Clinical Case Report

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Myxedema coma

A case report of pediatric emergency care

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Abstract

Raionale: Myxedema coma (MC) is extremely rare but lethal in pediatric patients with hypothyroidism leading to altered mental status and hypothermia. But there is no clinical guideline for such cases.

Patient concerns: A 6-year-old Chinese girl presented with coma and hypothermia preceded by pneumonia. Her lab results were: free thyroxin (T4) 4.18 pmol/L and thyroid-stimulating hormone (TSH) > 150 μIU/mL with extremely elevated anti-thyroid peroxidase (TPO-Ab) and anti-thyroglobulin. Pneumonia, mild pleural, and pericardial effusion were seen on computed tomographic (CT) scan.

Diagnoses: MC, autoimmune hypothyroidism, pneumonia and sepsis were diagnosed.

Intervention: Gastric levothyroxine, intravenous dexamethasone and antibiotics were administered.

Outcome: Her consciousness was restored and temperature returned to normal 2 days after starting levothyroxine. She was discharged two weeks later.

Conclusion: MC is rare but may be the initial presentation in pediatric patients with prolonged untreated hypothyroidism. Autoimmune thyroiditis could cause hypothyroidism in children. MC should be suspected in pediatric patients with altered mental status, hypothermia and cardiovascular instability. Treatment with 100 mg/m^2 of gastric levothyroxine is an option for pediatric patients with MC.

Abbreviations: MC = myxedema coma, T4 = thyroxin, TPO-Ab = anti-thyroid peroxidase, TSH = thyroid-stimulating hormone.

Keywords: autoimmune thyroiditis, case report, child, coma, hypothermia, myxedema coma, primary hypothyroidism

1. Introduction

Myxedema coma (MC) is a rare but lethal clinical condition in patients with longstanding, severe, untreated hypothyroidism with an estimated incidence rate of 0.22 cases per million people per year.[1] MC is a life-threatening emergency with mortality as high as 60%.[2] MC in children is exceedingly rare with only few reported cases and limited therapeutic experience. We present a case of MC as the initial presentation of acquired hypothyroidism in childhood. Prompt diagnosis and treatment led to quick recovery of the patient.

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2. Case presentation

The patient was a 5-year-old Chinese woman. She presented to the emergency department with complaints of cough for 2 weeks and fever for 5 days. She also had headache, vomiting, and altered interactions with her parents for 1 day. She was admitted to the pediatric intensive care unit. She hailed from a large island in East China Sea (6-hours drive to the mainland city center). She had an uncomplicated birth and roughly normal growth during the first 3 years of life but retarded height growth and decreased activity in the recent 2 years (as reported by her parents) without further medical assessment. The patient had no history of medication. On physical examination, the patient's height and weight were 109 cm and 22 kg ($z = 0.5$ and -1, respectively). Her vital signs included temperature of 38.7 °C, heart rate of 105 beats per minute, respiratory rate of 35 breaths per minute, and blood pressure of 90/55 mmHg. Her oxyhemoglobin saturation was 90% in room air. She showed generalized puffiness and non-pitting edema of the face and extremities capillary refilled time was >3 seconds (Fig. 1). Rales were found on the auscultation of both lungs. The cardiac auscultation was normal. Her abdomen was soft, mildly distended with normal bowel sounds. Neurological examination revealed that the patient was slightly confused and could not properly respond to commands.

Additional laboratory examinations were conducted immediately after admission. A complete blood count showed hemoglobin level of 97 g/L, white blood cell count of 2.5×10^9/L, with 70% neutrophils and blood platelet was 75×10^9/L. The levels of electrolytes, glucose, albumin, and creatine kinase were normal. The blood gas was also normal at admission. Chest computed tomographic (CT) scan confirmed left lobe pneumonia and mild pleural effusion (Fig. 2). The echocardiogram showed mild pericardial effusion with normal cardiac ejection fraction. The magnetic resonance imaging (MRI) scan of the brain and

