Published in final edited form as:

Endocrinologist. 2004 ; 14(4): 212–215.

Pericardial Effusion in the Emergency Department

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Abstract

We report the first child presenting to the emergency department with undiagnosed myxedema in whom incidental detection of pericardial effusion led to diagnosis. Moreover, this patient presented with the highest serum thyrotropin concentration reported to date, a phenomenon that caused the hook effect during laboratory analysis. We discuss key elements of the recognition and management of hypothyroidism in the pediatric population and emphasize the importance of annual screening for hypothyroidism in all patients with Down syndrome.

Keywords

pericardial effusion; Down syndrome; Hashimoto thyroiditis; hook effect; growth failure; myxedema

Although pericardial effusion has been recognized as a complication of long-standing hypothyroidism in adults since 1918,¹ it is rarely the first presenting sign of the disease. Only 3 pediatric case reports exist, and this presentation of myxedema has not been reported in the emergency medicine literature. Appropriate administration of L-thyroxine typically resolves the effusion in a reasonable period of time; thus, prompt diagnosis prevents unwarranted pericardiocentesis. We describe a child with Down syndrome who presented to the emergency department with acute facial swelling. In the course of evaluation, a pericardial effusion was noted, which prompted evaluation of thyroid status. Our purpose is to familiarize all physicians with the diagnosis and treatment of myxedema in children with hypothyroidism and to emphasize the importance of annual screening for hypothyroidism in all patients with Down syndrome.

CASE REPORT

An 11-year-old boy with Down syndrome presented to the emergency department with swelling of his face, in particular the eyelids and shoulders over the last week (Fig. 1). He had gradually become more listless over the past 6 weeks, and has had a decreased energy level for the past few months. There was no history of headache, neck pain, vision problems, eye pain, ocular discharge, ocular protrusion, or head trauma. His medical history was

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The authors have disclosed that they have no significant relationships with or financial interests in any commercial company that pertains to this educational activity.

significant only for Down syndrome. He was not on any medications. No laboratory examination had been performed at his most recent health maintenance visit 7 months ago. His mother reported that he has been complaining of “feeling cold” more often, and his lips had been “very dry.” In addition, he has gained 10 pounds over the past 2 months.

Physical examination revealed a child with Down’s facies in no distress. Brachial blood pressure was 104/64 mm Hg, heart rate 73 beats/min, respiratory rate 20 breaths/min, oral temperature 96.0°F, and pulse oximetry 95% on room air. He weighed 32 kg (25th percentile for Down syndrome) and was 109 cm tall (below the third percentile, –2.2 SDs for Down syndrome).² He had bilateral edema of both eyelids with symmetric supraclavicular and nuchal swelling. He had no rash, jaundice, or pallor. His testicular volume was 8 mL bilaterally (Tanner stage 2) with Tanner stage 1 pubic and axillary hair. The remainder of his examination was unremarkable.

Laboratory evaluation revealed a blood urea nitrogen level of 21 mg/dL, creatinine 1.5 mg/dL, glucose 83 mg/dL, albumin 4.1 g/dL, AST 116 U/L, ALT 187 U/L, and total bilirubin 0.4 mg/dL. Urinalysis was unremarkable. Additional testing showed a leukocyte count 5600/mm³, hematocrit 32%, and a platelet count of 230,000/mm³. Posteroanterior and lateral chest radiographs were normal. Electrocardiogram revealed normal sinus rhythm at a rate of 70 beats/min with slight T-wave inversions in leads II, III, and aVF. QRS axis was 104.

Elevation of the hepatic transaminases prompted abdominal ultrasonography, which was normal. However, the ultrasonography technician incidentally noted small bilateral pleural effusions and moderate pericardial effusion. Discovery of the pericardial effusion prompted an immediate echo-cardiogram, which confirmed the pericardial effusion and the absence of cardiac tamponade. After interdisciplinary discussion of the differential diagnosis of pericardial effusion and edema, the diagnosis of hypothyroidism was considered and serum thyrotropin (TSH) was assayed. After 4 hours and multiple dilutions of the original sample, the hospital laboratory reported the serum TSH level as “greater than 800 μ U/mL,” the highest level ever recorded at the institution. The patient was then transferred to the pediatric endocrine service of the closest academic medical center. At the time of transfer, the differential diagnosis included Down syndrome, hypothyroidism, possible pituitary pathology, renal insufficiency, elevated hepatic transaminases, and macrocytic anemia.

