




# Myxedema Heart Disease in a Teenage Child

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## Abstract

Myxedema heart disease is an exceptionally rare condition with few reported cases. We present a rare case of a child who presented with severe congestive heart failure secondary to myxedema heart disease complicated by preexisting valvular heart disease. The patient was admitted to the pediatric intensive care unit and medical management. An echocardiogram showed severe biventricular dysfunction and severe valvular disease. She was started on levothyroxine and liothyronine. During the patient's hospitalization, the thyroxine level normalized but the thyroid-stimulating hormone continued to remain elevated. Likewise, her cardiac ventricular function improved, though it did not return to baseline. Our case highlights the importance of maintaining a broad differential diagnosis in a child who presents with congestive heart failure, to include thyroid disease, which necessitates a rare but specific management strategy.

## Keywords

- ▶ myxedema heart
- ▶ hypothyroidism
- ▶ heart failure

## Introduction

Myxedema heart disease is an exceptionally rare disease with few reported cases in adults. Our case is the first reported in children and discusses the diagnosis and management of myxedema heart. It also highlights the differences in management between pediatric and adult patients.

## Case Presentation

A 13-year-old obese girl with short stature presented to the emergency department for perioral cyanosis in the setting of 4 weeks of worsening fatigue, dyspnea on exertion, lower extremity edema, and orthopnea. Her medical history is notable for Hashimoto thyroiditis and type 2 diabetes melli-

tus, diagnosed 18 months prior to presentation, with medication nonadherence. There was no known family history of thyroid or other autoimmune diseases. Menarche occurred approximately 1 year prior to admission, but she had been with amenorrhea for the preceding 8 months. She denied any recent illnesses or travel outside of the United States.

The patient presented in acute respiratory distress with grunting on initial examination. Vital signs demonstrated normothermia, tachycardia, tachypnea, and mild hypotension. Pulse oximetry was 98% on room air, and her body mass index was 42.1 kg/m<sup>2</sup>. Her lung sounds were diminished bilaterally with crackles and she utilized accessory muscles to breathe. Her cardiac exam revealed distant heart sounds with an S3 gallop. Her abdomen was protuberant, soft, nontender and demonstrated a palpable liver edge approximately 4 cm below the right costal margin. Additionally, diffuse abdominal striae were present. She had 4+ pitting edema to the lower extremities with overlying nonblanching

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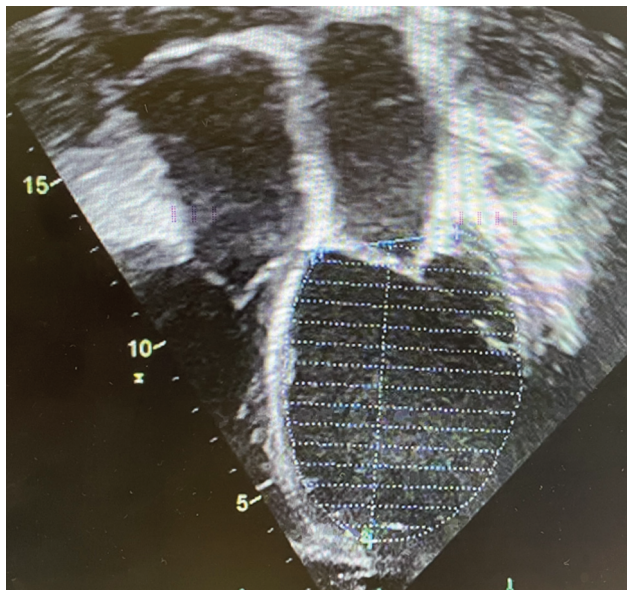
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**Table 1** Initial laboratory results

Laboratory test	Result	Normal range
Sodium	137 mmol/L	133–143 mmol/L
Potassium	4.5 mmol/L	3.5–5.1 mmol/L
Bicarbonate	17 mmol/L	20–28 mmol/L
Blood urea nitrogen	29 mg/dL	7–21 mg/dL
Creatinine	1.5 mg/dL	0.5–1.0
Alanine aminotransferase	32 units/L	0–55 units/L
Aspartate aminotransferase	81 units/L	5–34 units/L
Bilirubin	3.2 mg/dL	0.2–1.2 mg/dL
White cell count	15,800 cells/mm <sup>3</sup>	4.5–12.5 cells/mm <sup>3</sup>
Hemoglobin	9.2 mg/dL	13–16 g/dL
Platelets	288,000 cells/mm <sup>3</sup>	140–400 10 <sup>3</sup> /mm <sup>3</sup>
Brain natriuretic peptide	2,707 pg/mL	<100 pg/mL
Troponin	0.01 ng/mL	0–0.03 ng/mL
Thyroid-stimulating hormone	273.20 uIU/mL	0.5–4.94 uIU/mL
Free thyroxine	0.40 ng/dL	4.87–11.72 ng/dL
Lactate	4.83 mmol/L	<2.0 mmol/L

