Turkish Archives of Pediatrics

ORIGINAL ARTICLE
DOI: 10.5152/TurkArchPediatr.2025.25061

A Rare Endocrinological Emergency in Children with Hypothyroidism: Clinical Evaluation of Cases Presenting with Myxedema Coma

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What is already known on this topic?

- *Myxedema coma is a rare and serious clinical form of long-term untreated hypothyroidism in children.*
- *Myxedema coma should be considered in patients presenting with impaired consciousness, hypothermia, edema, and cardiopulmonary failure.*
- *Thyroid hormone replacement is the mainstay of treatment for MC. According to the American Thyroid Association, the initial thyroid hormone replacement for MC should be intravenous levothyroxine.*

What this study adds?

- *Children with MC present with better clinical findings than adults, and children usually do not present with a coma picture.*
- *Rhabdomyolysis and temporary muscle weakness may be observed in MC. With appropriate hormone replacement and supportive therapy, recovery can be achieved in a short time.*

ABSTRACT

Objective: Myxedema coma (MC) is a severe and rare clinical form of hypothyroidism that causes multiple organ failure and altered consciousness. The aim of reporting this case series is to evaluate the clinical presentation, diagnostic findings, and outcomes in pediatric patients diagnosed with MC.

Materials and Methods: This article presents a case series of 8 patients diagnosed with MC between January 1, 2020, and October 31, 2024, at pediatric endocrinology department of the authors' hospital. The clinical and laboratory data of the cases were obtained from the hospital records system, and the cases were scored using the diagnostic scoring system for MC.

Results: The mean age was 10.36 ± 3.56 years, with a male-to-female ratio of 1:3. Four of the patients were diagnosed with hypothyroidism upon admission with MC, while the remaining 4 had a history of hypothyroidism but presented with MC due to non-compliance with treatment. The majority of patients presented with edema, rapid weight gain, lethargy, and other symptoms of hypothyroidism. Six patients had Hashimoto's thyroiditis, 1 had thyroid hypoplasia, and 1 had thyroid aplasia. Laboratory tests revealed severely elevated thyroid-stimulating hormone (TSH) and low free thyroxine (fT_4) and free triiodothyronine (fT_3) levels. Six patients had elevated CK and myoglobin levels, indicating secondary rhabdomyolysis. Following levothyroxine (LT4) therapy, significant improvements were observed in muscle strength, thyroid function, and other clinical parameters. None of the patients required intensive care, and all recovered with 100% survival rate.

Conclusion: Early diagnosis and appropriate thyroid hormone replacement therapy are crucial for reversing the metabolic abnormalities and preventing life-threatening complications. This study highlights the importance of timely intervention and emphasizes the need for strict adherence to thyroid hormone therapy in children with hypothyroidism.

Keywords: Hypothyroidism, myxedema coma, Hashimoto's thyroiditis , levothyroxine

INTRODUCTION

Myxedema coma (MC), or more recently termed decompensated hypothyroidism,[1] is a rare and severe clinical form of long-standing untreated hypothyroidism.[2-6] Myxedema is non-pitting edema resulting from hyaluronic acid accumulation in the skin and soft tissues.[7] The term "coma" is generally not an accurate term for pediatric patients with MC, as patients usually present with changes in consciousness that are not as severe as coma. The exact frequency of MC in adults is not well-established, but some authors estimate an incidence of approximately 0.22 per million per year.[3,8] Myxedema coma is more common in women and in winter months.[9,10] Deep hypothyroidism leading to coma is rarely reported in children and adolescents.

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Received: March 5, 2025
Revision Requested: May 1, 2025
Last Revision Received: July 1, 2025
Accepted: July 5, 2025
Publication Date: September 1, 2025

Cite this article as: Çetin K, Donbaloğlu Z, Bahar YF, et al. A rare endocrinological emergency in children with hypothyroidism: Clinical evaluation of cases presenting with myxedema coma. *Turk Arch Pediatr.* 2025;60(5):474-482.

