

Levothyroxine-associated lichenoid drug eruption: A case report and review of levothyroxine-induced adverse reactions

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Abstract

Levothyroxine (LT4) is frequently used as thyroid hormone replacement to treat hypothyroidism. Adverse skin reactions are not common. Lichenoid drug eruption is a one such medication-related reaction. the lesion morphology and pathology mimic lichen planus. The current case describes a 47-year-old man who presented to us with a diffuse levothyroxine-induced lichenoid drug eruption. The Naranjo adverse drug reaction probability assessment score suggested this was likely an ADR to levothyroxine. The eruption resolved after discontinuation of the medication. We also reviewed the literature on levothyroxine-associated adverse events.

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Levothyroxine-associated lichenoid drug eruption: A case report and review of levothyroxine-induced adverse reactions

Levothyroxine (LT₄) is frequently used as thyroid hormone replacement to treat hypothyroidism. Adverse skin reactions are not common. Lichenoid drug eruption is a one such medication-related reaction. the lesion morphology and pathology mimic lichen planus. The current case describes a 47-year-old man who presented to us with a diffuse levothyroxine-induced lichenoid drug eruption. The Naranjo adverse drug reaction probability assessment score suggested this was likely an ADR to levothyroxine. The eruption resolved after discontinuation of the medication. We also reviewed the literature on levothyroxine-associated adverse events.

Keywords: Lichenoid drug eruption, levothyroxine

1 | BACKGROUND

Thyroid hormone replacement is the first-line treatment of hypothyroidism, and levothyroxine (LT₄) is the drug of choice. The basic principle is to convert exogenous thyroxine (T₄) into the active metabolite tri-iodothyronine (T₃) in peripheral tissues.¹ Long-term experience has proved its strengths, including efficacy in alleviating symptoms, good compliance, high intestinal absorption (70%–80%), long serum half-life (about 7 days), and low cost.² Nevertheless, several adverse reactions have been reported in the context of over-treatment with levothyroxine, mainly involving the cardiovascular and locomotor systems. Iatrogenic thyrotoxicosis may be characterized by atrial fibrillation and osteoporosis, especially in older people and postmenopausal women.²

Adverse skin reactions to levothyroxine are rarely reported. Only a few skin lesions have been reported to be induced by levothyroxine as consequences of anaphylactic reactions, including pruritic rashes, eczematiform skin eruptions, and lichenoid eruptions.^{3–5} Cutaneous lichenoid or lichen-planus-like eruptions may be induced by ingestion, contact or inhalation of a variety of drugs and chemicals. It is similar to lichen planus clinically and pathologically, with purple-red papules, obvious scales and eczematous change. The lesions are extensive, invading both trunk and limbs.⁶ There are many types of medications that cause lichenoid drug eruptions, with antipyretic analgesics and cardiovascular drugs being the most common.⁷ Delayed-type hypersensitivity is considered to mediate the reaction.

In the present case report, a lichenoid drug eruption was found to be an adverse skin reaction of levothyroxine. To the best of our knowledge, this is the first report of such a reaction caused by a conventional dose of levothyroxine; there has been a report that subacute lichenoid eruption due to L-thyroxine overdose.³

1.1 | Case presentation

A 47-year-old man with a history of hypothyroidism presented to the emergency department with complaints of multiple scaly, erythematous plaques over the extensor aspect of limbs, back, scalp, and neck for a 2-month duration. His lesions were non-painful, but itchy. On reviewing his drug history, it was found that he had been received thyroid hormone substitutive therapy with levothyroxine 50 µg daily for more than 2 months. Four months prior, a similar lesion occurred after ingesting oral levothyroxine.

Cutaneous examination revealed multiple scaly, erythematous plaques on the scalp (Figure 1A, B). There were generalized, confluent, scaly, purplish erythematous plaques all over the body (Figure 1C, D). A biopsy obtained from his back revealed epidermal hyperkeratosis accompanied by focal keratosis, acanthotic cell layer thickening, liquefaction degeneration of basal cells, a few dyskeratotic cells in spinous layer, zonal dense lymphocytes, and few eosinophils in the superficial dermis (Figure 2). These findings are actually consistent with a diagnosis of lichenoid drug eruption. We then used the Naranjo adverse drug reaction

(ADR) probability scale⁸ to assess the likelihood of lichenoid eruption being an ADR to levothyroxine, and attained a total score of 7, which suggests a ‘probable ADR’.

1.2 | Progression

At 2 months after withdrawal of the levothyroxine, the skin lesions regressed without any treatment.

2 | DISCUSSION AND REVIEW

The most commonly seen adverse reactions of levothyroxine are symptoms of hyperthyroidism due to overtreatment, including arrhythmias, dyspnea, and muscle weakness. Some less often reported special adverse reactions are shown in Table 1. In cases of adverse skin reactions, patch tests were all positive, suggesting the involvement of delayed type hypersensitivity (DTH).³⁻⁵

As a biological substance, levothyroxine cannot be recognized by the immune system as antigen. Nevertheless, lymphocytes of patients who had taken levothyroxine were indeed sensitized to the drug.¹⁶ Similarly, other biological medications (insulin and heparin) are able to induce hypersensitivity.¹⁷⁻¹⁸ Hence, the following hypotheses are proposed: (1) levothyroxine serves as a hapten and combines with carrier protein or adjuvants to become an antigen that recognized by antigen-presenting cells; (2) the additives or excipients of tablets causes the hypersensitivity rather than drug ingredient; (3) different brands of preparations have differences in terms sensitization; or (4) potential drug-induced immunologic responses of genetically susceptible individuals may mediate an autoimmune mechanism.

In the case of lichenoid drug eruption, cessation of the offending drug remains the mainstay treatment. Most authors believe that mild cases can be managed with topical steroids and systemic anti-histamines. In severe cases, administration of systemic corticosteroids is often required. In our case, the eruption resolves after discontinuation of levothyroxine.

3 | CONCLUSION

This case report presents a rare adverse effect of levothyroxine. Nevertheless, the detailed immunological and molecular mechanisms remain unknown, and further clinical observation and research are need.

What is already known about this subject

To the best of our knowledge, routine doses levothyroxine have not previously been reported associated with lichenoid drug eruption.

What this study adds

The authors wish to emphasize that lichenoid drug eruption can occur with routine dosing of levothyroxine. It could be self-limiting after withdrawal of levothyroxine.

COMPETING INTERESTS

There are no competing interests to declare.

CONTRIBUTORS

Nianfang Hu and Yajing Long drafted the manuscript. Nianfang, Yan Xian and Long Li had managed the case and finelised the manuscript

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Table 1 Reported cases of adverse drug reactions of levothyroxine

Publication year	Sex/Age	Dose	Treatment dura
2019 ⁹	F/49	25µg~50µg	39 days

Publication year	Sex/Age	Dose	Treatment dura
2019 ¹⁰	F/34	50µg	10 days
2019 ¹¹	F/31	100µg	26 days
2017 ¹²	M/34	100µg	24 hours
2015 ¹³	F/54	25µg~50µg	6 months
2015 ⁵	F/65	50µg	20 days
2010 ⁴	F/41	100µg	Few days
2007 ¹⁴	M/63	25µg~50µg	2 months
2003 ³	F/10	100µg per day for 7 years and accidental overdosage with intake of 9,000µg	100µg per day f
1999 ¹⁵	F/13	50µg~150µg	27 days
1986 ¹⁶	F/63	5µg	4 months

F=Female, M=Male



