Case Series

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Reversible Manifestations of Hypothyroidism causing Diagnostic Dilemma: A Case Series

Internal Medicine Section

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ABSTRACT

Hypothyroidism causes a wide spectrum of clinical manifestations, with various signs and symptoms. Some symptoms are common and aid in diagnosis, while the uncommon manifestations may be the sole feature causing diagnostic delays, leading to increased morbidity and mortality. Hereby the authors present a combination of three cases (50-year-old female, 22-year-old female, 56-year-old female): ascites, congenital hypothyroidism and myxoedema coma, respectively. Ascites in hypothyroidism responds to treatment and can help avoid unnecessary investigations; however, since this presentation is rare, clinicians should remain alert for low Serum Ascites Albumin Gradient (SAAG) with high protein ascites. myxoedema coma was diagnosed after excluding cerebrovascular accident, sepsis and dyselectrolytemia, with low body temperature serving as a diagnostic clue. Congenital hypothyroidism should be identified and treated promptly to prevent complications in newborns, as thyroid hormone is crucial for growth and development. Deficiency may lead to severe complications in newborns, so it is essential to rule out other causes. The importance of the present case series lies in the fact that hypothyroidism may present with variable manifestations. It is crucial to identify this hormone deficiency, as replacement with widely available thyroid hormone supplementation can promptly reverse some of the clinical manifestations, thereby aiding in accurate diagnosis and timely management with appropriate therapy.

Keywords: Ascites, Coma, Congenital hypothyroidism, Serum ascites albumin gradient

INTRODUCTION

Hypothyroidism is a prevalent endocrine disorder caused by insufficient production of thyroid hormones, resulting in metabolic and organ dysfunction [1]. Its clinical manifestations vary widely, ranging from subtle symptoms to life-threatening complications [2]. The present case series highlights three distinct presentations of hypothyroidism, each posing unique diagnostic and management challenges. The first case discusses hypothyroid-induced ascites, a rare condition that can mimic chronic liver disease or malignancies. The second focuses on congenital hypothyroidism in a late preterm infant with multisystem complications, including omphalocele and cleft palate. The third case examines myxoedema coma, a critical and life-threatening manifestation of severe hypothyroidism. Collectively, these cases emphasise the importance of timely diagnosis and a multidisciplinary approach to prevent morbidity and mortality.

CASE SERIES

Case 1

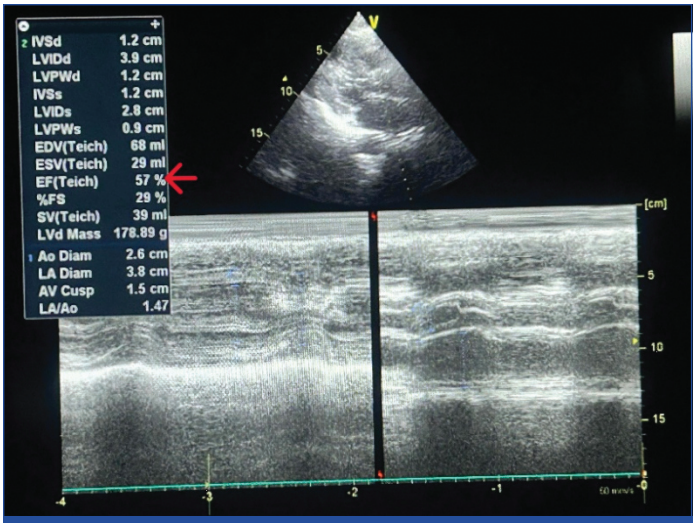
Hypothyroid-associated ascites in a 50-year-old female: A 50-year-old female with a known history of hypothyroidism presented to the Outpatient Department (OPD) with complaints of chronic fatigue and gradual abdominal distension over the past 3-4 weeks. She also reported a dull, non radiating pain in the right upper quadrant of the abdomen, without any obvious precipitating or relieving factors. The patient denied experiencing fever, vomiting, weight loss, haematemesis, or melena. Her medical history was negative for jaundice, blood transfusion, orthopnoea, or palpitations. The patient had been on alternate medications for hypothyroidism for several years. However, upon further questioning, she admitted to missing her thyroxine doses for the past three weeks. On physical examination, the patient had dry skin, periorbital oedema and bradycardia, with a heart rate of 52 bpm [Table/Fig-1].