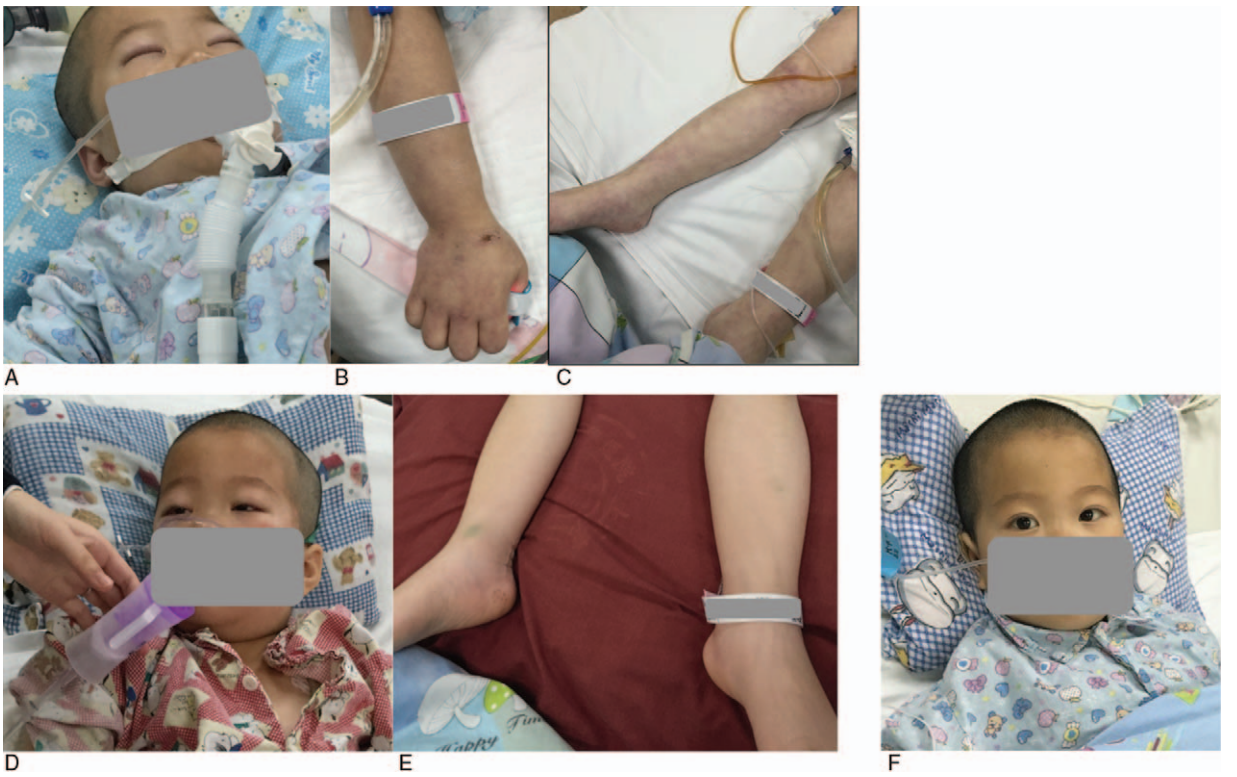

Figure 1. A. Photograph on the second day of admission demonstrates myxedema finding: generalized puffiness, periorbital edema, and hypoventilation. B and C. Photograph of the limbs on the second day of admission shows the extremities with non-pitting edema and shock skin. D and E. Photograph on the fifth day after hormone replacement shows consciousness was restored and the shock skin sign disappeared. F. Photograph 2 weeks after hormone replacement. Demonstrates the periorbital edema disappeared.

cerebrospinal fluid exam was normal. The patient was initially diagnosed as pneumonia and sepsis. Empiric antibiotic therapy, immunoglobulin supply (IVIG 2 g/kg) as immune supportive therapy, and restricted fluid administration were given immediately after admission.

Her mental status subsequently deteriorated. She became comatose on the second day after the admission, her temperature dropped to 35 °C. She also developed hypotension, arrhythmia, and hypoxia with SaO_2 decreased to 75% (Fig. 1). Electrocardiogram confirmed prolonged Q–T interval (Fig. 3). Thyroid studies were ordered at admission due to the retarded growth. The thyroid test results were received on the next day while the patient developed coma. Thyroxin (T4) was undetectable in the plasma (reference range, 58.1–140.6 nmol/L, Table 1). The thyroid stimulating hormone (TSH) level was extremely high (>150 uIU/mL; reference range, 0.55–4.78 uIU/mL). Laboratory results revealed extremely elevated anti-thyroid peroxidase (TPO-Ab) and anti-thyroglobulin (TgAb) levels in plasma (Table 1) after 2 days. Ultrasound of the thyroid revealed mild bilateral enlargement with small tubercles in the left side.

