

Drug Rash Induced by Levothyroxine Tablets

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Dear Editor:

Synthetic thyroxine (T₄) is the treatment of choice for the correction of hypothyroidism. We recently encountered an interesting case of drug rash apparently induced by the levothyroxine (as "Synthyroid" tablet; Bukwang Pharmaceutical Co., LTD., Seoul, Korea) tablets he was taking.

[Editor's Note: Readers should be aware that "Synthyroid" tablets from Bukwang Pharmaceutical Co. are not the same as Synthroid[®] tablets produced by Abbott Laboratories, Abbott Park, IL. The two names sound similar but are different. According to Abbott's Director of Professional and Advocacy Relations, "Synthyroid" manufactured by Bukwang Pharmaceutical Co. is not Synthroid[®] manufactured by Abbott, and Synthroid[®] manufactured by Abbott does not contain tartrazine yellow No. 4 or red No. 3. —C.H. Emerson, Editor-in-Chief]

A 77-year-old man presented with left lower-leg cellulitis. He had a history of old pulmonary tuberculosis that was apparently cured, hypertension, diabetes mellitus, deep vein thrombosis of the left lower leg, and old cerebral infarction. In addition, the patient had a history of drug rash caused by the antibiotic cefazolin. Therefore, the antibiotics cefoperazone plus sulbactam (Cefobactam, Hanmi Pharmaceutical Co., Seoul, Korea) and teicoplanin (Targocid, Sanofi Aventis, Seoul, Korea) were intravenously administered. After 2 weeks, the cellulitis improved, but general weakness, cold intolerance, and myxedema in both legs persisted. To address these persistent problems, thyroid function was tested. Laboratory examination yielded the following results: free T₄, 0.57 ng/dL (reference range [RR] 0.8–1.54); triiodothyronine (T₃), 0.74 ng/dL (RR 0.6–1.6); thyrotropin (TSH), 65.6 μ IU/mL (RR 0.35–5.5); thyrotropin-binding inhibiting immunoglobulin (TBII), 8% (RR 0–15%); and antimicrobial antibodies, 15.82 IU/mL (RR 0–34). Thus, hypothyroidism was diagnosed. Sonography of the thyroid gland showed mild atrophy of both lobes of the thyroid gland with multiple adenomatous goiter, a characteristic of chronic thyroiditis. We prescribed 0.05 mg levothyroxine in the form of "Synthyroid" (Bukwang Pharm.) for the correction of hypothyroidism. One day later, a generalized maculopapular rash began to develop and spread (see Supplementary Data, available online at www.liebertpub.com/thy). Given the patient's history of allergy to antibiotics, we discontinued antibiotic treatment and administered antihistamines (4 mg intravenous chlorpheniramine maleate for 6 hours, 60 mg oral hydroxyzine hydrochloride, 180 mg oral fexofenadine hydrochloride, and 5 mg levocetirizine hydrochloride). However, despite the discontinuation of antibiotics and the administration of antihistamines, the generalized skin rash was aggra-

vated during the 5 days of levothyroxine treatment. Therefore, levothyroxine treatment was discontinued, and 30 mg oral prednisolone was administered for 10 days; this resulted in the improvement of the skin lesions. We performed extensive skin tests for a wide variety of substances, including a ground preparation of "Synthyroid" (Bukwang Pharm.) (0.05, 0.1, and 0.15 mg) and 0.05 mg Comthyroid (Bukwang Pharm.), which did not yield definitive results. Therefore, we performed an oral-drug provocation test with 0.05 mg "Synthyroid" (Bukwang Pharm.) dissolved in 100 mL of drinking water. Provocation with 1% and 2% of the drug preparation on the first and second day, respectively, did not elicit any response. However, provocation with 10% of the drug preparation (0.005 mg) for 3 hours elicited a generalized maculopapular skin rash. We suspected a reaction to the dyes used in "Synthyroid" (Bukwang Pharm.)—tartrazine yellow No. 4 and red No. 3—and changed the medication to Comthyroid, which does not contain these dyes. Comthyroid treatment did not cause the rash to reappear. After 1 month of Comthyroid treatment, hyponatremia, general weakness, and thyroid function improved (free T₄ 0.86 ng/dL; T₃ 0.98 ng/dL; and TSH, 5 μ IU/mL).

Dyes are an important ingredient in processed foods, drugs, and cosmetics. The widespread use of such dyes has been accepted. However, dyes have often been reported to cause allergic reactions (1). In this case, the azo-dyes tartrazine yellow No. 4 and red No. 3 in the "Synthyroid" tablet (Bukwang Pharm.) were implicated in the allergic reaction.

In conclusion, certain levothyroxine tablets—and not levothyroxine *per se*—can rarely induce an allergic reaction in susceptible patients. It is likely that other brands of levothyroxine that contain certain dyes have the same potential to cause allergic reactions. Therefore, clinicians should be alert to the possibility of allergic reactions associated with the use of levothyroxine tablets containing dyes.

Reference

1. Desmond RE, Trautlein JJ 1981 Tartrazine (FD & C yellow #5) anaphylaxis: a case report. *Ann Allergy* 46:81–82.

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