The Gastrointestinal (GI) system examination revealed positive shifting dullness and a positive fluid thrill, indicating the presence of ascites with hepatomegaly. A tender, palpable left lobe measuring approximately 17 cm was noted. The liver had a smooth surface, but no bruit was heard and the spleen was not palpable.

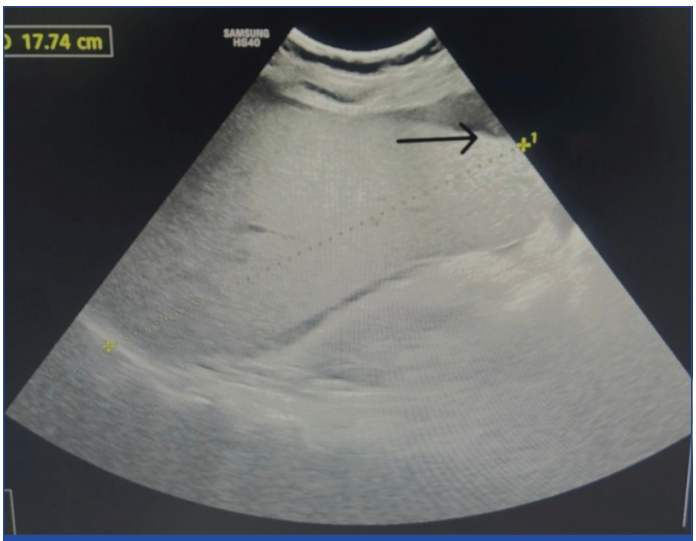
[Table/Fig-1]: Sinus bradycardia on the monitor and periorbital oedema.

Laboratory investigations revealed a haemoglobin level of 11.6 g/dL with a macrocytic Mean Corpuscular Volume (MCV) of 92 fL. Liver Function Tests (LFT) showed Serum Glutamic Oxaloacetic Transaminase (SGOT) (Aspartate Aminotransferase) at 56 IU/L and Serum Glutamate Pyruvate Transaminase (SGPT) (Alanine Aminotransferase) at 27 IU/L. Serum Creatine Phosphokinase (CPK) was normal. Ascitic fluid analysis indicated a Serum Ascites Albumin Gradient (SAAG) of 0.9, a protein content of 4.4 g/dL and no malignant cells. Echocardiography revealed cardiomegaly with Left Ventricular Diastolic Dysfunction (LVDD) grade II and the ejection fraction of the left ventricle was 57% [Table/Fig-2].

The thyroid function test showed a significantly elevated TSH level of 89.5 µIU/mL. Upper GI endoscopy identified antral gastritis but no varices. The patient's serum triglyceride level was high at 167 mg/dL. Abdominal Ultrasound (USG) detected grade II fatty liver, gross ascites, no splenomegaly, a normal portal vein and no evidence of portal hypertension [Table/Fig-3].

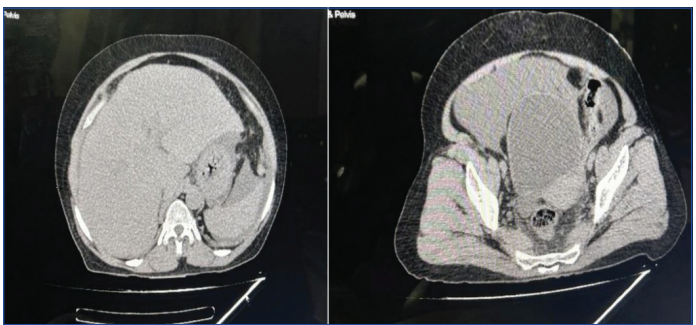


[Table/Fig-2]: Normal ejection fraction.



[Table/Fig-3]: USG showing ascites and hepatomegaly with smooth liver margins.

