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Severe hypothyroidism as the cause of rhabdomyolysis and acute kidney injury – a case report

Ciężka niedoczynność tarczycy jako przyczyna rabdomiolizy i ostrego uszkodzenia nerek – opis przypadku

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Abstract

Hypothyroidism is a set of clinical symptoms associated with a deficiency of thyroid hormones. Musculoskeletal symptoms, i.e. stiffness, pain or muscle fatigue, are among the many manifestations of the disorder. Rhabdomyolysis, a syndrome accompanying muscle tissue damage, which leads to acute kidney injury, may be a complication of hypothyroidism. In this paper, we present a case of a 35-year-old patient with hypothyroidism due to Hashimoto's disease, with a 4-year history of diagnosis for periodic pain and muscle weakness in the lower extremities. The patient presented to the hospital due to the recurring symptoms. One month before admission, she had discontinued thyroid hormone supplementation. Laboratory tests showed unquantifiable low levels of free thyroid hormones, elevated creatine kinase levels, and elevated kidney function parameters. Non-compliance can lead to potentially life-threatening complications in hypothyroid patients. Prompt diagnosis and implementation of treatment can lead to symptom resolution.

Keywords: hypothyroidism, rhabdomyolysis, acute kidney injury, thyroid hormones

Streszczenie

Niedoczynność tarczycy jest zespołem objawów klinicznych związanych z niedoborem hormonów tarczycy. Jedną z licznych manifestacji choroby są objawy ze strony układu mięśniowo-szkieletowego, takie jak sztywność, bóle czy męczliwość mięśni. Jej powikłaniem może być rabdomioliza – zespół chorobowy towarzyszący uszkodzeniu tkanki mięśniowej, który prowadzi do ostrego uszkodzenia nerek. W niniejszej pracy przedstawiono przypadek 35-letniej pacjentki z niedoczynnością tarczycy na podłożu choroby Hashimoto, diagnozowanej od 4 lat z powodu okresowego bólu i osłabienia mięśni kończyn dolnych. Pacjentka zgłosiła się do szpitala ze względu na ponowne wystąpienie objawów. Miesiąc przed przyjęciem zaprzestała suplementacji hormonów tarczycy. W badaniach laboratoryjnych odnotowano nieoznaczalnie niskie stężenia wolnych hormonów tarczycy, podwyższone stężenie kinazy kreatynowej, podwyższone parametry funkcji nerek. W grupie chorych z niedoczynnością tarczycy niestosowanie się do zaleceń lekarskich może prowadzić do potencjalnie zagrażających życiu powikłań. Szybka diagnostyka i wdrożenie leczenia mogą prowadzić do ustąpienia objawów.

Słowa kluczowe: niedoczynność tarczycy, rabdomioliza, ostre uszkodzenie nerek, hormony tarczycy

INTRODUCTION

Hypothyroidism is a group of clinical symptoms associated with a deficiency of thyroid hormones. Overt hypothyroidism is defined as a thyroid stimulating hormone (TSH) level above the upper limit of normal and a free thyroxine (fT4) level below the lower limit of normal. Overt hypothyroidism is usually preceded by subclinical hypothyroidism, diagnosed as normal fT4 and elevated TSH[1]. The prevalence of hypothyroidism varies depending on the population being analysed and the cut-off points for normal levels of TSH and thyroid hormones. Studies in the European population showed the prevalence of overt and subclinical hypothyroidism of 0.2–5.3%[2]. Many individuals are unaware of having the disorder; according to the authors of a meta-analysis of European data, further 5% of the population remain undiagnosed[3]. These rates may be even higher in populations with dietary iodine deficiency. Women and people over 65 years are more likely to be affected[4].

Symptoms of hypothyroidism are non-specific and may include fatigue, weight gain and dry skin, and if left untreated, the disorder may have serious consequences and lead to a life-threatening myxedema coma[5]. The paper presents a case of a patient with hypothyroidism who developed rhabdomyolysis and acute kidney injury due to the lack of thyroid hormone supplementation.

CASE REPORT

A 35-year-old woman presented to hospital due to symmetrical pain and muscle weakness in the lower limbs. She spent the last 2 days prior to admission lying in bed and being able to move about only with the help of an accompanying person.

