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CASE REPORT

Lethal thyroid storm after uncontrolled intake of liothyronine in order to lose weight

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Abstract Thyroid hormones are sometimes used for purposes for which they are not approved. Reasons for off-label use can be overweight, prevailing depressive mood, or various somatic symptoms. Information about the intake of thyroid hormones in order to lose weight can be easily obtained from inappropriate/nonmedical websites. The objective of this case report is to describe the first case of a lethal abuse of liothyronine. The case was a 29-year-old male (BMI 32) without relevant illnesses. An autopsy was performed and followed by histological, toxicological, and clinical chemistry examinations. The autopsy revealed no relevant pathology. Histology showed multiple areas of focal cell necrosis in the myocardium and signs of acute heart failure including severe edema of the lungs; the follicles of the thyroid gland were markedly plump. Postmortem laboratory results indicated lethal liothyronine intoxication. Despite prevailing opinion, uncontrolled intake of liothyronine can cause lethal thyroid storm in a euthyroid patient without manifested cardiac illnesses.

Keywords Liothyronine · Triiodothyronine · Abuse · Thyroid storm

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Introduction

Off-label use of thyroid hormones

Levothyroxine (L-Thyroxine, T4) and liothyronine (triiodothyronine, T3, Thybon®) are usually prescribed for different reasons of thyroid hypofunction or for thyroid suppression tests. Somatic symptoms like depressive mood or memory and cognitive impairment are sometimes associated with subclinical hypothyroidism. Levothyroxine can correct these symptoms [1]. In clinical practice, levothyroxine is preferred to liothyronine as it has fewer side effects. Off-label refers to the prescription of thyroid hormones to cure somatic symptoms without underlying hypothyreosis. Nevertheless, there is evidence that off-label use of levothyroxine can be helpful in patients with chronic depressive disorder [2]. Stimulating effects to the basal metabolic rate and the heat balance can induce weight loss which is only one of many side effects. A double-blind, randomized, placebo-controlled trial showed significant loss of weight in grossly obese patients after 1 month of high-dose liothyronine intake [3]. Manufacturers explicitly advise against intake of thyroid hormones for weight reduction as overdoses could cause severe health damage. However, the product information for Thybon® [4] states that there is no described case of thyrotoxic crisis induced by liothyronine overdose and that it would be doubtful if a thyrotoxic crisis after liothyronine intake could occur at all.

An excessive intake of liothyronine downregulates thyrotropin-releasing hormone and thyroid-stimulating hormone (TSH) levels to inhibit endogen synthesis and release of T4 and T3 out of thyroglobulin. An exacerbation of the hyperthyroid state, a thyrotoxic crisis, is characterized by decompensation of one or more organ systems. The clinical picture is characterized by four main features: fever,

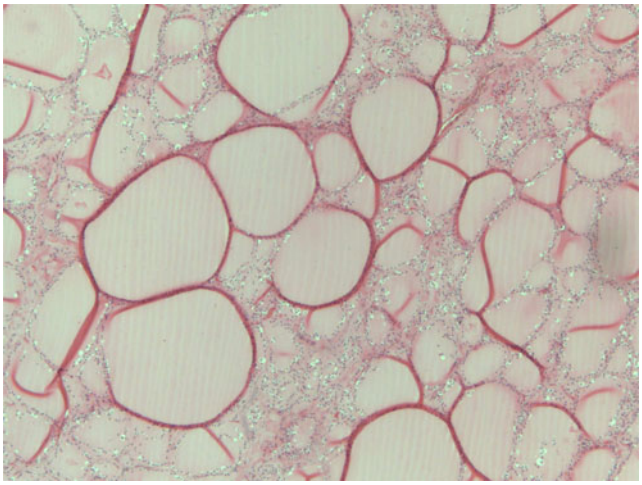

Fig. 1 Thyroid gland with plump follicles and flattened epithelial layer (hematoxylin and eosin staining, ×100)

tachycardia or supraventricular arrhythmias, central nervous system symptoms, and gastrointestinal symptoms [5]. A thyroid storm represents the extreme manifestation of thyrotoxicosis and its rate of mortality is considered to lie between 20% and 50% [6].

Bhasin et al. describe three cases of death that were associated with levothyroxine abuse [7]. An autopsy was performed in a 50-year-old female who took up to 600 μg/day after subtotal thyroidectomy to lose weight. Presumably, she died from ventricular fibrillation as multiple areas with focal necrosis were found histologically.

Several acute myocardial infarctions in association with hyperthyroidism are described even without underlying pathology of the coronary arteries [8–10]. It is assumed that thyroid hormones trigger coronary spasms and increase oxygen demand. Other authors report excessive intake of thyroid hormones without severe health damage. For example, in a suicide attempt, a 30-year-old female ingested, among other things, 1,600 μg liothyronine. A gastric lavage followed 1 h later at the hospital. Two hours after ingestion, the circulating level of T3 was approximately 5,200 ng/L and values of free T4, total T4, and TSH were normal; thyrotoxic signs were moderate. After 7 days, T4 and TSH values fell below normal. This illustrated the suppressive action of T3 on TSH secretion from the pituitary with consequent reduction of thyroxine release from the thyroid [11].

According to our literature search, this is the first case of death caused by deliberate intake of liothyronine.

Patient

A 29-year-old male was found dead at home. Despite chilly weather, he was covered with a thin blanket and the window was open. Liothyronine tablets (Thybon®) were found in the flat, which a general practitioner had prescribed twice. The second prescription contained 200 tablets of Thybon® 100 μg which were dispensed 8 months before death. Only ten of these 200 tablets could be found at home.