Carcinoembryonic Antigen (CEA) levels were normal. A Computed Tomography (CT) scan of the abdomen was performed and there was no evidence of any gastrointestinal malignancy [Table/Fig-4].



[Table/Fig-4]: CT abdomen showing hepatomegaly with no pelvic mass.

The diagnosis of hypothyroid-associated ascites was established based on clinical and investigative findings. The patient was advised to resume her thyroxine medication. Levothyroxine supplementation was initiated, leading to a gradual improvement in the patient's symptoms. Within seven days, her heart rate increased to above 60 bpm.

Case 2

Congenital hypothyroidism in a late preterm infant with omphalocele and cleft palate: A 22-year-old female was admitted with pregnancy-induced hypertension and hypothyroidism at 35 weeks and five days of gestation. She underwent an emergency Lower Uterine Segment Caesarean Section (LUCS) and delivered a baby girl. There was no significant medical or surgical history apart from hypothyroidism diagnosed during pregnancy.

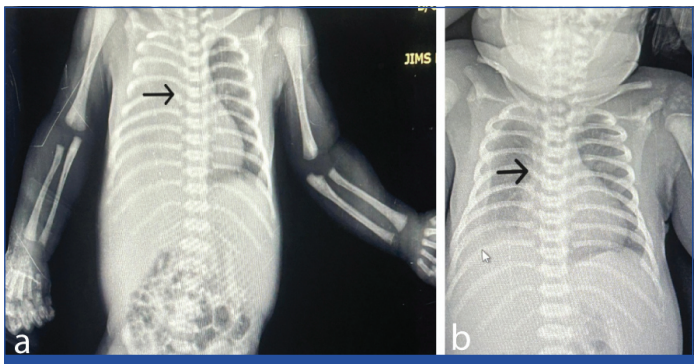
The newborn weighed 2.715 kg, cried immediately after birth and required routine resuscitation. Shortly thereafter, the baby developed respiratory distress with peripheral cyanosis, chest retractions and nasal flaring, necessitating transfer to the Neonatal Intensive Care Unit (NICU).

On admission to the NICU, the newborn presented with signs of respiratory distress, including tachypnea, retractions and grunting, as well as congenital anomalies such as a cleft in the soft palate. Initial investigations revealed a haemoglobin level of 21.4 g/dL and a Packed Cell Volume (PCV) of 64.3%. A chest X-ray showed opacity in the right hemithorax, suggestive of effusion [Table/Fig-5a] and echocardiography identified a 3 mm Patent Foramen Ovale (PFO). An USG of the abdomen revealed an omphalocele with herniation of bowel loops and mesentery. Despite normal sepsis screening results, antibiotics (Piperacillin tazobactam and Amikacin) were started empirically due to suspected early-onset neonatal sepsis.

The newborn's condition worsened on day 6, with increased respiratory distress requiring Continuous Positive Airway Pressure (CPAP) support, dobutamine administration and parenteral nutrition via Nasogastric (NG) feeding. Antibiotics were escalated to meropenem, vancomycin and fluconazole following an increase in total leukocyte count, CRP and worsening chest X-ray findings. Repeat echocardiography revealed a Patent Ductus Arteriosus (PDA) measuring 3 mm, trivial Tricuspid Regurgitation (TR) and grade 1 Left Ventricular Diastolic Dysfunction (LVDD).

On day 15, thyroid function tests demonstrated significantly elevated TSH levels (52.7 µIU/mL) and a low free T4 level (0.74 ng/dL). Congenital hypothyroidism was diagnosed and thyroxine therapy was initiated at 25 µg/day. Over the next two weeks, the baby's respiratory status improved, with successful weaning from CPAP and oxygen support, resolution of jaundice and the re-establishment of oral feeding. Constipation was managed with saline rectal washes and glycerin suppositories.

The newborn completed a 21-day course of antibiotics, with colistin and fluconazole administered for 14 days. Follow-up chest X-rays and laboratory investigations showed normalisation of findings [Table/Fig-5b].



[Table/Fig-5]: a) Right-sided pleural effusion. b) Resolution of the effusion.