The patient was diagnosed with MC complicated with untreated hypothyroidism on the second day after her admission. The thyroid test indicated that the hypothyroidism was secondary to autoimmune thyroiditis (Hashimoto's thyroiditis). Hormone replacement was immediately started. Intravenous dexamethasone at a dosage of 0.3 mg/kg/d divided every 12 hours was administered for the stressed state early morning on the second day of admission. Later that day, once the thyroid test results were obtained, oral levothyroxine was administered at a dose of 100 $\mu g/m^2/d$ (4 $\mu g/kg/d$) once daily by nasogastric tube. The patient also received vasopressor, mechanical ventilation, and continuous renal replacement treatment for hypotension,

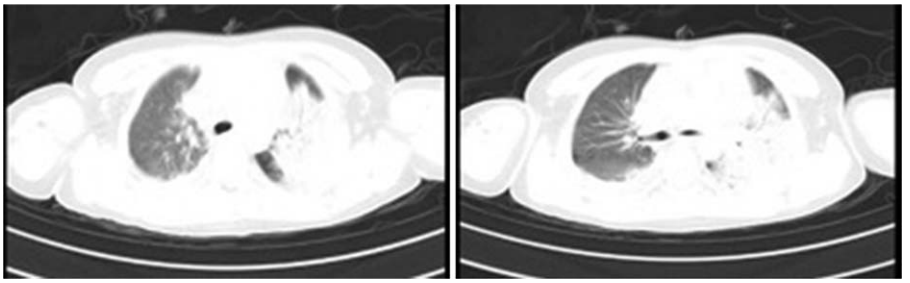

Figure 2. CT scan of chest at admission. Left lobe pneumonia and mild pleural effusion were found. CT = computed tomography.

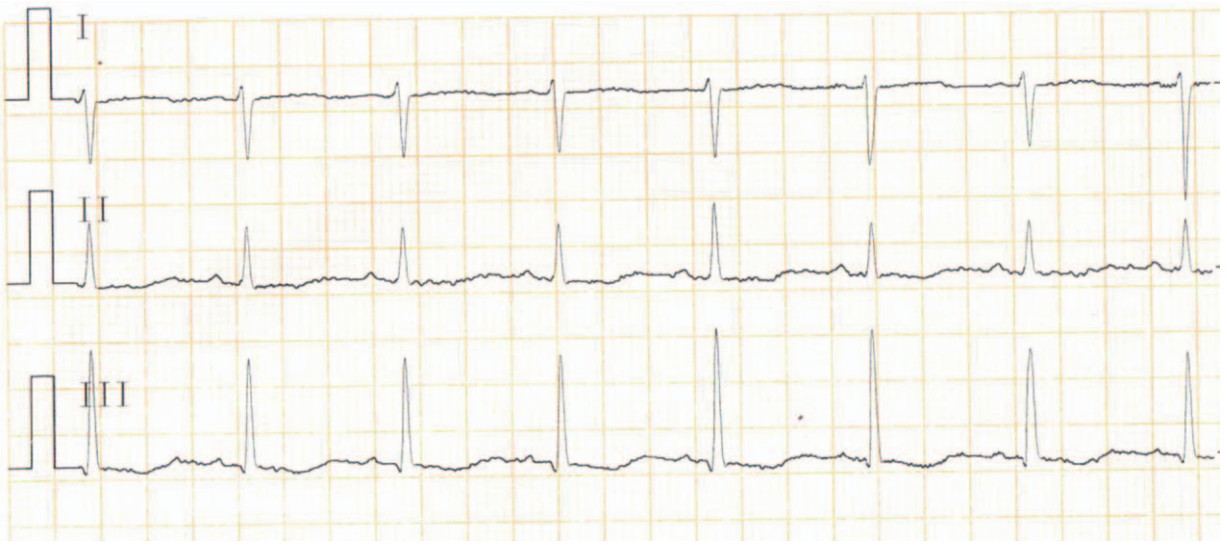

Figure 3. Electrocardiogram on the second day after admission revealed prolonged Q–T interval.

hypoxemia, and anuria, respectively. Two days after starting levothyroxine, her consciousness was restored and temperature returned to normal. She was extubated on the fifth day after the initial hormone administration (Fig. 1).

The dosage of oral levothyroxine was reduced to 3 μg/kg/d once daily 2 weeks after initial administration (Fig. 4). She was discharged on this regimen and continues to do well (Fig. 4).

Eight months after discharge, her height reached 118 cm, and had increased 9 cm since the initial hormone therapy. She was also reported to be more active than before. Her family was recommended to undergo thyroid tests. Her father and grandmother were confirmed with Hashimoto's thyroiditis as well.