- *The MC criteria established for adults are not suitable for evaluating children with severe hypothyroidism. Therefore, new MC criteria specific to pediatric patients should be developed through multicenter studies involving large pediatric populations.*

The clinical picture is characterized by symptoms related to a generalized slowing of metabolism.[2,3] Common symptoms of hypothyroidism in children include delayed growth, fatigue, cold intolerance, constipation, and menstrual irregularities. Myxedema coma can be triggered by infections, metabolic disturbances, trauma, and certain medications.[11] Pneumonia and sepsis are commonly reported as leading triggers.[3] Physical findings include generalized edema, macroglossia, ptosis, sparse hair, and coarse facial features, characteristic of the classic myxedematous face.[3,4,12]

Thyroid hormones influence almost all anatomical and physiological processes of the cardiovascular system. They positively affect heart contraction, heart rate, and vascular tone.[13] In severe hypothyroidism, electrocardiographic (ECG) findings may include bradycardia, flattened T waves, low voltage, and multiple bundle branch blocks.[14] Pericardial effusion may occur due to the accumulation of mucopolysaccharide-rich fluid, though it generally has no significant clinical impact due to its slow accumulation.[15,16] Severe hypothyroidism affects erythrocytes, thus tissue oxygenation is impaired, and ventilation is also impaired due to the decrease in the central response to hypoxia and hypercapnia.[17-19] Severe hypothyroidism may also lead to reduced glomerular filtration and inappropriate antidiuretic hormone (ADH) secretion, resulting in dilutional hyponatremia, which can cause altered mental status ranging from lethargy to coma.[20]

Treatment should be initiated without delay upon clinical suspicion.[4,21] The treatment regimen includes correcting electrolyte imbalances, passive warming, treating infections, respiratory and hemodynamic support, stress-dose glucocorticoid administration, and thyroid hormone replacement. Thyroid hormone replacement is the cornerstone of MC treatment. According to the American Thyroid Association, initial thyroid hormone replacement for MC should be intravenous (iv) LT4 because, in severe cases, gastrointestinal absorption may be impaired, making enteral drug replacement unreliable.[11] Intravenous thyroid hormone administration is replaced by oral administration once the patient is fully awake.

The therapeutic effects of thyroid replacement in MC are seen as improvement in consciousness, cardiac, and pulmonary functions.[21] Given the potential for secondary hypothyroidism and associated hypopituitarism in MC, hydrocortisone therapy is recommended until adrenal insufficiency is ruled out.[22] Respiratory and airway management, as well as monitoring and support of cardiac function, are critical in MC treatment. Early initiation of broad-spectrum antibiotic therapy is crucial if there is suspicion of a triggering infection, as is the treatment of any other identified triggers.[3,6,10,20]

Describing the prognosis of MC is difficult due to the limited number of reported cases. Studies in the literature report high mortality rates, ranging from 20% to 60%. Factors associated with poor prognosis include advanced age, bradycardia, and refractory hypothermia.[2,8,23] Prognosis is generally better in children and adolescents than in adults.[24] Myxedema coma criteria established for adults are not suitable for evaluating children with severe hypothyroidism. This study aims to raise awareness of MC in pediatric patients and contribute to the diagnosis and treatment process.

MATERIALS AND METHODS

This study included 8 patients diagnosed with MC and followed up and treated at pediatric endocrinology department of Akdeniz University Hospital between 01.01.2020 and 31.10.2024. The study was designed as a single-center, retrospective investigation.

Inclusion Criteria

1. Patients who were younger than 18 years of age at the time of application.
2. Patients with severe hypothyroidism: serum free T4 (fT4) levels <0.5 ng/dL and free T3 (fT3) levels <1.0 ng/L.
3. Patients who are regularly followed up in the authors' clinic.

Exclusion Criteria

1. Patients with other systemic diseases that may cause impaired consciousness or coma.
2. Patients with suspected substance/medication that may cause impaired consciousness or coma.
3. Patients with inadequate medical records.

Table 1. The Diagnostic Scoring System for Myxedema Coma

Thermoregulatory Dysfunction (Temperature °F/°C)	Points	No.1	No.2	No.3	No.4	No.5	No.6	No.7	No.8
>95/35	0	0	0	0	0	0	0	0	0
89.6-95/32-35	10								
<89.6/32	20								
Central Nervous System Effects									
Absent	0		0	0				0	0
Somnolent/Lethargy	10	10			10	10	10		
Obtunded	15								
Stupor	20								
Coma/seizures	30								
Gastrointestinal Findings									
Absent		0			0	0	0	0	
Anorexia/abdominal pain/constipation	5		5	5					5
Decreased intestinal motility	15								
Paralytic ileus	20								
Precipitating Event									
Absent		0			0		0	0	
Present	10		10	10		10			10
Cardiovascular Dysfuntion									
Bradycardia/Heart rate									
Absent	0			0					
50-59	10				10	10	10		
40-49	20								
<40	30								
Other ECG changes*	10	10						10	10
Pericardial/pleural effusion	10	10	10		10	10		10	10
Pulmonary edema	15								
Cardiomegaly	15							15	
Hypotension	20								
Metabolic Disturbances									
Hyponatremia	10		10	10	10		10		
Hypoglycemia	10								
Hypoxemia	10								
Hypercarbia	10								
Decrease in GFR	10	10				10		10	
Total score		40	35	25	40	50	30	45	35

*Other EKG changes: QT prolongation, or low voltage complex, or bundle branch blocks, or nonspecific ST-T changes, or heart blocks. °F fahrenheit; °C, celcius; ECG: elektrocardiography; GFR: glomerular filtration rate. Adapted from Popoveniuc G, ChaNdra T, Sud A, et al. Endocr Pract 2014; 11:1-36.