On presentation, review of systems revealed poor growth for at least 3 years. His mother did not recall any recent thyroid function tests. The combination of Down syndrome, myxedema, growth failure, and the presenting constellation of laboratory findings was attributed to longstanding Hashimoto’s hypothyroidism. Elevated thyroid peroxidase immunoglobulin (IgG) titer at 126.5 IU/mL (normal range, <2.0) confirmed the diagnosis of Hashimoto’s hypothyroidism. Thyroglobulin IgG titer was <2.0 IU/mL (normal range, <2.0). Repeat thyroid function studies were obtained, and one third the usual replacement dose of L-thyroxine for this age was immediately initiated at 37.5 μ g orally daily. Serial laboratory assessments are summarized in Table 1. The patient was discharged from the hospital on the fifth hospital day after close monitoring for cardiac or renal decompensation revealed no instability. He demonstrated normal serum concentration of free thyroxine by the 45th day of replacement therapy (Table 1), and by the 60th day, the pericardial and pleural effusions had completely resolved. By this time, the serum transaminase concentrations and serum creatinine had also returned to the normal ranges.

DISCUSSION

We have reported the first case of pericardial effusion as the herald sign of myxedematous hypothyroidism presenting to an emergency department. Our patient had Hashimoto’s

hypothyroidism, the most common acquired thyroid disorder in children and adolescents.³ Hashimoto disease is very common in Down's patients, in whom the prevalence approaches 30% before age 18,⁴ more than 300-fold that of the general pediatric population.⁵ Like in our patient, auto-immune hypothyroidism is often not associated with goiter as a result of destruction of the thyroid gland.

Pericardial effusion is a common finding in hypothyroid patients and has been reported in a fetus⁶ as well as children with⁷ or without⁸ Down syndrome. Although pericardial effusion has been recognized as a complication of long-standing hypothyroidism in adults since 1918,¹ it is rarely the first presenting sign of the disease. In our patient, the concern for a primary cardiac etiology for the edema initially superseded the consideration of myxedema from hypothyroidism. Incidental evaluation of the pericardium by the sonography technician fortuitously expanded the differential diagnosis resulting in timely intervention.

Administration of L-thyroxine typically resolves pericardial effusion related to myxedema within a month. Thus, prompt diagnosis prevents unwarranted pericardiocentesis. Cardiac tamponade is a rare but most dangerous complication associated with pericardial effusion^{9,10} and appears to occur more often in children with structural cardiac disease.¹¹ Recognition of hypothyroidism as a cause of pericardial effusion is critical, because even massive effusions have completely resolved simply with L-thyroxine replacement without resorting to pericardiocentesis.¹² Aside from infectious pericarditis and primary cardiac disorders, the differential diagnosis of pericardial effusion in the pediatric population includes AIDS, hypothyroidism, sarcoidosis, systemic lupus erythematosus, rheumatic fever, tuberculosis, and malignant invasion.

To our knowledge, the extraordinarily elevated serum TSH level in our patient is the highest ever reported in the literature and is much higher than any value observed in one of the nation's busiest, most established and renowned reference laboratories (personal communication to R.F. from Michael Moxness, PhD, of Esoterix Endocrinology, Inc., Calabasas Hills, CA, May 23, 2002). It exceeds the values reported with TSH-secreting adenomas¹³ and reflects the robust pediatric thyrotrope function in the face of longstanding hypothyroidism (at least 3 years in our patient based on the documented growth failure). TSH concentrations in serum were determined by the latest generation electrochemiluminescent technique. Based on the sandwich principle, specific monoclonal antibody to TSH is ruthenium-labeled and coupled to streptavidin-coated paramagnetic beads (all reagents from Roche-Boehringer Mannheim, Los Angeles, CA). After incubation with serum, beads are separated in the fully automated Elecsys 2010 Analyzer (software version 3.08, Roche-Boehringer Mannheim), which holds the electrochemiluminescence (ECL) detection cell. After addition of tripropylamine, voltage is applied and the resulting luminescence is measured.¹⁴ We use TSH-specific reagents and calibrators (Roche part 1731459; Los Angeles, CA) with internal Liquicheck controls (Bio-Rad, Hercules, CA). In part as a result of limitations on the linearity of the assay at extreme ranges, our laboratory performed serial dilutions of the fresh serum sample in this patient (obtained before L-thyroxine administration). This approach also reduced the possibility of an erroneously low reading from the hook effect, which results in a falsely low absorbance reading when high analyte concentration saturates the primary antibody and prevents secondary antibody binding.¹⁵ The absorbance curve hooks at high concentration toward basal (low) values, and serial dilutions of the specimen are required for accurate results (Fig. 2).

