-751.
3. Masa JF, Pépin J-L, Borel J-C, Mokhlesi B, Murphy PB, Sánchez-Quiroga MA. Obesity hypoventilation syndrome. Eur Respir Rev 2019; 28:180097.
4. Elkattawy S, Dhanoa P, Kotys J, Fichadiya H, Eckman A. Myxedema coma: case report and literature review. Cureus 2021; 13:e15277.
5. BaHammam AS, Aleissi S, Olaish AH, Almeneessier AS, Jammah AA. Prevalence of hypothyroidism in a large sample of patients with obesity hypoventilation syndrome. Nat Sci Sleep 2020; 12:649-59.
6. Zwillich CW, Pierson DJ, Hofeldt FD, Lufkin EG, Weil JV. Ventilatory control in myxedema and hypothyroidism. Engl J Med 1975; 292:662-5.
7. Saaresranta T, Polo O. Hormones and breathing. Chest 2002; 122:2165-82.
8. BaHammam AS, Pandi-Perumal SR, Piper A, *et al*. Gender differences in patients with obesity hypoventilation syndrome. J Sleep Res 2016; 25:445-53.
9. Devdhar M, Ousman YH, Burman KD. Hypothyroidism. Endocrinol Metab Clin North Am 2007; 36:595-615.
10. Batniji RK, Cevera JJ, Gavin JP, Seymour PE, Parnes SM, Parnes SM. Supraglottic myxedema presenting as acute upper airway obstruction. Otolaryngol Head Neck Surg 2006; 134:348-50.
11. Watson EM, Pearce RH. The mucopolysaccharide content of the skin in localized (pretibial) myxedema. Am J Clin Pathol 1949; 19:442–7.
12. Petrof BJ, Kelly AM, Rubinstein NA, Pack AI. Effect of hypothyroidism on myosin heavy chain expression in rat pharyngeal dilator muscles. J Appl Physiol 1992; 73:179-87.
13. Duranti R, Gheri RG, Gorini M, *et al*. Control of breathing in patients with severe hypothyroidism. Am J Med 1993; 95:29-37.
14. Massumi RAWJ, Winnacker JL. Severe depression of the respiratory center in myxedema. Am J Med 1964; 36:876-82.
15. Ladenson PW, Goldenheim PD, Ridgway EC. Prediction and reversal of blunted ventilatory responsiveness in patients with hypothyroidism. Am J Med 1988; 84:877-83.
16. Wilson WR, Bedell GN. The pulmonary abnormalities in myxedema. J Clin Invest 1960; 39:42-55.
17. Randerath W, Verbraecken J, Andreas S, *et al*. Definition, discrimination, diagnosis and treatment of central breathing disturbances during sleep. Eur Respir J 2017; 49:1600959.

บทคัดย่อ: ณัฐพงษ์ บุญรอด[1], นิธิพัฒน์ เจียรกุล[2], นพรัตน์ สกลสนธิเศรษฐ์[2]. รายงานผู้ป่วยภาวะหมดสติจากการขาดฮอร์โมนไทรอยด์ร่วมกับภาวะอ้วนจนหายใจต่ำ. วารสารวัณโรค โรคทรวงอกและเวชบำบัดวิกฤต 2567; 43: 110-115.

[1] กลุ่มงานอายุรกรรม โรงพยาบาลตราด
[2] ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์ศิริราชพยาบาล

ความสัมพันธ์ระหว่างการขาดฮอร์โมนไทรอยด์กับการหายใจผิดปกติเป็นที่รับทราบกันดี ในประเทศไทยยังไม่มีรายงานผู้ป่วยที่หมดสติจากภาวะต่อมไทรอยด์ทำงานต่ำร่วมกับภาวะอ้วนจนหายใจต่ำ รายงานผู้ป่วยหญิงหนึ่งรายอายุ 47 ปี มีอาการหอบเหนื่อยที่เป็นมากขึ้นเรื่อย ๆ จนกระทั่งเมื่อเข้ารับการรักษาในโรงพยาบาลแล้วสงสัยภาวะหัวใจล้มเหลว ตรวจพบน้ำหนักตัว 120 กิโลกรัม ส่วนสูง 1.67 เมตร คิดเป็นดัชนีมวลกาย 43 กก./ม.^{2} ร่วมกับมีอุณหภูมิร่างกายต่ำและหัวใจเต้นช้า ขนคิ้วน้อย และเคาะรีเฟล็กซ์พบมีการคลายตัวช้า วัดระดับฮอร์โมน T3 ในเลือดได้ 0.578 นก./มล. (0.87-1.78), FT4 0.163 นก./ดล. (0.58-1.64), และ TSH 45.440 mIU/มล. (0.64-5.60) ภายหลังรักษาในโรงพยาบาลเกิดอาการหมดสติและหยุดหายใจ เมื่อเริ่มให้ฮอร์โมนไทรอยด์ทางปากโดยค่อย ๆ เพิ่มขนาดร่วมกับการบริบาลในระบบการหายใจ อาการของผู้ป่วยดีขึ้นตามลำดับสามารถหยุดการช่วยหายใจและเอาท่อช่วยหายใจออกได้ แต่ยังต้องใช้การช่วยหายใจแบบไม่รุกล้ำผ่านทางหน้ากาก ผลการตรวจก๊าซในเลือดแดงพบภาวะพร่องออกซิเจนร่วมกับภาวะคาร์บอนไดออกไซด์คั่งในเลือด จึงวางแผนว่าเมื่อผู้ป่วยอาการดีขึ้นเพียงพอแล้วจะส่งไปทำการตรวจการนอนหลับเพิ่มเติมเพื่อยืนยันภาวะอ้วนจนหายใจต่ำที่อาจพบร่วมด้วย