The general practitioner declared that the young man needed the liothyronine tablets for a relative abroad with a tumor of the thyroid gland. As liothyronine has no addictive somatic effects, he prescribed the medication for this unknown person and invented diagnoses to balance accounts with the health insurance.

Relatives stated that the deceased had been taking unspecified heart-activating and fat-burning tablets for about 6 months. A family member with a tumor of the thyroid gland could not be found.

The deceased was a healthy young man without severe illnesses. A pre-employment medical examination a few months before death only showed a slightly elevated blood cholesterol level.

Results

Autopsy

The autopsy of the slightly overweight young man (BMI 32) did not reveal the cause of death as the macromorphological findings were unspecific. The brain showed signs of highly elevated intracranial pressure and the lungs exhibited edema. The coronary arteries showed decent arteriosclerosis, and the heart was slightly enlarged. There was no macroscopical sign of myocardial infarction. The thyroid and pituitary glands had a normal appearance. The musculature and internal organs were highly congested with blood.

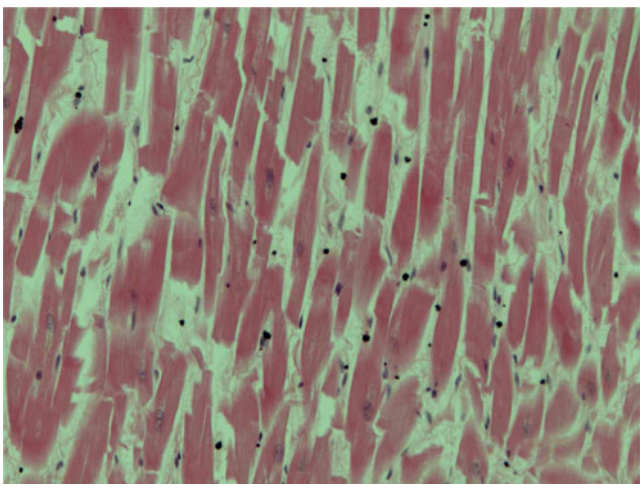

Fig. 2 Myocardial cell necroses (hematoxylin and eosin staining, ×200)

Histopathology

Histologically, the follicles of the thyroid gland were markedly plump and the follicular epithelial layer was flattened (Fig. 1). The pituitary gland was congested with blood but showed a normal morphology. The myocardium presented multiple fresh cell necroses (Fig. 2). The small heart vessels showed slight arteriolosclerosis. The lungs showed a remarkable intra-alveolar edema resulting from a prolonged heart failure.

Toxicology

Screening tests for pharmaceuticals and common drugs (e.g., cannabinoids, cocaine metabolites, amphetamines, opiates, benzodiazepines, and methadone) in blood, liver, and stomach contents showed negative results. The blood alcohol concentration was 0.014% but this may probably be due to the start of decomposition as phenylethylamine was present at higher concentration in blood and kidney.

FT3, FT4, TSH, and thyroglobulin in femoral blood were quantified showing a substantial elevation of FT3 [FT3, >32.5 ng/L (reference range, 2.6–5.1 ng/L); FT4, 7.8 pg/ml (reference range, 9.1–19.1 pg/ml); TSH, <0.01 μIU/ml (reference range, 0.27–4.20 μIU/ml); TG, 3.1 ng/ml; TG recovery, 86%].

Discussion

Cases with unspecific macromorphological findings bear diagnostic challenges and need a thorough examination. Recent publications describe other rare causes of death who could be revealed only in combination with clinical history, toxicological results, histopathological, and/or immunohistochemical examinations [12–15].

The sole combination of excessively elevated FT3, low FT4, and extremely low TSH and TG would clinically allow the conclusion of prolonged liothyronine intoxication. However, clinical reference values have to be used with care as defined postmortem reference values do not exist. Previous investigations of thyroxine in postmortem blood mainly showed a decrease [16–18] and triiodothyronine is supposed to rise or fall after death [16, 18]. TSH values showed minor variations and remained in the normal range for at least 1 day after death [17]. Thyroglobulin is said to either stay within the normal range or rise in certain types of death with mechanical pressure on the thyroid gland, for example, in traffic accidents or hanging [19]. Nevertheless, it is possible to use postmortem measurements of thyroid function if they are combined with histology and if the upper normal limit of FT4 is adjusted [20].

In this case, histology of the thyroid gland showed markedly plump follicles and the follicular epithelial layer was flattened. At this point, the question comes up of how prolonged liothyronine abuse would affect thyroid follicles. On one hand, one could expect thyroid follicles to be empty after prolonged substitution as the synthesis is inhibited. On the other hand, one could assume inhibition of endogen thyroid hormone liberation with plump follicles as liothyronine has immediate active effects in contrast to levothyroxine. We could not certainly clarify this question as a comparable case does not exist. Fever as a main feature of a thyrotoxic crisis could explain the situation in which the body was found—sparsely covered with an open window despite chilly weather. Multiple fresh cell necroses and signs of acute heart failure without relevant heart disease are further details that can be brought in line with thyroid storm. Finally, witness statements confirmed the intake of drugs that stress the heart and increase metabolism.

In summary of the findings and after exclusion of other possible reasons of death, it has to be concluded that the young man died from a thyroid storm after uncontrolled intake of liothyronine.

In contrast to the manufacturer's product information, liothyronine can obviously cause thyrotoxic crisis and even lethal thyroid storm.

It has to be assumed that thyroid storm is an underdiagnosed reason of death because specific morphological changes cannot be expected and the determination of thyroid hormones does not factor in routinely run, postmortem clinical chemistry examinations.

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