erythema and roughened, dry skin along her upper extremities bilaterally in addition to acanthosis nigricans along her neck. Initial laboratory results are summarized in ► **Table 1**. A chest radiograph revealed an enlarged cardiac silhouette and a right pleural effusion. Electrocardiogram (ECG) demonstrated left axis deviation and sinus tachycardia. An echocardiogram revealed severe biventricular dysfunction with an ejection fraction of 13%, diastolic dysfunction, bicuspid aortic valve, severe tricuspid insufficiency, moderate mitral valve regurgitation, and a moderate pericardial effusion (► **Fig. 1**). She was diagnosed with severe congestive heart failure secondary to myxedema heart disease.

**Fig. 1** Echocardiogram.

She was categorized using New York Heart Association (NYHA) with stage IV heart failure. Milrinone and epinephrine infusions were initiated, while judicious furosemide infusion provided essential diuresis. Noninvasive positive pressure ventilation was used to aid left ventricular function. Levothyroxine was initiated at 50 µg intravenously daily along with liothyronine 5 µg loading dose, followed by 2.5 µg orally every 8 hours.

After 2 months of inpatient intensive care management, her ventricular function improved and she was transitioned to oral medications. Her thyroid-stimulating hormone (TSH) level decreased significantly but had not normalized, with a TSH of 5.49 uIU/mL on discharge. She was discharged home with instructions to maintain a heart failure diet with fluid restriction and to continue regular outpatient follow-up care with cardiology and endocrinology.

## Discussion

First described in 1918, myxedema heart is seen in patients who develop cardiomegaly, left ventricular systolic dysfunction, and ECG changes to include low voltage, sinus bradycardia, nonspecific ST-T wave changes, and junctional rhythm.<sup>1–3</sup> Additionally, serum enzyme changes including elevated levels of homocysteine, creatine kinase, aspartate aminotransferase, and lactate dehydrogenase have been described in myxedema heart.<sup>3</sup> The absence of thyroid hormone results in decreased cardiac output, due to a combination of slowed heart rate, decreased stroke volume, decreased blood volume, and increased peripheral vascular resistance.<sup>3–5</sup> In reported histological evaluation, mucinous vacuolization, intercellular and intracellular thickening, and edema are seen with progression to irreversible fibrotic

changes to the myocardium and vasculature.<sup>1,2</sup> These structural changes cause valvular dysfunction, left ventricular hypertrophy, and impaired systolic and left ventricular function.<sup>1,2</sup> These patients present with signs and symptoms of heart failure. Simultaneously, these patients may show dermatologic manifestations of hypothyroidism, including cold intolerance, alopecia, dry skin, and periorbital edema.<sup>2,6</sup> Although mild to moderate pericardial effusions have also been described in myxedema heart disease, it is generally not associated with tamponade physiology or hemodynamic compromise given the slow rate of fluid accumulation and distensibility of the pericardium. However, one case report described a 5-year-old girl who presented with cardiac tamponade secondary to unrecognized hypothyroidism.<sup>2,7</sup> The typical course of myxedema heart disease is reversible with thyroid hormone supplementation.<sup>3,8,9</sup> In one study, mRNA levels encoding for selected cardiac proteins important for contractility and cardiac strength were found to be low when serially measured from myocardial biopsy, and normalized when euthyroid state was attained.<sup>10</sup>

