Case Report

Myxedema Coma and Acute Respiratory Failure in a Young Child: A Case Report

Rinah Elaisse R Dolores¹* and Marion O Sanchez¹,²

¹Department of Pediatrics, National Children’s Hospital, 264 E. Rodriguez Sr. Blvd Quezon City, 1102 (02) 8724 0656, Philippines
²Institute of Pulmonary Medicine, St. Luke’s Medical Center, 279 E. Rodriguez Sr. Blvd Quezon City, 1102 (02) 8723 0101, Philippines

Abstract

Background: Myxedema is an extreme manifestation seen in patients with untreated hypothyroidism. It is a lethal endocrine emergency, which arises when a precipitating cause overwhelms the compensatory mechanisms of the hypothyroid state.

Objectives: This case report aims to present a case of myxedema coma secondary to cretinism. It also aims to discuss how hypothyroidism leads to hypoventilation and eventually respiratory failure, as well as to discuss the epidemiology, pathophysiology, clinical manifestation, diagnosis, and management of a child with myxedema coma.

Case presentation: This is a case of a 7-year-old female, diagnosed with congenital hypothyroidism at 5 months of age, but eventually was lost to follow-up. She came back after 7 years presenting with difficulty of breathing. She was seen hypothermic, obtunded, and in severe respiratory distress. She was severely stunted and underweight with coarse facial features. Initial laboratory work-up showed elevated Thyroid Stimulating Hormone (TSH) as well as decreased tri-iodothyronine (FT3) and thyroxine (FT4). She was immediately started on levothyroxine, with noted resolution of the edema and improvement in sensorium. There was also noted improvement in the patient’s ventilation and was sent home on Continuous Positive Airway Pressure (CPAP) while asleep.

Conclusion: This case highlights the importance of having a high index of suspicion of its clinical manifestations, which could lead to earlier intervention thereby preventing further complications. A multidimensional approach is essential in managing this case, as various organ systems are involved in this condition.

Introduction

Myxedema coma, also known as decompensated hypothyroidism in recent literature [1], is a rare and fatal complication of longstanding, severe, and untreated hypothyroidism [2]. It is a medical emergency, and even with early diagnosis and treatment, mortality can be as high as 30% - 60%, due to significant medical complications. In children, there are only a few reported cases and limited therapeutic experiences ([2], having an estimated incidence rate of 0.22 cases per million people per year [3]. In the Philippines, there were only 6 reported pediatric cases of myxedema coma and only 12 reported cases of congenital iodine-deficiency syndrome (cretinism) in the Philippine Pediatric Society registry.

Thyroid hormones play an essential role in metabolism and development, which have a profound impact on various organ systems. Low intracellular levels of triiodothyronine affect the functioning of the central nervous, cardiovascular, and respiratory systems as well as thermogenesis, metabolism, and fluid balance [1]. In cases of prolonged and severe hypothyroidism, compensatory mechanisms that maintain homeostasis are disrupted after a precipitating event causing the constellation of findings presenting as myxedema coma [4].

Respiratory failure associated with myxedema coma has a high mortality. Three mechanisms are presumed to cause respiratory failure associated with hypothyroidism. These are (1) impaired ventilatory response to hypoxia...
and hypercapnia, resulting in respiratory acidosis, (2) hypoventilation due to weakness of respiratory muscles and diaphragm causing a restrictive respiratory pattern, and (3) obstructive sleep apnea syndrome due to soft tissue infiltration by mucopolysaccharides and protein causing pharyngeal narrowing [5,6].

Here is a case of a young child with congenital hypothyroidism. For years she was lost to follow-up, and then was brought to the same institution 7 years later in acute respiratory failure and was managed as myxedema coma due to the presence of edema associated with altered sensorium and hypothermia. She was promptly started on antibiotics and levothyroxine, with a remarkable resolution of edema and improvement in sensorium. This highlights the importance of prompt diagnosis and treatment to prevent further deterioration.

Case report

This is a case of a 7-year-old Filipino female, from Bulacan, Philippines, seen at the National Children’s Hospital for the second time due to difficulty of breathing. The patient is a known case of Congenital hypothyroidism, initially presenting as failure to gain weight at 5 months of age with associated microcephaly, macroglossia, and dry skin. She was severely stunted and underweight. Subsequent work-up showed elevated TSH (>100 uIU/ml) and decreased FT3 (<0.4100 uIU/ml) and FT4 (0.34 uIU/ml). She was sent home with Levothyroxine at 12 mcg/kg/day. Relatives have been noncompliant in administering medications and the patient was eventually lost to follow-up. 7 years later she presented to the emergency room with a month history of productive cough, fever, and noisy breathing and with generalized edema. On presentation, she was in a critical state, obtunded, and in hypoxicemic respiratory failure.