Clinical and Laboratory Evaluation in Patients

Clinical and laboratory data obtained by screening the hospital's electronic patient records database were included in the study. The triggering factors for MC and comorbidities that developed in the patients were examined. The patients' consciousness levels, vital signs, complaints, and demographic characteristics were recorded in the study form. Height was measured using a standard stadiometer with precision to the nearest 0.1 cm. Height SDS was calculated based on age and sex-specific reference standards. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). BMI SDS was also derived using age and sex-specific reference data.[25] Extensive biochemical data of the patients were noted. Chest X-ray findings, ECG, echocardiography (ECHO), and thyroid ultrasonography (USG) findings were also included in the study. When the patients' lethargy and drowsiness improved and their consciousness returned to normal, muscle strength measurements were taken. Muscle strength was measured using a dynamometer device (GRIP-D dynamometer), and the measurements were repeated at the first follow-up visit after normalization of thyroid function tests (average of 1 month after discharge). The posterior-anterior X-ray findings of the left wrist at the time of MC presentation were evaluated according to the Greulich and Pyle bone age atlas and compared with the patients' chronological age.[26] The levothyroxine (LT4) dosage and administration routes, the duration required to return thyroid function tests to normal range, and hospitalization periods were examined.

Myxedema Coma Scoring System

Using all these data, the diagnostic scoring system for MC was performed according to the criteria developed by Popoveniuc et al[27] (Table 1). Myxedema coma severity can be assessed using a diagnostic scoring system that evaluates multiple

clinical parameters. These include thermoregulatory dysfunction (temperature), central nervous system effects (level of consciousness), gastrointestinal findings, precipitating events, cardiovascular dysfunction (heart rate, ECG changes, and effusions), and metabolic disturbances (e.g., hyponatremia and hypoglycemia). Each parameter is assigned a specific point value, with higher scores indicating more severe manifestations of MC. A score of 60 or higher is highly suggestive/diagnostic of MC; a score of 25-59 is suggestive of risk for MC, a score below 25 is unlikely to indicate MC.[27] Initially, 13 patients were included in the study, but 3 patients with less than 25 points on the MC score, 1 patient with severe hypothyroidism who presented with a coma secondary to stimulant-drug use, and 1 patient who did not attend their clinical follow-up were excluded, leaving a total of 8 patients for analysis. The study was approved by Akdeniz University Ethics Committee (date: 28.11.2024, number: KAEK-766). Written informed consent was obtained from the patients' parents.

Statistical Analysis

The analyses were performed using The Statistical Package for the Social Sciences (SPSS) version 23.0 for Windows (IBM SPSS Corp.; Armonk, NY, USA). Descriptive statistics were presented as n (%) or mean ± SD, or minimum and maximum, or median values. The Shapiro-Wilk test was used to assess the assumption of normality. Wilcoxon Paired 2 Sample Test was used to analyze the differences between the initial and final measurements. The Spearman correlation test was used to analyze the strength and direction of the relationship between 2 non-parametric variables. A correlation coefficient (*r*) value of <0.25 was interpreted as indicating a very weak association; 0.26-0.49 a weak association; 0.50-0.69 a moderate association; 0.70-0.89 a strong association, and 0.90-1.0 a very strong association. *P* values less than .05 were considered statistically significant.

RESULTS

The mean age of the eight pediatric patients included in the authors' study was 10.36 ± 3.56 years (range: 5.3-15.0 years). The male-to-female ratio was 1:3. Four (50%) patients were diagnosed with de novo hypothyroidism; the other patients developed MC due to treatment non-compliance. The infection parameters of the patients were negative. None of the patients had a history of external drug use or trauma. No MC trigger factors were identified in patients other than treatment non-compliance. All 8 patients had primary hypothyroidism, 6 (75%) had Hashimoto's thyroiditis, 1 (12.5%) had thyroid aplasia, and 1 (12.5%) had thyroid hypoplasia (Table 2).

