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Hypersensitivity to levothyroxine: A case report of a successful oral desensitization

Desensitization to levothyroxine

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KEYWORDS

Levothyroxine; Drug hypersensitivity; Desensitization; Skin test; Skin prick test

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Abbreviations

L-T4: levothyroxine

TSH: thyroid-stimulating hormone

Introduction

Levothyroxine (L-T4) is the mainstay of treatment of hypothyroidism. Unlike majority of patients tolerate this drug well, hypersensitivity reactions to L-T4 have been rarely reported [1-4]. In this case, there is a problem of alternative treatment of hypothyroidism.

We report a case of acute hypersensitivity reaction induced by LT-4 and currently a successful oral desensitization.

Case report

A 47-year-old woman, who had a known history of asthma since childhood, was admitted to the endocrinology department to initiate brand of L-T4 for hypothyroidism (thyroid-stimulating hormone [TSH] = 100 mIU/L [reference range 0.5-4.5 mIU/L]). This drug contained the following excipients: lactose monohydrate, maize starch, gelatin, croscarmellose sodium and magnesium Stearate. LT-4 was started (day 1) at a dose of 50 µg daily and it was gradually increased for 7 days up to 100 µg/day. The thyroid function test showed improvement within a week (TSH = 5 mIU/L). However, she reported dyspnea and fatigue one hour after the first dose of 25 µg L-T4. The same symptoms had appeared when she took the drug for the six consecutive days (day 7). On day 8, she had generalized urticaria (thighs, abdomen, back) accompanied by facial angioedema. These symptoms were accentuated when she continued to take the medication. On day 10, the patient was referred to the regional pharmacovigilance center of Sfax (Tunisia): the L-T4 was stopped and 10 mg of oral cetirizine was prescribed for three days. The symptoms gradually disappeared after three

days, and L-T4 was not reinstated. The score of imputability of L-T4, according to the French imputability method [5], was plausible. Few days later, the patient presented with increased symptoms of hypothyroidism, including fatigue, depression, irritability.

After obtaining the patient's informed consent, skin test was performed according to a published protocol (day 7 after withdrawal of L-T4) [6]. Briefly, LT-4 stock solution was prepared by crushing 25 µg levothyroxine tablet and dissolved in 1 ml of 0.9% phosphate-buffered saline (Table 1). Positive skin tests were defined according to internationally accepted guidelines [7]. Prick test was negative to: (i) undiluted stock solution, (ii) 0.9% phosphate-buffered saline (negative control 1) and (iii) physiological saline (negative control 2). Prick test to histamine (0.01%) was positive (a wheal 3x4 mm and a flare 22x13 mm). Results of intradermal testing was positive with 0.01 ml of the LT-4 solution in concentrations of 1:100 (8 mm wheal), and negative with negative saline control. Due to a lack of treatment alternatives, oral desensitization to LT-4 was decided with the patient permission and after signing informed consent. The scheme of desensitization was performed in a hospital setting according to the modified protocol published by Fevzi D et al [1]. The procedure was started at a dose of 0.04 µg LT-4, with progressive dose increments every 30 minutes until a cumulative dose of 100 µg (Table 2). No other medication was taken during the time of desensitization. The patient successfully completed the entire desensitization protocol and did not experience similar skin reactions. Since then, the patient has tolerated the daily dose of 100 µg L-T4, with complete resolution of the symptoms of hypothyroidism (TSH = 0.5 mIU/L). The total tolerance time from the moment of performing desensitization to present was 14 months.

Based on the intradermal test result, immediate hypersensitivity reaction (type I) to

levothyroxine was retained in this patient. Oral desensitization was well established procedure for severe IgE-mediated reactions to drugs. The desensitization scheme in our patient was adapted from that published by Fevzi D et al [1]. These authors successfully induced tolerance to LT-4 in a patient who experienced acute systemic symptoms reactions. Given the risk of anaphylaxis with desensitization, it is crucial that it is performed at a hospital by experienced health care professionals.

Disclosure of interest

The authors declare that they have no competing interest.

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Table 1. Reagents and results of skin testing to levothyroxine

Reagents	Concentration (µg/mL)	Prick test	Intradermal test
LT-4	25	-	ND
	0.25	ND	8 mm W
Solvent*		-	ND
Normal Saline		-	-
Histamine		3x4 mm W	ND
		22x13 mm F	

*****0.9% phosphate-buffered saline

F: flare; LT-4: levothyroxine; ND: not done; W: wheal

Table 2. Oral desensitization schedule to levothyroxine

Time	Dose (µg)	Cumulative dose (µg)
0 h	0.04	0.04
1 h	0.1	0.14
1 h 30 min	0.2	0.34
2 h	0.6	0.94
2 h 30min	1	1.94
3 h	2	2.94
3 h 30min	4	6.94
4 h	8	14.94
4 h 30min	16	30.94
5 h	19	49.94
5 h 30min	22	71.94
6 h	29	100.94