The baby was discharged on day 30 in stable condition, exclusively breastfeeding and was prescribed thyroxine (25 µg once daily), vitamin D and multivitamin supplements. At the time of discharge, repeat thyroid tests showed a TSH level of 10.99 µIU/mL and free T4 of 0.74 ng/dL. At the 2-week follow-up, the baby was clinically well and thyroid function tests were suggested to monitor progress. At the 6-week follow-up, the baby was maintaining developmental milestones and thyroid function tests showed a normal TSH level of 3.2 µIU/mL, indicating effective treatment.

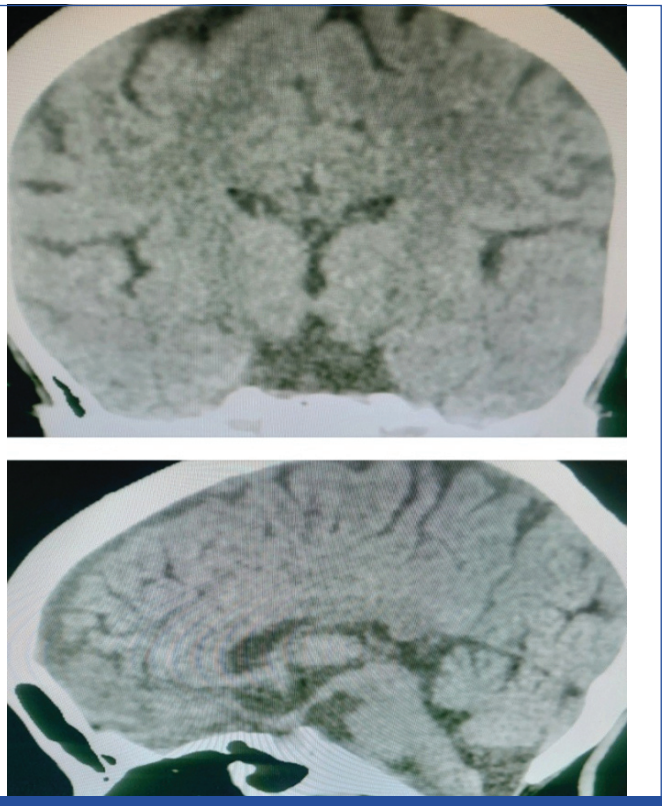
The final diagnosis was congenital hypothyroidism in a late preterm infant (35 weeks and five days) with omphalocele, cleft palate, neonatal jaundice, constipation and early-onset neonatal sepsis (bilateral pneumonia with right-sided pleural effusion).

Case 3

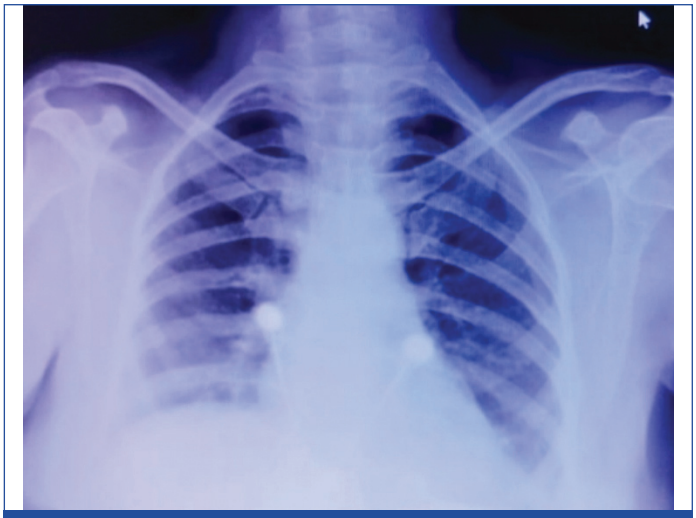
A case of myxoedema coma: A 56-year-old non diabetic, non hypertensive, non smoker female housewife presented with gradually progressive generalised weakness over the past two weeks, accompanied by drowsiness for the last two days. Her relatives denied any history of fever, headache, vomiting, diarrhoea, yellowish discolouration of urine, abdominal swelling, bleeding from any site, or shortness of breath. Additionally, there was no history of falls, weakness on one side of the body, abnormal movements, or any recent drug intake. She followed a mixed diet.