Thyroid Function Test Results

At the time of MC diagnosis, the mean TSH level was 742.2 ± 265.1 mIU/L (N: 0.51-4.30), the mean fT4 level was 0.18 ± 0.13 ng/dL (N: 0.93-1.63), and the mean fT3 level was 1.04 ± 0.67 ng/L (N: 2.56-5.01) (Table 2). Six patients had Hashimoto's thyroiditis, and high positive antibody levels were observed in

Table 2. The Characteristics of Hypothyroidism, Thyroid Hormone Levels, Medication Doses, and Hospitalization Durations in Patients with Myxedema Coma

Patient No.	Date of Admission	Reason of MC	TSH* (mIU/L) fT4** (ng/dL) fT3*** (ng/L)	Treatment LT4 initial/maximum dose (mcg po)	Duration of Hospitalization (days)
1	May 2024	Hashimoto's thyroiditis; new diagnosis	888 0.04 0.39	LT4 6.25/25	7
2	Jul 2024	Hashimoto's thyroiditis; non-compliance to treatment	>1000 0.24 0.71	LT4 20/75	7
3	Jul 2022	Hashimoto's thyroiditis; non-compliance to treatment	550 0.33 2.29	LT4 37.5/50	4
4	Jan 2023	Hashimoto's thyroiditis; new diagnosis	>1000 0.25 1.70	LT4 12.5/50	4
5	Sep 2023	Congenital hypothyroidism (Hypoplasia); non-compliance to treatment	666 0.07 0.39	LT4 15/100	14
6	Sep 2023	Hashimoto's thyroiditis; new diagnosis	>1000 0.05 0.54	LT4 12.5/75	15
7	Jun 2020	Hashimoto's thyroiditis; new diagnosis	310 0.15 1.10	LT4 12.5/75 digoxin, furosemide 25/100 mcg po	5
8	Sep 2022	Congenital hypothyroidism (Aplasia); non-compliance to treatment	532 0.38 1.20	LT4 12.5/62.5	12

*Normal range for TSH: 0.51-4.30 mIU/L **Normal range for fT4: 0.93-1.63 ng/dL ***Normal range for fT3: 2.56-5.01 ng/dL fT4, free tetraiodothronin; fT3, free-triiodothronin; LT4, levothyroxine; LTSH, thyroid-stimulating hormone; MC, myxedema coma.

Table 3. The Clinical Characteristics and Laboratory Findings of Patients with Myxedema Coma

No	Sex	Age (years)	Central Nervous System Impairment	Precipitating Event	eGFR* (mL/dk/1.73 m²)	Na** (meq/L) Glucose*** (mgl/dL)	Total**** CK (U/L)	Temp (°C) Hypoxemia	Heart rate (/min) Hypotension Pericardial effusion	ECG Change	Chest X-Ray Findings	Gastro-Intestinal Findings	Muscle Strength (newtons) Initial Measurement Follow- up Measurement
1	F	5.3	Lethargy	None	63	137 99	807	36.8 –	90 - +	Low voltage	–	–	5.4 6.1
2	F	9.4	No	Therapy non-compliance	90	130 97	459	36.6 –	84 - +	–	–	Pain, constipation	10.2 12.7
3	F	12.9	No	Therapy non-compliance	139	129 75	140	36.7 –	80 - -	–	–	Pain, constipation	15.9 17.5
4	F	11.0	Lethargy	None	97	133 81	111	36.8 –	58 - -	Sinus brady cardia	Pleural effusion	–	14.8 17.3
5	M	14.2	Lethargy	Therapy non-compliance	70	135 88	6113	36.6 –	56 - +	Sinus brady cardia	Pleural effusion	–	25.1 28.8
6	F	6.2	Lethargy	None	91	132 90	4874	36.7 –	64 - +	–		–	6.9 8.6
7	M	15.0	No	None	74	139 86	8505	36.8 –	90 - +	Low voltage	Cardiomegaly pleural effusion	–	20.1 30.0
8	F	8.9	No	Therapy non-compliance	91	137 79	1717	36.6 –	72 - +	Low voltage	–	Pain, constipation	13.5 18.8

*Normal range for eGFR>90°mL/min/1.73m² **Normal range for Na 135-145°mEq/L ***Normal range for Glucose 70-100°mg/dL ****Normal range for Total CK 0-180 U/L symptom present (+), symptom absent (–). ECG, electrocardiography; Egfr, estimated glomerular filtration rate; F, female; M, male; Na, sodium; Temp, body temperature; Total CK, total creatine kinase.

