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HYPOTHYROIDISM – DIAGNOSTIC CHALLENGE IN CHILDREN – CASE REPORT

Abstract: Hypothyroidism is an endocrine disorder with a wide range of symptoms and multi-organ involvement. Almost all cells of the body have receptors for thyroid hormones, and the clinical picture of hypothyroidism is a result of the reduced effect of thyroid hormones on target organs and can be nonspecific, especially in children and adolescents, and thus may remain unrecognized for a longer period of time. Pericardial effusion, which occurs with a frequency of 10%–30% in adult patients with hypothyroidism, is very rare in children. Pericardial effusion, as well as all other symptoms of hypothyroidism, is reversible after the initiation of hormone replacement therapy. This is a report of a girl in whom pericardial effusion was the most significant manifestation of autoimmune thyroiditis, and in whom, at the time of diagnosis, other disorders due to the prolonged effect of low levels of thyroid hormones on target organs were also observed.

Keywords: children, hypothyroidism

Introduction

Hypothyroidism is an endocrine disorder with a wide range of symptoms and multi-organ involvement [1].

Almost all cells of the body have receptors for thyroid hormones [2], and the clinical picture of hypothyroidism is a result of the reduced effect of thyroid hormones on target organs and can be nonspecific, especially in children and adolescents, and thus may remain unrecognized for a longer time period [3].

Autoimmune thyroiditis is the most common cause of acquired hypothyroidism in the pediatric population. It is usually diagnosed in older children and adolescents, more frequently in females [4].

Pericardial effusion, which occurs with a frequency of 10%–30% in adult patients with hypothyroidism, is very rare in children [5].

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This is a report of a girl in whom pericardial effusion was the most significant manifestation of autoimmune thyroiditis, and in whom, at the time of diagnosis, other disorders due to the prolonged effect of low levels of thyroid hormones on target organs were also observed.

Case Report

A 17-year-old girl was referred to our institution due to abdominal pain, which she described as starting in the stomach area and then descending along the left side of the abdomen, lasting for the past 5 days, and fatigue. She had no fever. She had recovered from a COVID-19 infection a month earlier, with her only symptom being a slightly elevated body temperature. Laboratory findings, performed 5 days before admission, included ESR 28 mm/h, WBC 4.5 (Neu 44,1%, Lym 43,5%, Mo 8,5%, Eos 2,4%, Bas 1,49%), RBC 3.35, Hgb 109 g/L, Hct 0,318 L/L, PTL 232, total cholesterol 6,92 mmol/L, triglycerides 0,79 mmol/L, creatinine 129,9 µmol/L, total protein 83 g/l, albumin 49 g/L, ALT 67 U/L, AST 67 U/L, serum amylase 70 U/L, K 3,6 mmol/L, other electrolytes were within reference ranges; urine: normal; urine culture without growth of pathogenic bacteria. Abdominal and pelvic ultrasound revealed the presence of a free fluid collection in the intrapelvic region up to 2mm thick, normal-sized ovaries with multiple cystic changes. She was treated for 5 days on an outpatient basis with oral antimicrobial therapy Cefixime (Pancef).

Upon admission, the girl's weight was 63,5kg, height 172,5cm, BMI 21,3 kg/m^2, afebrile, eupneic, blood pressure 100/70mmHg, pale skin without pathological efflorescence, conscious, mobile. Upper eyelids slightly swollen. Throat calm. The thyroid gland was not enlarged. Normal auscultatory findings on lungs. Heart action rhythmic, tones clear without pathological murmurs. Palpable femoral artery pulses symmetrical with brachial. Abdomen soft, not tender on palpation, without palpable organomegaly. Mild pretibial edema. Meningeal signs negative.

