Syndrome T

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Contributor: Johannes W. Dietrich

Syndrome T, or SORSHOT, refers to persistent symptoms in patients affected by hypothyroidism who appear euthyroid by TSH levels. Seen in about 10% of hypothyroid patients, causes are unclear but likely include psychosomatic factors, inadequate treatment, autoimmunity, and neuropathy. Common symptoms are fatigue, heart-related issues, mood changes, weight gain, and pain. No standard treatment exists, but options may include combined hormone therapy, personalised dosing, and nutritional supplementation.

thyroid hypothyroidism syndrome T SORSHOT quality of life endocrinology

1. Introduction

Syndrome T (aka SORSHOT) is the designation for the complex of continued symptoms and reduced quality of life in patients with hypothyroidism that seem to be sufficiently treated from a TSH-centric perspective. The affected suffer from persistent complaints despite being in a formally euthyroid condition (i.e. thyrotropin concentration is in its reference range) [1][2][3][4].

2. Terminology

The term “syndrome T”, which is more common in Europe, traces back to “syndrome thyroiditis”, recognising a clustering of symptoms in autoimmune thyroiditis [5][6]. In the USA, the alternative term SORSHOT ("syndrome of residual symptoms of hypothyroidism on T4") is partly favoured, including hypothyroidism after thyroidectomy or radioiodine therapy [7]. On the other hand, the term “syndrome T” also includes latent autoimmune thyroid disease, i.e., autoimmune thyroiditis with preserved euthyroidism.

3. Epidemiology

The prevalence of syndrome T is estimated to be between 5 and 15% of all patients with hypothyroidism or autoimmune thyroiditis [8]. Since about 5% of the population of developed countries suffers from hypothyroidism, this translates to a population prevalence of about 0.5%.

4. Aetiology

Up to now, the exact cause of the syndrome T remains unknown. It is probably one of the multifactorial symptom complexes. Potential reasons to be discussed include [8][9]:

- awareness of being affected by a chronic disease (psychosomatic aspects, nocebo effect)
- insufficient dosage of substitutive therapy with L-thyroxine (i.e. under treatment, the concentrations for TSH and free thyroxine are in their respective reference ranges, but they miss the personal set point of the feedback loop, a non-ergodic system)
- insufficient modality of therapy (i.e. treatment with L-thyroxine alone, missing an increased need for L3 or Liothyronine in the setting of step-up-hypodeiodination)
- immunity of the thyroid with consecutive release of inflammatory mediators and, potentially, cross-immunity, e.g. to epitopes of the peripheral and central nervous system
- clustering of other autoimmune conditions in cases of chronic thyroiditis (including, but not limited to, adrenal failure, type 1 diabetes and hypoparathyroidism)
- Autonomic and sensorimotor neuropathy (probably resulting from both impaired thyroid signalling and autoimmunity) [10]

5. Symptoms

Typical complaints include fatigue, tachycardia (both postural and at rest), palpitations, gastrointestinal symptoms, depression, anxiety, unstable weight (and, especially, weight gain), intolerance to both heat and cold, and diffuse, fibromyalgia-like pain [1][2][8].

6. Therapy

Currently, a universal treatment program has not been established [11]. A significant subgroup of the affected may benefit from a combination therapy with levothyroxine (L-T4) and liothyronine (L-T3) [12][3][4], especially in cases of some polymorphic variants of the DIO2 gene, which encodes the type 2 deiodinase [13]. Other promising approaches include dosage of L-T4 based on reconstructing the setpoint of thyroid homeostasis with cybernetic methods (Thyroid SPOT), treatment of comorbidities, and immunomodulation with selenium and vitamin D [14].

Therefore, treatment of syndrome T requires a personalised approach [15].

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