On examination, the patient was conscious but appeared drowsy. She had mild pallor without icterus, bilateral non pitting oedema and was haemodynamically stable; however, her pulse rate was 50 beats per minute and her temperature was 95°F. Systemic examination showed no signs of meningeal irritation, although the bilateral plantar responses were extensor, with preserved tendon reflexes. The gastrointestinal examination revealed no organomegaly or ascites and examinations of the respiratory and cardiovascular systems were unremarkable. Based on these findings, a provisional diagnosis of metabolic encephalopathy was considered, with septic encephalopathy as a differential diagnosis.

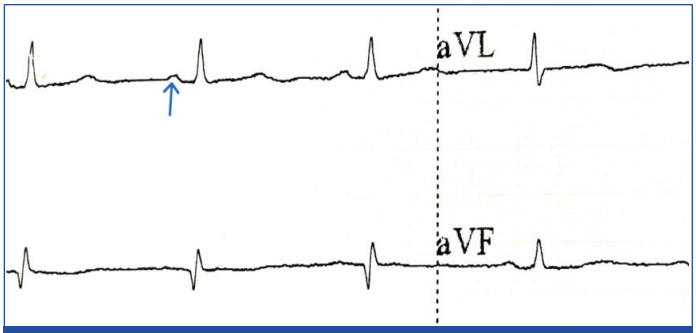
The patient underwent extensive investigations to determine the underlying cause of her condition. A fever profile, including MP slide, dual antigen tests, Immunoglobulin G (IgG) and Immunoglobulin M (IgM) dengue antibody tests and Typhi Dot IgM, was negative. Blood cultures and sensitivity, as well as urine routine examination and culture, revealed no pathogen growth. Random Blood Sugar (RBS) was 72 mg/dL, serum sodium was 130 mmol/L and calcium, magnesium and phosphate levels were within normal limits. Serum procalcitonin, Complete Blood Count (CBC), Liver Function Tests (LFTs) and renal function tests (creatinine and urea) were normal. Thyroid function tests demonstrated hypothyroidism, with Thyroid Stimulating Hormone (TSH) >100 mU/L and free T4 at 0.5 ng/dL. Cortisol, urine sodium, osmolality and Adrenocorticotropic Hormone (ACTH) levels were normal. Neurological assessments revealed evidence of encephalopathy on the Electroencephalogram (EEG), while a CT scan of the brain [Table/Fig-6] and chest X-ray (PA view, [Table/Fig-7]) were unremarkable. An Electrocardiogram (ECG) showed sinus bradycardia [Table/Fig-8].



[Table/Fig-6]: Normal CT brain.



[Table/Fig-7]: Normal chest X-ray.



[Table/Fig-8]: Electrocardiogram (ECG) with a heart rate of 58/min and presence of P waves as marked, suggestive of sinus bradycardia.

A diagnosis of myxoedema coma was made and the patient received a loading dose of L-Thyroxine (400 mcg) via Ryle's tube, with regular monitoring of vitals and supportive care, including warm blankets. By day two, the patient showed improvement, with corrected sodium levels, a temperature increase to 98.8°F and the ability to resume oral feeding. Antithyroid Peroxidase (Anti-TPO) antibody levels were normal. She was discharged on day 14 and her TSH level was 34 mU/L at the time of discharge. She was prescribed L-Thyroxine 75 mcg daily before breakfast with proper instructions. The patient was doing well during follow-up, with TSH levels having normalised to 2.8 µIU/mL. She was on a daily dose of L-Thyroxine 50 mcg and an endocrinology consultation was recommended. A follow-up visit is scheduled in two months.