3. Discussion

MC is an extreme manifestation in patients with untreated hypothyroidism. The typical presentation includes altered mental status, hypothermia, hypoventilation, hypotension, bradycardia, and hypoglycemia. Very few cases of MC have been reported till date, with the first case reported in London in 1879 and described as a condition with a myriad of symptoms related to "mucous edema" that resulted in vascular and nervous disorders.[3] Given the rarity of MC, actual prevalence is unclear with the estimated incidence rate of 0.22 cases per million people per year.[1] MC is extremely rare in children and the first such case was reported in 1980.[4] Till date, there are only 3 published cases of MC in children, of which MC was the initial presentation of hypothyroidism in 2.[4–6] MC usually occurs after long-standing hypothyroidism. It is characterized by altered mental status and symptoms related to general decrease in metabolism. The mortality of MC ranges from 30% to 60% due to significant medical complications.[2,7] The diagnosis could be delayed because diagnostic laboratory data may not be available in a timely manner during emergency presentation. Our patient was also reported to have delayed growth recently when she was initially admitted for pneumonia and sepsis. We requested a thyroid test on the first day of her admission and the results were received the following day while she developed MC.

Primary hypothyroidism accounts for more than 95% of cases of MC, and 5% occur due to hypothalamic or pituitary causes.[8] Autoimmune hypothyroidism (Hashimoto's thyroiditis) is the most common cause of acquired hypothyroidism in children and adolescents, since congenital hypothyroidism is usually diagnosed during regular neonatal screening. The most common symptoms of hypothyroidism in children are delayed growth, fatigue, cold intolerance, constipation, and menstrual irregularities. These physiological alterations compensate for the lack of thyroid hormones. The hypothyroid patient may decompensate

Table 1

Patient's thyroid function test results.

Test	Hospital day			8 months after discharged	Reference range
	1	4*	15†		
TT3 (nmol/L)	0.03	0.97	2.29	1.93	0.92–2.79
TT4 (nmol/L)	0.00	54.20	185.9	113.1	58.1–140.6
FT3 (pmol/L)	0.00	2.10	4.91	5.81	3.5–6.5
FT4 (pmol/L)	4.18	8.79	21.43	19.75	11.5–22.7
TSH (ulU/mL)	>150	137.95	80.46	4.01	0.55–4.78
TPO-Ab (IU/mL)		>1300	>1300	>1300	<60
TgAb (u/mL)		>500	>500	>500	0–60

FT4 = free thyroxine.

* Denotes 3 days after L-thyroxine therapy initiation.

† Denotes 14 days after L-thyroxine therapy initiation.

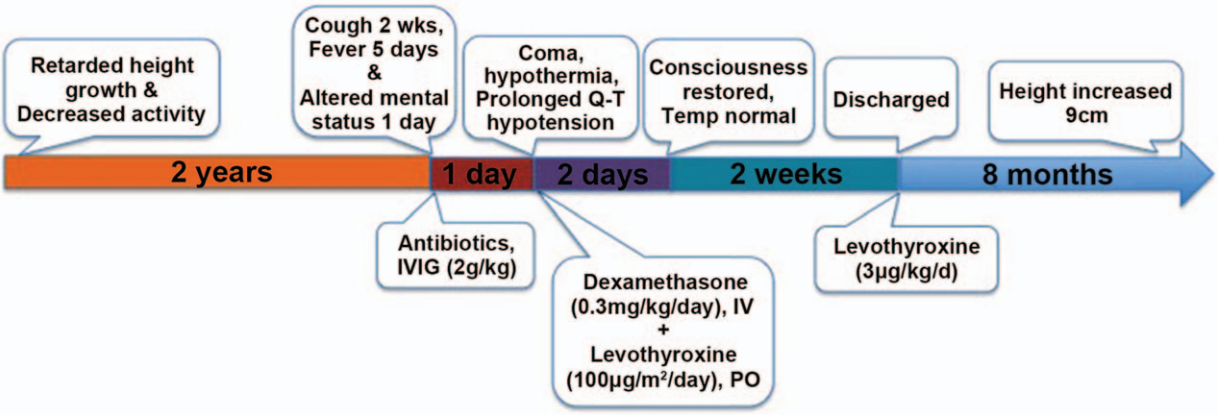

Figure 4. Timeline of presentation and therapy.

into MC when the homeostatic mechanisms are overwhelmed by factors such as infection, metabolic disturbances, and certain medications.[9] Infections are the leading precipitating factor of MC, particularly pneumonia and sepsis.[2,7] Our patient suffered from untreated acquired thyroiditis with severe hypothyroidism, and her T4 level was almost 0 and TSH value was above 150 uIU/mL. She was initially diagnosed as pneumonia and sepsis, and these infections induced the onset of MC.