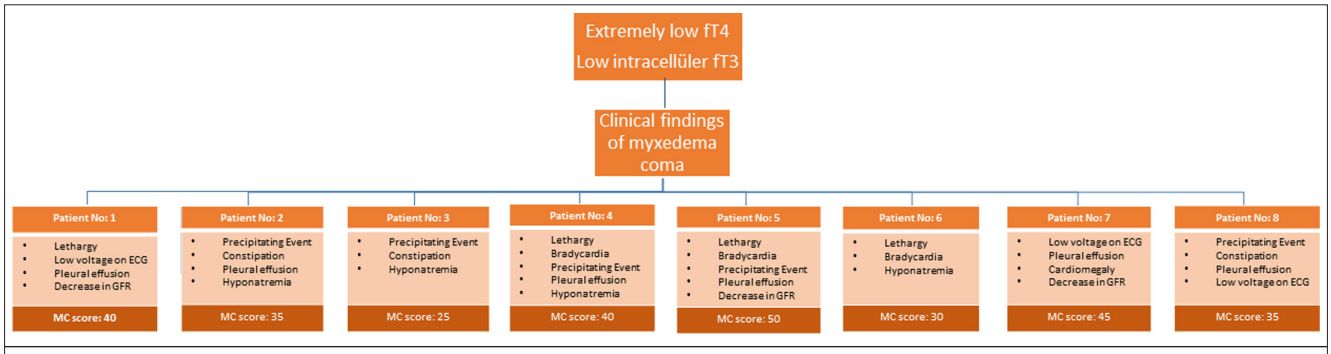

Figure 1. Diagnostic scoring of patients for myxedema coma.

these patients (mean anti-TPO: 464 ± 62.76 IU/mL and median anti-hTG: 122 IU/mL [min:13, max:796]). The mean hospital stay was 8.5 ± 1.59 days (range: 4-15 days) (Table 2).

Other Laboratory Findings

None of the patients had hypoglycemia. All patients presented with MC showed dyslipidemia (elevated total cholesterol and LDL cholesterol). However, after 1 month of treatment, all patients had normal fasting lipid profiles. The mean total creatine kinase (CK) level in the patients was 2840.7 ± 1139.7 U/L, and 6 (75%) patients had CK levels above the normal range (N: 0-180). Secondary rhabdomyolysis due to MC was suspected in these patients, and with controlled high-volume hydration, bicarbonate fluid therapy, and thyroid hormone replacement, the elevated CK and myoglobin levels were brought within the normal range. During this process, only 3 (12.5%) patients had high creatinine levels for their age (GFR values: 63, 70, 74 mL/dk/1.73m^2), which improved with hydration. None of the patients required dialysis. Four (50%) patients had mild hyponatremia (sodium levels: 129, 130, 132, and 133 mEq/L, N: 135-140), which was quickly corrected with fluid and electrolyte therapy (Table 3) (Figure 1). No patient had metabolic or respiratory acidosis at the time of presentation.

Physical Examination Findings

Upon presentation, 5 (62.5%) patients had edema, 5 (62.5%) had rapid weight gain, 4 (50%) had lethargy, 3 (37.5%) had constipation, 2 (25%) had short stature, 2 (25%) had sweating, 2 (25%) had goiter, 1 (12.5%) had leg pain, and 1 (12.5%) had hair loss (Figure 1). The consciousness of 4 (50%) patients who were lethargic at admission improved completely by the second day of LT4 replacement therapy. The mean height SDS was −0.75 ± 1.17, the mean weight SDS was 1.25 ± 1.24, and the mean BMI SDS was 1.44 ± 1.18, indicating obesity. On physical examination, edema without pitting, especially in the lower extremities, was found in 5 (62.5%) patients, 4 (50%) had dry and brittle hair, 4 (50%) had a coarse facial appearance, 3 (37.5%) had dry skin, and 2 (25%) had palpable goiter. Upon MC presentation, only 3 (37.5%) patients had borderline sinus bradycardia (58 beats/min, 56 beats/min, and 60 beats/min), while all other vital signs were stable. None of the patients had hypothermia, hypoxia, bradypnea, or hypotension (Table 3) (Figure 1).