Laboratory analyses on admission: ESR 19mm/h, CRP <1mg/L fibrinogen 2,52g/L, ASOT: negative, WBC 4,1 (Neu 49,4%, Lym 37,7%, Mo 8,3%, Eos 3,4%, Bas 1,2%), RBC 3,4, Hgb 104 g/L, Hct 0,32 L/L, PTL 208. Electrolytes were within reference ranges, total cholesterol 6,76 mmol/L, LDL cholesterol 4,42 mmol/L, HDL cholesterol 1,84 mmol/L, urea 4,7 mmol/L, creatinine 116,5 µmol/L, uric acid 190 µmol/L, ALT 21 U/L, AST 81 U/L, alkaline phosphatase 46 U/L, Latex RF: negative, Waaler Rose Test: negative, rapid antigen test for SARS-CoV-2: negative.

Electrocardiography: HR 74/min, sinus rhytm, negative T wave in D2, D3, aVF, V4-V5, flattened in D1, V6, low QRS complex voltages in leads D1, V4-V6, QTc 0,44s (Figure 1).

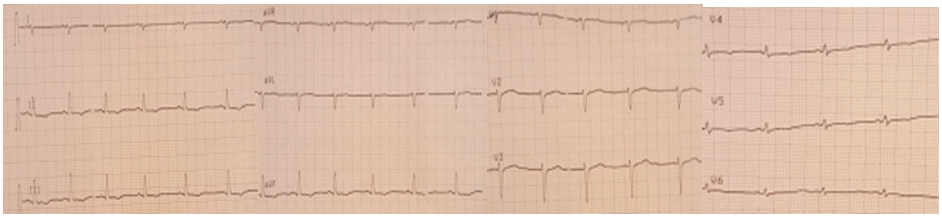

Figure 1. Electrocardiography of 17-year-old girl with hypothyroidism and pericardial effusion: HR 74/min, sinus rhytm, negative T wave in D2, D3, aVF, V4-V5, flattened in D1, V6, low QRS complex voltages in leads D1, V4-V6, QTc 0,44s.

After electrocardiography, additional laboratory tests were performed: CK 1975 U/L, CK-MB 88 U/L, LDH 421 U/L, Troponin I <10 (ref. up to 40), D-dimer 0,19 mg/l (ref. <0.50), and an echocardiographic examination was also performed, which showed pericardial effusion of about 12mm in diastole with preserved left ventricular contractility (Figure 2).

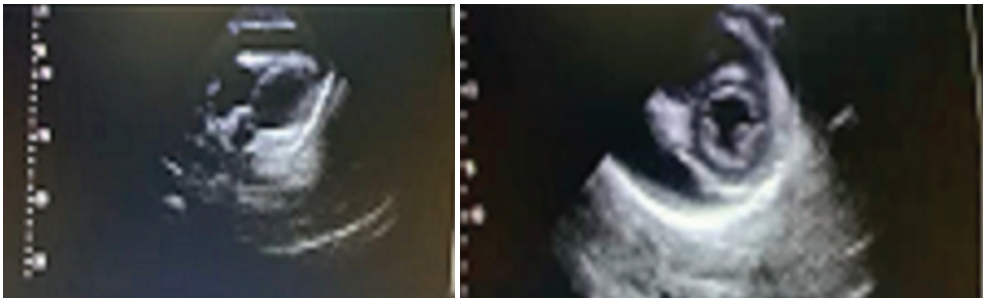

Figure 2. Echocardiography with evidence of a pericardial effusion in 17-year-old girl with hypothyroidism

The girl was referred to a tertiary care institution for further investigation, where she was diagnosed with autoimmune thyroiditis with the thyroid gland hypofunction.

Discussion

In hypothyroidism, an increased protein extravasation and slowing of lymphatic drainage occurs which can lead to the development of myxedema with fluid accumulation in serous spaces, including the pericardial space. Fluid accumulation is usually very slow, allowing the heart time to adapt, patients are mostly asymptomatic, and it is usually discovered when the clinical picture of hypothyroidism is fully developed or incidentally during examination. However, if pericardial effusion is not detected

and adequately treated in time, fluid accumulation in the pericardial space can lead to the development of cardiac tamponade [6].

Thyroid hormones, through their direct effect on cardiomyocytes, affect their electrophysiological properties as well as heart rate and expression of beta-adrenergic receptors in the heart [7]. Therefore, in patients with hypothyroidism, various disturbances of heart rhythm and conduction can be observed.