The etiology and manifestations of pediatric heart failure are diverse, varying considerably based on a child's age.<sup>11,12</sup> Causes of heart failure can be divided into cardiac and noncardiac etiologies. In a patient without known congenital cardiac malformations, noncardiac causes of heart failure to consider include anemia, sepsis, hypoglycemia, diabetic ketoacidosis, hypothyroidism and other endocrinopathies, arteriovenous fistula, renal failure, and muscular dystrophies.<sup>11-13</sup> The principles of managing heart failure involve identifying and treating the precipitating event while managing systemic and pulmonary vascular congestion. In determining heart failure therapy, pediatricians rely on extrapolated evidence from large trials performed in adults.<sup>14</sup> Afterload reduction is achieved through the use of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, milrinone, or nitrates; and diuretics are used for preload reduction. Beta-blockers are considered for sympathetic nervous system inhibition, while mineralocorticoid inhibitors are used for cardiac remodeling prevention. Digoxin can be considered for inotropy.<sup>12</sup> In the case of myxedema heart, thyroid replacement hormone is paramount in correcting underlying physiologic derangements. Levothyroxine (T4) and liothyronine (T3) are used in these cases, though evidence-based treatment of myxedema has not yet been established given the lack of large-scale controlled studies.<sup>15</sup> Moreover, treating underlying precipitants, including infections, electrolyte abnormalities, anemia, arrhythmias, and drug toxicity, is equally crucial.<sup>16</sup> Due to the possibility of secondary hypothyroidism with associated hypopituitarism, hydrocortisone should be considered if there is concern for adrenal insufficiency, as increasing thyroxine levels in a patient with underlying adrenal insufficiency can result in increased metabolism of cortisol and precipitate adrenal crisis.<sup>2</sup> Patients who do not respond to initial treatment for heart failure should be considered for extracorporeal membrane oxygenation or ventricular assist device. Further, cardiac transplantation may be considered if the patient is refractory to the aforementioned treatment modalities.<sup>12</sup>

The outcome for children with heart failure depends upon the etiology.<sup>16</sup> In a reported autopsy finding of a 36-year-old woman who was diagnosed with myxedema heart disease, mucoid changes were persistent in the myocardial fibers despite adequate thyroid replacement therapy.<sup>17</sup> Prior to her death, she had clinically recovered with resolved physical signs of myxedema and normalized basal metabolic rate and ECG.

Levothyroxine has a 7-day half-life; therefore, to avoid continued complications or a risk for myxedema coma, liothyronine can be used, given its rapid onset within 24 hours.<sup>3</sup> In the setting of severe hypothyroidism with myxedema heart disease or myxedema coma, medications should be given through intravenous route due to the sluggish alimentary system and risk for decreased absorption.<sup>3</sup> Additionally, hypotonic fluids should be avoided.<sup>3</sup> Caution with rapid thyroid hormone replacement is often a concern in the intensive care unit setting due to the concern that liothyronine may increase the risk of arrhythmia; however, studies evaluating euthyroid adults with known cardiac disease have demonstrated liothyronine supplementation may improve cardiac output and decrease systemic vascular resistance in the absence of adverse effects.<sup>18,19</sup> Likewise, liothyronine has been used in postoperative euthyroid children with congenital heart disease and has been associated with improvements, without negative outcomes.<sup>3</sup> In the 2014 guidelines from the American Thyroid Association's Task Force on thyroid hormone replacement, it is discussed that in adults, intravenous synthetic T3 can be started with a loading dose of 5 to 25 µg, followed by a maintenance dose at 2.5 to 10 µg every 8 hours.<sup>18</sup> However, further discussion recognizes that while T3 is the activated form of thyroid hormone, it may increase the risk of arrhythmia.<sup>18</sup> Therefore, the use of combination therapy with lower doses of levothyroxine at 4 µg/kg of ideal body weight and liothyronine at 10 µg every 8 to 12 hours can successfully treat patients with decompensated hypothyroidism. Smaller doses of liothyronine may be needed for smaller and younger patients.<sup>20</sup> Importantly, high-dose hormone therapy has been shown to increase 1-month mortality in adults with myxedema; therefore, caution with thyroid hormone replacement is sensible.<sup>21</sup> Small prospective studies evaluating children with hypothyroidism before and after thyroid replacement therapy has demonstrated alteration of myocardial function and subsequent reversal with therapy.<sup>22</sup>

## Conclusion

This case underscores immediate considerations in the treatment of myxedema heart disease. Clinicians should consider the temporal delay that may occur between initiating hypothyroid treatments and clinical improvement after levothyroxine and liothyronine supplementation. This case highlights the unique management in a critically ill pediatric patient population not previously described.

## Disclaimer

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#### Contributors' Statement Page

Dr. Bennett and Dr. Bridwell contributed to conception and design and drafted the initial manuscript, and reviewed and revised the manuscript.

Dr. Percival, Dr. Appachi, Dr. Gupta-Malhorta, and Dr. Salameh contributed to conception and design, acquisition of data, analysis and interpretation of data and critically reviewed the manuscript for important intellectual content.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

#### Conflict of Interest

None declared.

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