On physical examination, the patient was obtunded, with stridor, and in severe respiratory distress. She was normotensive, with a normal heart rate, but hypothermic at 34 °C and hypoxemic with an oxygen saturation of 88%. Her anthropometrics revealed severe underweight, severe stunting, and microcephaly. There was generalized pallor and non-pitting edema. Her skin was dry and rough, along with fine scales and her nails were also dry, dull, and brittle. There was also diffuse alopecia, with fine and soft hair. This was also observed from her eyebrows. Examination of the oral cavity revealed thick and dry lips with inflamed gingiva and aphthous ulcers seen on the gums and tongue. There was also noted absence of teeth and macroglossia. Respiratory findings include intercostal and substernal retractions, with bilateral coarse crackles. The cardiac examination was unremarkable. The abdomen was globular, with everted umbilicus and fluid wave. Examination of the breast and pubic hair graded Tanner stage I. She was also noted to have cool peripheral extremities and non-pitting edema on both upper and lower extremities. She only showed a reaction to painful stimuli (Figure 1).

The patient was subsequently intubated and admitted to Pediatric Intensive Care Unit. She was started on Ceftriaxone and Levothyroxine at 4.6 mcg/kg/day. Baseline thyroid function tests revealed decreased levels of FT3 (<0.4 uIU/ml) and FT4 (<0.5 uIU/ml) and elevated TSH (>100 uIU/ml), hence levothyroxine was adjusted to 9.25 mcg/kg/day. The patient underwent a blood transfusion due to anemia with initial hemoglobin of 45 and hematocrit of 14. After 48 hours of treatment with levothyroxine, there was noted improvement in the sensorium of the patient, with spontaneous movement of extremities, and ventilatory support was shifted to Non-Invasive Positive Pressure Ventilation (NIPPV) with minimal oxygen requirement on the 3rd day. In the interim, the patient still had generalized edema, with a 24% increase in weight. Abdominal circumference also increased by 8%. Macroglossia was still prominent at this time. Repeat thyroid function tests revealed that FT3 and FT4 levels were now at their normal range. While TSH was still elevated, levothyroxine was continued at 7.4 mcg/kg/day. 2D echocardiography revealed concentric left ventricular hypertrophy with evidence of dynamic left ventricular outflow tract obstruction hence Metoprolol was started at 0.25mg/kg/dose. After a month of levothyroxine, the patient was noted to have a cheerful disposition, but still with no verbal output. Skin texture was still mostly dry except on the face. Moreover, there was a 17% decrease in the weight of the patient. There was a further decrease in the TSH level when the dose was adjusted to 9mcg/kg/day. Bilevel Positive Airway Pressure (BIPAP) was administered only during sleep and gradually weaned down to Continuous Positive Airway Pressure (CPAP) which she tolerated well.

Unfortunately, the patient developed complications along the way. She presented with focal seizure, characterized as jerking movement of the left upper and lower extremities, lasting for 5 - 10 seconds. CT scan was immediately done, with a note of a brain abscess at the right frontoparietotemporal region, and subsequently underwent an emergency burr hole and then drainage of the abscess three times during her...
entire hospitalization. She was also started on appropriate antibiotics based on culture and sensitivity results. On the 8th postoperative day and 2nd month of levothyroxine, the patient was awake, with spontaneous eye-opening, with no neurologic deficits. There was a 20% further decrease in the weight. There was the resolution of the edema on the face, trunk, and extremities. The tongue was still slightly protruded but with a remarkable decrease in its size. Thyroid function tests reveal FT3 below the normal range and increasing levels of TSH. The current dose of levothyroxine was continued at 11.2 mcg/kg/day and on the course, eventually maintained at 5 mcg/kg/day.

The patient maintained her weight at 8 kg - 9 kg. There was a significant improvement in the skin texture, becoming soft and smooth from her previously dry skin. Hair started to grow and macroglossia resolved. There was no recurrence of edema and abdominal distention. With the aim of nutritional upbuilding, the patient underwent gastrostomy tube insertion. She was eventually discharged after almost 7 months of stay in the hospital on levothyroxine at 5 mcg/kg/day, with regular follow-ups at the outpatient clinics (Figure 2).

Discussion

Myxedema coma is often considered a misnomer because patients rarely present with myxedema or in a coma. However, patients more often than not manifest lesser degrees of altered consciousness. A focused history with attention to precipitating factors as well as careful physical examination for hypothyroidism can lead to this diagnosis [7] as patients are often recognized through a high index of suspicion.

On presentation to the emergency department, the patient had fast breathing and was in severe respiratory distress. Is the respiratory distress a result of her pre-existing condition? Or is the respiratory distress the precipitating factor of her current condition?