DISCUSSION

The diverse presentations of hypothyroidism underscore its complexity and potential to mimic other conditions, often leading to diagnostic delays [3]. In hypothyroid-associated ascites, fluid retention arises from increased capillary permeability, reduced oncotic pressure and altered lymphatic drainage, leading to exudative ascites with variable SAAG values ranging from 0.8 to 2.3 g/dL [4]. Other factors, such as hyaluronic acid accumulation, excess Antidiuretic Hormone (ADH) and Vascular Endothelial Growth Factor (VEGF)-mediated permeability, normalise with thyroid hormone replacement [5]. This rare condition necessitates a high index of suspicion, especially when common causes of ascites are excluded. The resolution of ascites upon thyroid hormone replacement highlights the reversible nature of this manifestation with appropriate therapy.

Congenital hypothyroidism, as seen in the second case, represents a critical condition requiring early intervention to prevent irreversible neurodevelopmental damage [6]. The challenges in managing associated congenital anomalies, including omphalocele and cleft palate, necessitate a multidisciplinary approach [7]. Prompt initiation of thyroxine therapy, alongside supportive care for respiratory and nutritional needs, was pivotal in achieving a favourable outcome [8].

Myxoedema coma, illustrated in the third case, is a rare, severe complication of severe hypothyroidism characterised by altered consciousness and multiorgan dysfunction, with mortality rates of 20-60% even under critical care [9]. Predisposing factors include infections, hypothermia, trauma and medications like amiodarone and lithium [10]. The typical presentations of myxoedema coma include altered mental status and hypothermia, with temperatures below 95.9°F indicating a worse prognosis. The absence of mild diastolic hypertension in severe hypothyroidism can signal impending myxoedema coma [11]. Symptoms vary from subtle changes in consciousness to coma and may include hypoventilation, facial puffiness, bradycardia and abdominal distension, among others [12]. Aggressive management with thyroid hormone replacement and supportive care can dramatically improve prognosis, as demonstrated by the patient's recovery [13].

A few similar cases have been found in the literature. One case involved a 61-year-old diabetic woman with unexplained isolated ascites, who was ultimately diagnosed with hypothyroidism after exhaustive investigations. Hormone replacement with levothyroxine led to the rapid resolution of ascites, emphasising the importance of thyroid function evaluation in cases of unexplained ascites [14]. Another case report described two instances of congenital hypothyroidism that were initially missed due to non specific symptoms, including respiratory distress requiring mechanical ventilation, cardiac and feeding difficulties, reduced muscle tone and delayed neurocognitive function. The diagnosis confirmed thyroid agenesis and abnormal hormone levels, with hormonal therapy leading to significant improvements. This study emphasises the need for timely congenital hypothyroidism screening and thorough evaluation in neonates with persistent respiratory, cardiac, or neurological issues [15]. A similar case involved an 82-year-old patient with multiple co-morbidities diagnosed with myxoedema coma, complicated by chronic amiodarone use and sepsis, who presented with progressive dysopnea, hypotension, bradycardia and refractory hypothermia. Timely treatment with intravenous levothyroxine and glucocorticoids led to recovery. This case underscores the diagnostic challenges associated with myxoedema coma and the importance of early recognition and management of this rare endocrine emergency [10].

These cases collectively highlight the importance of maintaining a high index of suspicion for hypothyroidism in atypical presentations, employing targeted investigations and initiating timely treatment. Early recognition and intervention are key to reducing morbidity and improving patient outcomes in diverse clinical scenarios.

CONCLUSION(S)

In conclusion, the present case series highlights the varied and severe complications associated with hypothyroidism, including hypothyroid ascites with low SAAG and high protein content, congenital hypothyroidism with complex multisystem involvement and myxoedema coma. These cases emphasise the importance of considering hypothyroid-related complications as differential diagnosis in patients presenting with unexplained ascites, developmental issues, or altered mental status, especially when other systemic findings align with thyroid dysfunction. Prompt recognition and treatment of these hypothyroid-related complications are crucial to preventing further morbidity and ensuring effective patient management. The present case series underscores the need for a high index of suspicion and a multidisciplinary approach in managing the diverse manifestations of hypothyroidism to avoid potential complications and improve patient outcomes.