The patient had a history of chronic hypothyroidism in the course of Hashimoto's disease and anxiety disorders. Additionally, she had experienced recurrent episodes of pain in the muscles of the lower limbs for 4 years; according to the patient, no cause was found, she had no documentation or past test results. Due to hypothyroidism, she remained under the care of an endocrinology clinic, where treatment with high doses of levothyroxine filed to achieve euthyroidism, and the drug was switched to combination therapy with levothyroxine plus liothyronine. Absorption disorders were suspected, but no appropriate diagnosis was ordered. The patient reported that she had discontinued thyroid hormone supplementation about a month earlier due to the unavailability of the drug in pharmacies; however, she did not consult her doctor. Due to anxiety disorders, she regularly took gabapentin and duloxetine.

On admission, the patient was cardiovascularly and respiratorily stable; physical examination showed significant symmetrical muscle weakness, especially in the thighs. She reported pain during palpation of the muscles of the lower limbs. She was unable to rise from bed unassisted. Blood count showed leukocytosis – 12.81 × 10^9/L (normal: 4.30–9.64 × 10^9/L), venous blood gas showed elevated lactates. Serum nitrogen retention parameters were elevated: creatinine 1.8 mg/dL (normal: 0.5–0.9 mg/dL), urea 48 mg/dL (normal: 15–43 mg/dL). Creatine kinase was elevated to 6,691 U/L (normal: 26–145 U/L), myocardial necrosis markers did not show dynamics typical of acute coronary syndrome. The laboratory workup also showed significantly elevated TSH of 452 µIU/mL (normal: 0.27–4.2 µIU/mL). Free thyroid hormone was below the lower limit of quantification for the tests available in the hospital laboratory: free triiodothyronine (fT3) <0.6 pmol/L (normal: 3.2–6.9 pmol/L), fT4 <0.5 pmol/L (normal: 12–22 pmol/L). Urinalysis showed red blood cells, squamous epithelium, minor bacteriuria and leukocyturia. Inflammatory parameters were not elevated. Liver enzymes were also measured; alanine aminotransferase and aspartate aminotransferase levels were slightly above normal; total bilirubin was increased to 1.9 mg/dL (normal: 0.0–1.1 mg/dL). Antinuclear antibodies against double-stranded DNA (anti-dsDNA), antibodies against neutrophil myeloperoxidase, and antibodies against granulocyte cytoplasmic peroxidase 3 were also measured and were negative. Diagnostic imaging, including abdominal ultrasound (US) and computed tomography (CT) of the head, was normal. Thyroid ultrasound was suggestive of autoimmune thyroiditis. A CT scan of the lumbar and sacral spine showed a multilevel disc herniation, without signs of compression of the nerve trunks.

Considering the clinical picture and laboratory findings, rhabdomyolysis and severe thyroid hormone deficiency due to untreated hypothyroidism were diagnosed. The patient was started on intensive intravenous fluid therapy with bicarbonate. Levothyroxine with liothyronine were resumed. Further laboratory workup performed during hospital stay showed a gradual decrease in creatinine until its normalisation, which allowed for the diagnosis of acute kidney injury (AKI) in the absence of a history of chronic kidney disease. Creatine kinase decreased significantly (Tab. 1). Free thyroid hormone levels returned to normal on day 9 of treatment. A follow-up urinalysis showed no haematuria or urinary tract infection. During hospital stay, the patient was consulted by a neurologist, but no grounds for further diagnosis were found. The patient's general condition improved significantly during hospital stay; the pain resolved and the woman was able to walk independently on the day of discharge. Regular pharmacotherapy and further follow-up in the endocrinology clinic were recommended.