Various vital organ systems are involved in respiration - nervous, cardiovascular, musculoskeletal, and respiratory systems. The cause of respiratory failure is extensive and can come from any of the mentioned systems [8]. Hence, a thorough history and physical examination can narrow our differential diagnosis.

At the outset, given a month-long history of cough, which eventually progressed, accompanied by a fever of one-week duration, one of the initial considerations is community-acquired pneumonia as a cause of the respiratory distress of the patient. However, considering the other circumstances of this patient, is the respiratory distress caused by airway obstruction due to macroglossia or is this a disorder in the respiratory center? Is this an infection in the Central Nervous System (CNS), given her altered state of consciousness? However, our neurologic examination at that time does not point out CNS infection. Or is this a case of septic shock, presenting with tachypnea and hypothermia coexisting with a suspected infection and possible end-organ damage? However, the patient was normotensive upon presentation.

Nonetheless, even a quick glance at this patient will tell us that there is more that we should investigate. Can a single entity explain everything that we see and recognize about this patient? Even without the knowledge that this patient is a known case of congenital hypothyroidism, we can already suspect this on the basis of the physical features – a severely underweight and severely stunted 7-year-old patient, with coarse facial features, macroglossia, and dry skin.

Hypothyroidism alters ventilation in several ways. Dyspnea as a result of hypothyroidism is presumed to be due to reduced inspiratory and expiratory muscle strength as well as restricted ventilator and cardiac reserve [9]. Furthermore, respiratory failure as a result of myxedema is associated with the diminished sensitivity of the central nervous system to hypoxia and hypercapnia [10]. In addition, our patient presented with a large protruding tongue causing significant airway obstruction and necessitating emergency intubation. There could also be increased fat pads in the neck muscles which could encroach the airway and in some patients, tracheostomy tube placement is even necessary. The large, protruding abdomen places the diaphragm at a mechanical disadvantage and may even contribute to the restrictive lung defect.

Figure 2: Patient from admission to discharge.

https://doi.org/10.29328/journal.acem.1001027
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Cretinism is defined as the extreme clinical picture secondary to a lack of thyroid hormone during critical phases of development [11]. It usually presents with delays in sexual development, prominent growth disturbances, and mental retardation.

Myxedema coma, on the other hand, is an extreme manifestation in patients with untreated hypothyroidism. It usually presents with the following physiological alterations such as growth delay, constipation, cold intolerance, and menstrual irregularities, which are compensatory mechanisms for thyroid hormone deficiency. It occurs when a precipitating cause, particularly infection, overwhelms the compensatory mechanisms of the hypothryroid state [2]. Literature would often point towards pneumonia and sepsis as the leading precipitating factors as we could surmise in our patient. Other confounding factors include metabolic disturbances, trauma, and certain medications [12]. The first case of myxedema coma was reported in London back in 1879 and describes as a condition with a myriad of symptoms related to mucous edema that resulted in vascular and nervous disorders. Physical findings include the classic myxo edematous face, which is characterized by generalized puffiness, macroglossia, and coarse, sparse hair [2], all of which are present in our patients. This generalized myxedema is due to the accumulation of hyaluronic acid, which acts on the skin as well as other organs including the tongue, myocardium, and kidney [13]. Myxedema coma can also affect mental status, temperature, ventilation, heart rate, blood pressure, and blood sugar. Deterioration of mental status and hypothermia are said to be the hallmark presentation in patients with myxedema coma [14]. Hypothermia is usually less than 35.5 °C (95.9°F) body temperature, wherein the prognosis is worse as the temperature goes lower [2]. However, the body temperature may sometimes be normal because of concurrent infections.

Early recognition is essential for timely management. The similarities in the presentation of phenotypic appearance, intellectual disability, and poor growth could make the diagnosis of myxedema coma often challenging as may these be attributable to other syndromes or comorbidities [7]. Moreover, some cases in the emergency room have similar presentations with myxedema coma – such as sepsis, stroke, and electrolyte imbalance, which delays the diagnosis further. These have been observed in the following cases of myxedema coma – a 5-year-old previously well girl presenting with altered mental status, which was initially believed to be secondary to hypoxia [15] and a 5-year-old Chinese girl who at first was managed as pneumonia and sepsis [2].

It is often possible to diagnose myxedema coma on clinical grounds alone and results of the total serum thyroxine and free thyroxine index tests usually will confirm the diagnosis [16]. Most patients with myxedema coma reveal low serum FT4 concentration and high serum TSH concentration, indicating primary hypothyroidism, which results from the inability of the thyroid gland to produce adequate amounts of thyroid hormone [2], such as in the case of our patient. On the other hand, TSH may be low, normal, or slightly high, indicating central hypothyroidism [14]. Other diagnostic findings are reported in patients with myxedema coma, which are also seen in our patient at baseline were anemia and elevated creatinine. Other laboratory abnormalities in myxedema coma are as follows, however not seen in our patient include elevated transaminases, hypercapnia, hyperlipidemia, hypoglycemia, hyponatremia, and respiratory acidosis [2,12].