REFERENCES

[1] Chaker L, Razvi S, Bensenor IM, Azizi F, Pearce EN, Peeters RP. Hypothyroidism. Nat Rev Dis Primers. 2022;8(1):30. Doi: 10.1038/s41572-022-00357-7.
[2] Chaker L, Bianco AC, Jonklaas J, Peeters RP. Hypothyroidism. Lancet. 2017;390(10101):1550-62. Doi: 10.1016/S0140-6736(17)30703-1.
[3] Ross DS, Cooper DS, Mulder JE. Patient education: Hypothyroidism (underactive thyroid) (Beyond the Basics). Literature review current through Nov 2024. Updated Apr 18, 2023. UpToDate. Available from: https://www.uptodate.com/contents/hypothyroidism-beyond-the-basics.
[4] Khalid S, Asad-Ur-Rahman F, Abbass A, Gordon D, Abusaada K. Myxedema ascites: A rare presentation of uncontrolled hypothyroidism. Cureus. 2016;8(12):e912. Doi: 10.7759/cureus.912. PMCID: PMC5215814. PMID: 28083456.
[5] Srinivasan RE, Estes S, Panda M. A rare complication of hypothyroidism: Myxedema ascites. Tennessee Medicine E-Journal. 2015;1(4):4. Available from: http://ejournal.tnmed.org/cgi/viewcontent.cgi?article=1024&context=home.
[6] Rose SR, Wassner AJ, Wintergerst KA, Yayah-Jones N, Hopkin RJ, Chuang J, et al. Congenital hypothyroidism: Screening and management. Pediatrics. 2023;151(1):e2022060419. Doi: 10.1542/peds.2022-060419. PMID: 36827523.
[7] Klosinska M, Kaczynska A, Ben-Skowronek I. Congenital hypothyroidism in preterm newborns - The challenges of diagnostics and treatment: A review. Front Endocrinol (Lausanne). 2022;13:860862. Doi: 10.3389/fendo.2022.860862. PMID: 35370986.
[8] Léger J, Olivieri A, Donaldson M, Torresani T, Krude H, van Vliet G, et al. European Society for Paediatric Endocrinology consensus guidelines on screening, diagnosis, and management of congenital hypothyroidism. J Clin Endocrinol Metab. 2014;99(2):363-84. Doi: 10.1210/jc.2013-1891. PMID: 24446653.
[9] Elshimy G, Chippa V, Correa R. Myxedema. 2023 Aug 14. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 31424777. (Bookshelf ID: NBK545193).
[10] Assis JG, Santos A. Myxedema coma: Recognition of a rare endocrine emergency. Cureus. 2024;16(8):e66053. Doi: 10.7759/cureus.66053.
[11] Gupta KJ. Myxedema coma: A sleeping giant in clinical practice. Am J Med. 2013;126(12):e3-e4. Doi: 10.1016/j.amjmed.2013.07.037. PMID: 24262739.
[12] Mathew V, Misgar RA, Ghosh S, Mukhopadhyay P, Roychowdhury P, Pandit K, et al. Myxedema coma: A new look into an old crisis. J Thyroid Res. 2011;2011:493462. Doi: 10.4061/2011/493462. PMCID: PMC3175396
[13] Jawed M, Osella J, Bani Hani D. A case of myxedema coma crisis induced by inhalation injury. Cureus. 2021;13(8):e17049. Doi: 10.7759/cureus.17049. PMID: 34522527; PMCID: PMC8428158.
[14] Mekni S, Ben Nacef I, Rojbi I, Mhedhebi C, Mchirgui N, Lakhoua Y, et al. Myxoedema ascites: An unusual situation revealing hypothyroidism. Endocrine Abstracts. 2020;70:EP414. Doi: 10.1530/endoabs.70.EP414.
[15] Năstase L, Cristea O, Diaconu A, Stoicescu SM, Mohora R, Pascu BM, et al. Two cases of congenital hypothyroidism revealing thyroid agenesis. Medicina (Kaunas). 2023;59(10):1887. Doi: 10.3390/medicina59101887. PMCID: PMC10608129. PMID: 37893606.

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