DISCUSSION

Hypothyroidism is one of the most common endocrine disorders. The treatment is based on thyroid hormone supplementation and aims to relieve symptoms and achieve euthyroidism[6]. Levothyroxine, a synthetic form of thyroxine, is the most commonly used drug for hypothyroidism. It is also one of the most commonly prescribed drugs in

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Parameter	Day 0 (admission)	Day 3 of hospital stay	Day 9 of hospital stay	Normal range
Creatinine[mg/dL]	1.8	1.2	1.0	0.5–0.9
Urea [mg/dL]	48	30	36	15–43
CK [U/L]	6,691	5,072	750	26–145
ALT [U/L]	40	–	47	0–33
AST [U/L]	109	–	50	0–31
TSH [µIU/mL]	452	–	8.4	0.27–4.2
fT3 [pmol/L]	<0.6	–	5.49	3.2–6.9
fT4 [pmol/L]	<0.5	–	12.1	12–22
ALT – alanine transaminase; **AST** – aspartate transaminase; **CK** – creatine kinase; **fT3** – free triiodothyronine; **fT4** – free thyroxine; **TSH** – thyroid stimulating hormone.				

Tab. 1. Laboratory findings on admission and on subsequent days of hospital stay

developed countries; according to the American Food and Drug Administration (FDA), 100 million prescriptions are issued annually for levothyroxine, which makes it the second most prescribed drug in this country[7]. In the case of failure of levothyroxine monotherapy, a more biologically active liothyronine (synthetic triiodothyronine) can be included in the treatment regimen[8]. Patients typically present with non-specific symptoms, which most often include fatigue, excessive sleepiness, intolerance to cold, weight gain, constipation, voice changes and dry skin[9]. Musculoskeletal symptoms, such as muscle stiffness, pain or fatigue, are relatively common. Rhabdomyolysis, defined as a complex condition in which skeletal muscle damage occurs, is a potentially life-threatening complication. In rhabdomyolysis, free myoglobin is released into the blood, and then filtered by the glomeruli. The causes of muscle fibre damage in hypothyroidism are complex and not fully understood; the role of, among other things, thyroid hormone deficiency in glycogen metabolism disorders and oxidative phosphorylation, as well as changes in sarcomere structure and impaired glycosaminoglycan metabolism is suggested[10]. The release of myoglobin into the bloodstream in rhabdomyolysis leads to kidney damage via a complex underlying mechanism[11]. This mechanism involves, among others, vasoconstriction leading to tubular damage as a result of ischemia and direct myoglobin cytotoxic effects on the tubules, as well as obstruction of the distal tubules as a result of precipitation of the Tamm–Horsfall protein-myoglobin complex[12]. Nephrotoxicity may be aggravated by thyroid hormone deficiency, which causes activation of the renin–angiotensin–aldosterone system and an increase in the sympathetic response, which in turn decreases renal blood flow[13]. Experimental studies have also shown the negative impact of thyroid hormone deficiency on the urethral mechanisms of urine concentration[14].

In the described case, our patient diagnosed with hypothyroidism due to Hashimoto's disease developed severe thyroid hormone deficiency. This was caused by discontinuation of combined levothyroxine and liothyronine treatment. As a consequence, serum free thyroid hormones were unquantifiably low for the tests available in the hospital laboratory. Myalgia and muscle weakness, which when combined with high serum creatine kinase (over 40 times the upper limit of normal) indicated rhabdomyolysis, were the main reasons for the patient's admission to the hospital. For this reason, the patient was urgently started on intravenous fluid therapy. Elevated serum creatinine on admission (which normalised during hospital stay) pointed to the diagnosis of acute kidney injury. During the patient's stay in the hospital, thyroid hormone supplementation was resumed, resulting in a significant reduction of symptoms, normalisation of serum fT3 and fT4 levels, and a significant decrease in TSH within a week.

Earlier episodes of myalgia and muscle weakness may indicate a longer history of non-compliance. However, this hypothesis requires confirmation and exclusion of other aetiology.

CONCLUSIONS

Special attention should be paid to compliance in a patient with previously diagnosed hypothyroidism. Lack of thyroid hormone supplementation can trigger many symptoms, which in turn lead to life-threatening conditions. Immediate diagnosis and prompt implementation of treatment play a key role in patients with rhabdomyolysis as they prevent renal toxicity of myoglobin.

Conflict of interest

The authors report no financial or personal relationships with other individuals or organisations that could adversely affect the content of the publication and claim ownership of this publication.

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