Imaging Findings

Chest X-ray was performed on all patients upon admission, and 3 (37.5%) patients had mild pleural effusion, while 1 (12.5%) had mild cardiomegaly. Electrocardiography showed mild sinus bradycardia in 3 (37.5%) patients and mild voltage reduction in 3 (37.5%) patients, which fully resolved by the third day of thyroid hormone replacement. All patients underwent ECHO, and minimal pericardial effusion was found in 6 (75%) patients (Table 3) (Figure 1). After thyroid hormone replacement, pericardial effusion findings regressed in all patients during the first-month follow-up. Only 1 (12.5%) patient had a low ejection fraction (EF) of 53% and was evaluated as having dilated cardiomyopathy. This patient received digoxin and furosemide treatment from the pediatric cardiology department. In follow-up ECHO, EF was 63% and dilated cardiomyopathy continued, although it regressed. All patients underwent thyroid USG, and 6 had findings consistent with Hashimoto's thyroiditis (hypoechoic, heterogeneous, and pseudonodular appearance). One patient had thyroid aplasia, and another had thyroid hypoplasia.

Treatment

Due to the unavailability of parenteral thyroid hormone forms and the absence of significant gastroenterological pathology causing malabsorption, oral LT4 was administered to all patients. Levothyroxine therapy was initiated at a dose, ranging from 6.25 mcg to 37.5 mcg (0.25-0.80 mcg/kg/day), with the mean starting dose of 0.40 ± 0.06 mcg/kg/day. The dose was gradually increased, and at discharge, the LT4 dose ranged from 25 mcg to 100 mcg (1.0-1.9 mcg/kg/day), with the mean dose of 1.50 ± 0.12 mcg/kg/day (Table 2). Four patients had a known history of hypothyroidism. As the remaining patients presented with stable vital signs and exhibited no clinical indicators suggestive of adrenal insufficiency (hypotension, hypoglycemia, or marked hyponatremia and hyperkalemia) or other hypothalamic–pituitary axis dysfunction at presentation, and serum cortisol levels were within normal ranges, corticosteroid therapy was not administered to any of the patient.

Muscle Strength Measurements

The patients' median muscle strength at the initial measurement was 14.1 newtons (min:5.4, max:25.1), and at the follow-up, it was 17.4 newtons (6.1-30.0), indicating a significant improvement in muscle strength (P = .012). A strong positive correlation was found between the total CK levels at presentation and the improvement in muscle strength during follow-up (P = .037, r = 0.738). The left wrist X-ray findings of the patients were evaluated, and the mean bone age was found to be −0.68 ± 1.03 years behind their chronological age.

Prognosis

None of the patients required intensive care. The survival rate during follow-up was 100%. The normalization of fT4 after MC diagnosis with LT4 therapy ranged from 6 days to 45 days. One patient's mother and another patient's brother had a history of autoimmune thyroiditis, but none of the other patients had a family history of hypothyroidism or autoimmune diseases. The scoring of the authors' cases according to the diagnostic scoring system for MC was provided in Table 1. The lowest score observed was 25, and the highest score was 50. None of the authors' cases were classified as severe MC according to the scoring system.

DISCUSSION

Myxedema coma is the decompensated form of hypothyroidism and can present with various clinical signs. Myxedema coma is a rare clinical condition that requires early diagnosis and treatment, as failure to treat can affect multiple organ systems and may lead to a fatal outcome. The first pediatric case of MC was reported in 1980.[28] Since MC is rare in children, its incidence remains undetermined. In the authors' clinic, between 2020 and 2024, an average of 200-250 hypothyroid patients were followed and treated annually. According to data from clinical patient admissions over 4 years, a total of 8 cases of myxedema coma were observed. Based on this, the incidence of MC among patients with primary and secondary hypothyroidism in the authors' clinic is approximately 0.8-1%.

Among the authors' patients, 2 (25%) were male, and as seen in the literature, the majority of MC patients are female (60-75%).[1,29] All 8 patients in this study had primary hypothyroidism, with 6 having Hashimoto's thyroiditis and 2 having congenital hypothyroidism. In the literature, the proportion of MC patients with Hashimoto's thyroiditis is reported to be high (35-45%).[1,29] Congenital hypothyroidism occurs in approximately 1 in 1500-4000 live births,[30] the incidence of chronic lymphocytic thyroiditis is 1:3000.[33] Congenital central hypothyroidism is even rarer, with an incidence of 1 in 25 000-100 000 births.[31] This explains why, in this study and in the literature, MC is most commonly seen in patients with primary hypothyroidism, particularly those with Hashimoto's thyroiditis.