Severe primary hypothyroidism has also been associated with true isosexual precocity (van Wyk-Grumbach syndrome), postulated to result when elevated hypothalamic thyrotropin-releasing hormone (TRH) stimulates pituitary TSH, follicle-stimulating hormone (FSH), and luteinizing hormone (LH) release. Highly concentrated TSH cross-stimulates the FSH and

LH receptors. At the time of diagnosis in our patient, serum testosterone level was 11 ng/dL (normal prepubertal range, 1–10 ng/dL) with plasma LH concentration of 1.10 mIU/mL (normal prepubertal range, 0.02–0.3 mIU/mL), and testicular volume appropriate for his Tanner staging. He was within the appropriate chronologic age range to have begun puberty. Unfortunately, precocious puberty can occur in patients with primary hypothyroidism despite normalization of serum TSH concentrations on L-thyroxine replacement.¹⁶ Overtreatment that results in elevated free thyroxine levels could advance osseous maturation, leading to premature physeal closure which, combined with sexual precocity, predisposes to short adult stature.¹⁷ Careful monitoring to avoid iatrogenic hyperthyroidism appears to reduce the risk of achieving final adult stature below the genetic potential.¹⁸

CONCLUSION

Given their high incidence of hypothyroidism, patients with Down syndrome should be screened annually by physical examination of growth pattern as well as determination of serum TSH concentration.^{19,20} Hypothyroidism must be excluded during the evaluation of any child with Down syndrome, particularly in settings of linear growth failure, edema, or pericardial effusion. Careful, timely replacement of L-thyroxine will restore expected growth and development. Pericardiocentesis is generally unwarranted in hypothyroid patients who are hemodynamically stable. The therapeutic goal with L-thyroxine replacement therapy is to restore euthyroidism while avoiding precocious sexual development and premature physeal closure.

Acknowledgments

Supported in part by NIH Grant K08 DK02876 and the Genentech Clinical Scholar Award of the Lawson Wilkins Pediatric Endocrine Society (to R.J.F.).

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Learning Objectives

- Identify the clinical and laboratory findings that point to a diagnosis of myxedema in children.
- Outline the preferred management of myxedematous children with pericardial effusion, emphasizing the possible sequelae of overtreatment.
- Recall the connection between Down syndrome and childhood hypothyroidism, and the authors' recommendations for screening.

FIGURE 1.
Clinical appearance of the facial and nuchal swelling on presentation.

FIGURE 2.
Classic hook effect at high analyte concentrations with radioimmunoassay.

TABLE 1

Laboratory Values Throughout Clinical Course

Days After Initial Presentation to ED	1	3	4	45	90	105
Serum TSH (0.3–4.7 μ U/mL)	3493	nd	nd	57	36	nd
Serum free T ₄ (0.7–2.2 ng/mL)	<0.2	nd	nd	0.9	nd	nd
Serum total T ₄ (4.5–12 μ g/dL)	0.5	nd	nd	nd	5.3	nd
Serum creatinine (0.7–1.2 mg/dL)	1.3	1.1	1.1	0.7	nd	nd
Blood urea nitrogen (8–20 mg/dL)	20	20	15	nd	nd	nd
Serum ALT (5–50 U/L)	126	nd	121	nd	nd	10
Serum AST (15–50 U/L)	105	nd	111	nd	nd	47

L-thyroxine replacement was initiated after obtaining the initial confirmatory sample on day 1; nd, not determined.