The most common changes that can be observed in patients with hypothyroidism on a 12-lead surface ECG are bradycardia, right bundle branch block, flattened or inverted T waves, wide QRS complexes, prolonged QTc interval, and low QRS complex voltage [8]. Prolongation of the QTc interval puts these patients at risk for developing ventricular arrhythmias (torsades de pointes) [7], and low QRS complex voltage can be seen in patients with hypothyroidism with or without pericardial effusion. However, since this ECG pattern is highly suggestive of pericardial effusion, it is recommended that an echocardiographic examination be performed in all patients [8].

In hypothyroidism, in addition to the aforementioned chronotropic and dromotropic changes, there is also a decrease in myocardial contractility and impaired relaxation (diastolic dysfunction) [7].

Thyroid hormones also affect the tone of smooth muscles in blood vessels and their reactivity. In hypothyroidism, due to decreased production of endothelin-producing relaxation factor (EDRF), there is a decrease in the relaxation of smooth muscles in blood vessels and their constriction, leading to increased systemic vascular resistance. This, along with decreased myocardial contractility, results in reduced cardiac output and tissue hypoperfusion [7].

Individuals with hypothyroidism may also have elevated diastolic blood pressure due to impaired function of the renin-angiotensin-aldosterone system, resulting from reduced plasma renin levels due to a decreased synthesis of its precursors in the liver [8].

All these hemodynamic disturbances probably affect kidney function as well, so in patients with hypothyroidism, a reduced glomerular filtration and increased serum creatinine levels are also observed [9].

Fatigue, muscle weakness, and weakened tendon reflexes (hypothyroid myopathy) are probably the consequences of skeletal muscle dysfunction that occurs in hypothyroidism [10, 11]. Namely, in patients with hypothyroidism, an increase in the muscle enzyme creatine phosphokinase, mainly the CK-MM isoenzyme, has been observed, while a smaller number of patients also exhibit an increase in CK-MB. This, along with an increase in lactate dehydrogenase (LDH) and aspartate aminotransferase (AST) but without an increase in troponin I [12] in patients with elevated CK-MB isoenzymes, indicates that the origin of this enzyme is from skeletal muscles [13, 14]. Why muscle enzymes increase in hypothyroidism is not entirely clear, but it is hypothesized that it may result from disturbances in glycogenolysis, direct cellular damage,

and/or decreased clearance of creatine phosphokinase, while creatine phosphokinase levels are usually positively correlated with TSH levels [10].

In hypothyroidism, there is a decrease in erythropoietin secretion, which can lead to the development of anemia in these patients [15].

Dyslipidemia is common in people with hypothyroidism, and they usually have elevated levels of total cholesterol and low-density lipoprotein cholesterol (LDL-cholesterol), although somewhat less frequently they may also have hypertriglyceridemia. Elevated levels of total cholesterol and LDL-cholesterol are most likely due to a decreased activity of proteins and enzymes involved in cholesterol metabolism in the liver, as well as a reduced expression of LDL receptors in the liver and its decreased hepatic and biliary clearance [7, 8].

Treatment involves substitution therapy with thyroid hormones, the administration of which leads to the resolution of hypothyroidism symptoms [1, 7], including pericardial effusion [6].

Conclusion

The clinical picture of hypothyroidism in children and adolescents can be very nonspecific. Therefore, it is advised to check the thyroid status in all children who have nonspecific symptoms such as fatigue, muscle pain, anemia (especially when not responding to substitution therapy), dyslipidemia, or newly developed heart rhythm and conduction disturbances or myocardial dysfunction. Additionally, thyroid status should be checked in all children with observed pericardial effusion without clear clinical signs for diagnosing pericarditis or the presence of other possible causes such as neoplasms, kidney diseases, or rheumatological diseases.

Conflict of interest: The autor declare no conflict of interest regarding the publication of this paper.

Ethical approval: This is case report and ethical committee approval was not sought.