X-ray of the hand in this patient showed bone age compatible with that of a newborn female, as untreated hypothyroidism causes a delay in bone maturation [17].

Myxedema coma is a fatal endocrine emergency [2]. Given its rarity in children, there is no guideline for treatment. They should be managed in an intensive care unit for cardiovascular and pulmonary support [2]. Treatment should be immediately initiated once the diagnosis is suspected, even without laboratory confirmation. The management is multidimensional with attention to the following principles: (a) intensive care treatment with ventilator support, central venous pressure monitoring, (b) appropriate fluid management and correction of hypotension and electrolyte imbalance, (c) aggressive management of precipitating factors and steroid supplementation if required and (d) thyroid hormone replacement [10]. In patients with altered consciousness, managing the airway should be prioritized in order to protect from aspiration. Upon arrival at the emergency department, our patient was obtunded and was in a very critical state. For years, she was lost to follow up and the myxedema crisis happened during the lockdown where the situation imposed additional difficulty of access to the outpatient clinics.

Thyroid hormone therapy is the cornerstone of management; however, controversial in children as there are few studies regarding its optimum dosages, frequency, and route of administration [7]. Triiodothyronine has greater biologic activity and rapid onset of action than thyroxine, whereas the latter has slower onset, less fluctuations, and fewer adverse events. Thyroxine is readily available, however, in severe illness, its conversion to active form triiodothyronine is diminished [7]. Most studies in children used intravenous thyroxine as an initial treatment to rapidly raise serum FT4 and avoid the problem of poor enteral absorption [18]. An intravenous dose of Levothyroxine administered at 10 mcg/kg/day in 3 divided doses for 24 hours, as a loading dose, achieved good results [3]. However, studies have shown thyroxine replacement through the nasogastric tube are as efficacious as intravenous drug, which is significant in countries where triiodothyronine is unavailable. In the recent studies by Zhu, et al. [2] and Wankanit, et al. [18], they used oral levothyroxine for the management of myxedema coma due to non-availability of commercial intravenous preparation. In our case, oral levothyroxine was also administered via

https://doi.org/10.29328/journal.acem.1001027

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nasogastric tube, since patient was intubated, with note of significant improvement in the thyroid function tests after 10 days.

The therapeutic effect of levothyroxine in myxedema coma should improve mental status, cardiac function, and pulmonary function [2]. In children, the long-term goal of hormone therapy in hypothyroidism is to maintain the FT4 and TSH levels within the reference range, particularly in the mid to upper half for the former and in the mid to the lower half for the latter [2]. During the first six months from diagnosis, it is important to monitor the patient’s growth and development monthly. Our patient was eventually weaned off the mechanical ventilator and eventually tolerated CPAP only when asleep. Unfortunately, she developed brain abscess during the course which further prolonged her recovery and hospital stay. Nonetheless, the holistic management despite the extreme challenge of the pandemic has successfully transitioned her to home care.

Before the introduction of newborn screening, diagnosis of congenital hypothyroidism was often delayed until the second or third month of life. Thyroid hormone levels influence brain development. In the absence of proper thyroid replacement, intellectual deterioration progresses with each passing week [19]. If untreated by 6 months of age, severe developmental and physical retardation will occur. However, treatment in infancy will only improve the physical differences, but not the neurological damage [19]. Our patient’s parents were made to understand regarding the possible neurological sequelae associated with her microcephaly and hypothyroidism and possibly the effects of severe hypoxemia to her developing brain. If congenital hypothyroidism is recognized at birth and treated immediately, there is a very favorable therapeutic outcome. For myxedema coma, despite vigorous therapy, prognosis is guarded; however, with recent advances in intensive care, mortality has decreased from 60 to 70 to 25 to 30% [7].

Conclusion

Myxedema coma is an extreme and life-threatening form of untreated hypothyroidism. Although this is rare in children, awareness of the condition in children with altered mental status, hypothermia, and bradycardia especially concomitant with signs of hypothyroidism is crucial for early diagnosis and treatment. A multidimensional approach should always be considered, with immediate attention to ventilation, hypotension, hypothermia, and steroid replacement. Early thyroid hormone supplementation is also essential, with the administration of oral levothyroxine also effective in treating myxedema coma. Early medical attention and ensuring continuation of thyroid supplements may prevent significant morbidity and mortality.

Acknowledgement

The authors would like to thank Dr. Wilson Cua for the expert guidance regarding this case.

Consent

Written informed consent was obtained from the patient’s parents for this case report and any accompanying images.

References