MC usually exhibits the physiological decompensation of hypothyroidism. The hallmark presentation includes decreased mental status, hypothermia, hypoventilation, bradycardia, hypotension, and hypoglycemia. Physical findings include the classic myxoedematous face, which is characterized by generalized puffiness, macroglossia, ptosis, and coarse.[7,10] Deterioration of mental status was reported in all patients with MC, with altered consciousness including confusion, psychosis, and even coma.[7] Lethargy may develop via stupor into a comatose state. Hypothermia in MC is usually less than 35.5 °C (95.9 °F) body temperature. The lower the temperature, the worse is the prognosis.[9] However, the body temperature may be normal because of concurrent infections.[11] Patients with MC may also show hypoventilation. Hypoxemia and hypercapnia were described in 80% and 54% of the patients, respectively.[10] A reduced ventilatory drive is accompanied by altered mental status and further hampered by intercurrent pulmonary infection. Bradycardia is common in MC patients, while electrocardiogram changes include decreased voltages, non-specific ST, and T changes, varying types of block and a prolonged Q–T interval.[8] Hypotension is also characteristically associated with MC, bradycardia, low cardiac output, and overall blood volume deficit frequently exacerbate the hypotension.[7] Hypoglycemia may occur due to the down-regulation of metabolism seen in serious hypothyroidism. Other abnormalities include anemia, hypernatremia, elevated creatine kinase, and high serum myocardium kinase. Laboratory examination may reveal low serum free thyroxine and high serum TSH. Serum TSH can be low or normal in case of central hypothyroidism. Our patient presented with all-common features of MC such as coma, hypothermia, hypoventilation, prolonged Q–T interval and hypotension with typical primary hypothyroidism. Though our patient did not present with hypernatremia, she showed non-pitting edema and pleural effusion, which may be caused by impaired excretion of free water loading due to the absence of normal thyroid functioning.

MC is a lethal endocrine emergency. Patients with suspected MC should be admitted to an intensive care unit for vigorous pulmonary and cardiovascular support.[12] Administration of thyroid hormone replacement is vital for survival of these patients. In adult it is recommended that initial replacement should be levothyroxine given intravenously at a loading dosage of 200 to 400 μg. The replacement dosage reduced to 1.6 μg/kg/d thereafter.[12] The therapeutic effect in myxedema coma should be improved mental status, improved cardiac function, and improved pulmonary function.[12] The therapy should be instituted on clinical suspicion without delay.[12] Given the rarity of MC in children, there is no guideline for treatment. The recommended therapy for children with autoimmune thyroiditis is levothyroxine replacement therapy. The dose for patients 1 to 3 years of age is 4 to 6 μg/kg/d, for patients 3 to 10 years the dose is 3 to 5 μg/kg/d, and for patients 10 to 16 years the dose is 2 to 4 μg/kg/d. Levothyroxine may also be dosed based on body surface area calculated at 100 $\mu g/m^2/d$.[12] It was reported that intravenous levothyroxine at the dosage of 6.3 to 10 μg/kg/d or 80 $\mu g/m^2/d$ without loading dose was effective and safe in pediatric patients with MC.[4–6] However, levothyroxine injections are currently unavailable in China. There was no serious gastrointestinal complication, such as intestinal obstruction or serious bleeding, observed in our patient at admission. The patient was treated with gastric levothyroxine at a dosage of 100 $\mu g/m^2/d$ (4 μg/kg/d) once daily, which is the recommended dosage of hormone replacement in children with acquired hypothyroidism caused by autoimmune thyroiditis. Her mental status recovered 2 days after hormone therapy and other major symptoms resolved after 2 weeks. The recovery time after hormone replacement varied from 24 hours to 3 weeks in previous reports.[5,10,13] Hormone treatment of myxedema coma is suggested to be started intravenously because gastrointestinal absorption may be impaired in severe cases.[9] In our case oral levothyroxine rescued the patient successfully. This may partially due to the reservation of the gastrointestinal absorption of the patient. Our case suggested that 100 $\mu g/m^2/d$ of oral levothyroxine could successfully rescue the patient MC without serious gastrointestinal complication. In children, the long-term aim of hormone therapy of hypothyroidism is to keep the T4 level in the mid to upper half of the reference range and the TSH in the mid to the lower half of the reference range. The growth and development should also be followed monthly during the first 6 months after diagnoses.[12] In our case, the patient developed

well at the levothyroxine dosage of 3 μg/kg/d 2 weeks following the initial therapy.

4. Conclusion

MC is extremely rare but lethal in children. It could be the initial presentation in pediatric patients suffering from longstanding untreated hypothyroidism. Our case highlights the importance of evaluating thyroid function in pediatric cases with altered mental status and hypothermia. Autoimmune thyroiditis may be the underlying cause of hypothyroidism in children. Gastric management with 100 μg/kg/d of levothyroxine is reported to be effective in pediatric patients without serious gastrointestinal complication and can be an option when the injection is unavailable.

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