Four of the authors' patients were diagnosed with de novo hypothyroidism, while the remaining 4 had known hypothyroidism and were noncompliant with treatment (50%). In the literature, most cases of MC in both adults and children are seen in patients who are noncompliant with treatment.[1,29] A large French cohort study also identified the discontinuation of LT4 therapy as one of the most common triggers of severe hypothyroidism.[31]

Only 3 of the authors' patients presented with borderline bradycardia, and all other vital signs were stable. In a pediatric MC case series presented by Sanctis et al. data were available for 7 patients, all of whom had comorbidities. These patients showed varying degrees of altered mental status, hypotension in 3 patients, hypothermia in 4, bradycardia in 4, hypercapnia in 1, hypoxemia in 1, and hypoglycemia in 1.[1] In the study by Sokołowski et al., all patients exhibited varying levels of altered consciousness, hypothermia in 4, and hypokarbia in 6 patients.[29] No hypoglycemia was observed in the authors' patients, and in the literature, hypoglycemia is not a commonly observed finding in MC.[29] During the course of treatment, 3 of the authors' patients showed mild-to-moderate GFR impairment, which resolved with hydration and hormone replacement. Renal function impairment in MC has been documented in the literature. For example, in a case study of a 7-year-old Filipino girl with congenital hypothyroidism, noncompliance, and MC, the patient required intubation and advanced respiratory support, followed by Continuous Renal Replacement Therapy (CRRT) due to acute renal failure.[32]

In this study, mild pleural effusion was detected in 3 patients, minimal pericardial effusion in 6 patients, and dilated cardiomyopathy and low EF in 1 patient. All these findings regressed after starting hormone replacement therapy. Literature reports pleural effusion, pulmonary edema, pericardial effusion, reduced ECG voltage, and bradycardia as common findings in MC patients.[1,4,29]

Six of the authors' patients developed rhabdomyolysis, 3 of whom had significant renal function impairment, and 1 patient experienced rhabdomyolysis severe enough to impair walking. All patients were treated with LT4 replacement, high-volume hydration, bicarbonate, and diuretics, and none required dialysis. Wankanit et al[33] reported a case of MC in a 2-year-old girl with congenital hypothyroidism and noncompliance. This patient developed respiratory failure, rhabdomyolysis, and acute renal failure and was successfully treated with LT4 and supportive care.[33]

In the study by Sokołowski et al,[29] 11 patients with MC and a diagnosis score of 60 or higher were included, whereas the mean MC diagnosis score in this study was 37.5 ± 8.0 (range 25-50). According to the MC scoring system, the authors' patients likely meet the criteria for MC as defined by Popoveniuc et al[27] (Table 1). The lower MC score in this study may be explained by the better prognosis of MC in children.

Levothyroxine can be used alone or in combination with triiodothyronine for treatment. In MC, the conversion of T4 to T3 is impaired, and therefore, the combined therapy could be potentially beneficial.[34] However, iv LT4 is unavailable in many countries. In patients with chronic illness, thyroid hormone replacement should be started at low doses, gradually increasing to reduce the risk of arrhythmias, heart failure and pseudotumor cerebri. Due to the rarity of MC in children, no standard treatment guideline exists.[6,24,28,35,36] Root et al[35] successfully treated a 5-year-old child with autoimmune thyroiditis using an initial dose of 3 mcg/kg/day iv LT4, and Schutt-Aine[28] treated an 8-year-old child with panhypopituitarism using an initial dose of 6.4 mcg/kg/day iv LT4. None of the patients in this study were unconscious, nor did they have serious gastrointestinal pathologies that could cause malabsorption, parenteral LT4 preparations were not available. Therefore, all patients were administered oral LT4, and favorable results were obtained. Similarly, Zhu et al[4] and Wankanit et al[33] also used oral LT4 in pediatric MC cases when commercial iv preparations were unavailable. Zhu et al[4] started treatment with an initial dose of 4 mcg/kg/day for a 6-year-old child, and Wankanit et al[33] began with 6.3 mcg/kg/day for a 2-year-old child, gradually

increasing the dose and achieving positive outcomes. In adult studies, when iv LT4 preparations were unavailable, oral LT4 was used successfully to treat MC.[29,37-39]

In this study, the mean initial LT4 dose was 0.40 ± 0.06 mcg/kg/day, which is lower than reported in the literature. The authors' started treatment with a lower dose due to concerns about secondary cardiac effects from aggressive LT4 therapy, and the mean discharge dose was also low (1.50 ± 0.12 mcg/kg/day). Despite this, all the authors' patients were treated successfully without requiring prolonged hospitalization. In this study, the time required for fT4 to return to the normal range after LT4 therapy was initiated varied from 6 days to 45 days, with an average hospital stay of 8.5 ± 1.59 days (min: 4, max: 15 days). In the study by Sokołowski et al,[29] the discharge time ranged from 6 days to 102 days, and the fT4 levels of patients returned to normal within 5 days to 70 days. In the literature, steroid replacement is typically provided to MC patients.[1,4,29,32] In this study, none of the patients had adrenal insufficiency, so hydrocortisone supplementation was not given.

None of the patients in this study experienced mortality. In a literature review by Sanctis et al[1] on 9 pediatric MC cases, the survival rate was also 100%. Mortality rates in the literature range from 20% to 40%,[24,29,31,40] and the better prognosis observed in this study can be explained by the fact that all patients in the authors' cohort were pediatric, and the prognosis of MC is generally better in children.

Our study is unique in its evaluation of rhabdomyolysis in pediatric patients with MC. The authors have shown that dyslipidemia can develop in children and may improve with hormone replacement therapy and the restoration of euthyroidism. Moreover, the authors observed significant improvement in muscle strength with hormone replacement therapy ($P = .012$). This result shows that muscle strength measurement may be an important parameter in the diagnosis and follow-up of MC. The authors' data on muscle strength monitoring using a dynamometer in pediatric MC patients have not been previously reported in the literature. Additionally, data on bone age in MC patients have not been presented in prior studies. In the authors' patients, the mean bone age was −0.68 ± 1.03 years behind their chronological age. As demonstrated in this study, severe hypothyroidism affects not only various organ systems but also muscle and bone metabolism. Rapid recovery from these effects can be achieved with hormone replacement therapy. As there are no published series of pediatric MC cases, this study is expected to contribute significantly to the literature.

Due to the absence of pediatric-specific MC scoring systems, adult-based scoring tools are insufficient for identifying pediatric patients who do not present with overt myxedema or coma. This is one of the most important limitations of this study. Another limitation of this study is the small number of patients. However, due to the low incidence of myxedema coma, large patient cohorts in the pediatric population are unfortunately lacking. To generate more robust evidence, multicenter studies or national database-based research are needed to expand the patient pool.

Myxedema coma is a severe and life-threatening form of untreated hypothyroidism. Although rare in children, it can be diagnosed through thyroid function tests when clinical suspicion arises in patients presenting with signs of severe hypothyroidism. The prognosis of MC in children is significantly better than in adults, and early diagnosis, rapid thyroid hormone replacement, and comprehensive supportive care can substantially reduce morbidity and mortality.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of University of Akdeniz University (Approval no: KAEK-766, Date: November 28, 2024).

Informed Consent: Written informed consent was obtained from the patients' parents who agreed to take part in the study.

Peer-review: Externally peer reviewed.

Author Contributions: Concept – K.Ç., M.P.; Design – K.Ç., M.P.; Supervision – Ö.T.K., H.T.; Resources – K.Ç., Y.F.B.; Materials – K.Ç., A.K.; Data Collection and/or Processing – K.Ç., A.K.; Analysis and/or Interpretation – K.Ç., Z.D.; Literature Search – K.Ç., H.T.; Writing – K.Ç., Z.D.; Critical Review – K.Ç., M.P.

Declaration of Interests: The authors have no conflicts of interest to declare.

Funding: The authors declare that this study received no financial support.

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Supplementary Table 1. Diagnostic Scoring System for Myxedema Coma*

Thermoregulatory dysfunction (Temperature °F/°C)	**Points**
>95/35	0
89.6-95/32-35	10
<89.6/32	20
Central Nervous System Effects	
Absent	0
Somnolent/Lethargy	10
Obtunded	15
Stupor	20
Coma/seizures	30
Gastrointestinal Findings	
Anorexia/abdominal pain/constipation	5
Decreased intestinal motility	15
Paralytic ileus	20
Precipitating Event	
Absent	0
Present	10
Cardiovascular Dysfuntion	
Bradycardia/Heart rate	
Absent	0
50-59	10
40-49	20
<40	30
Other EKG changes**	10
Pericardial/pleural effusion	10
Pulmonary edema	15
Cardiomegaly	15
Hypotension	20
Metabolic Disturbances	
Hyponatremia	10
Hypoglycemia	10
Hypoxemia	10
Hypercarbia	10
Decrease in GFR	10

*Adapted from Popoveniuc G, ChaNdra T, Sud A, et al. Endocr Pract 2014; 11:1-36.
**Other EKG changes: QT prolongation, or low voltage complex, or bundle branch blocks, or non- specific ST-T changes, or heart blocks.
Total score: >60 highly suggestive/diagnostic of myxedema coma 25-59 supportive of diagnosis of myxedema coma <25 myxedema coma unlikely