

CASE REPORT

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Soy isoflavones inducing overt hypothyroidism in a patient with chronic lymphocytic thyroiditis: a case report

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Abstract

Background: Many people have thyroid conditions that make them susceptible to hypothyroidism. If the foods they eat may interfere with the production of thyroid hormone, which can lead to development of serious hypothyroidism. The danger of health drinks should always be noted.

Case presentation: A 72-year-old Japanese woman was previously diagnosed with chronic lymphocytic thyroiditis caused by a goiter and had an elevated thyroid-stimulating hormone level (6.56 μ U/ml), a high anti-thyroid peroxidase antibody level (>600 IU/ml), and a high antithyroglobulin level (> 4000 IU/ml) but normal levels of free triiodothyronine (3.08 pg/ml) and thyroxine (1.18 ng/ml). She presented to our hospital with sudden-onset general malaise, edema, and hoarseness with an elevated thyroid-stimulating hormone (373.3 μ U/ml) level and very low triiodothyronine (< 0.26 pg/ml) and thyroxine (0.10 ng/ml) levels. It was determined that for 6 months she had been consuming a processed, solved health drink ("barley young leaf") in amounts of 9 g/day, which included soybean and kale powder extract. Hypothyroidism might be affected by ingredients of health drinks. She discontinued consumption of the health drink immediately and began taking 12.5 μ g of levothyroxine. The amount of levothyroxine was gradually increased every 3 days up to 100 μ g. At day 61, her thyroid-stimulating hormone level had decreased (6.12 μ U/ml), her free triiodothyronine (2.69 pg/ml) and thyroxine (1.56 ng/ml) levels had increased, and her general condition was improved. Among risky foods lowering thyroid function, some experimental studies have revealed that isoflavones reduce thyroid function. Therefore, we measured the presence of isoflavones in the patient's frozen serum with thin-layer chromatography. After she discontinued consumption of the health drink, two components quickly disappeared, and the other three components gradually decreased. On the basis of developing solvent composition and a positive ferric chloride reaction in thin-layer chromatography experiment, the five ingredients that disappeared or decreased were highly suspected to be soy isoflavones.

Conclusions: This case emphasizes that consuming health drinks that include soy isoflavone powder extracts can lead to severe hypothyroidism.

Keywords: Isoflavones, Soybean, Barley young leaf, kale, Hypothyroidism, Chronic lymphocytic thyroiditis, Thin-layer chromatography

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Background

Many people have thyroid conditions that make them susceptible to hypothyroidism. For example, 10% of a disease-free population was reported to have positive results for anti-thyroid peroxidase antibodies (TPOAb) or antithyroglobulin (anti-Tg) [1], indicating that many patients have potentially chronic lymphocytic thyroiditis. However, there are many exogenous foods influencing the thyroid. If the foods interfere with the production of thyroid hormone, they can cause serious hypothyroidism.

We report a case of a patient with severe hypothyroidism induced by consuming a health drink. To the best of our knowledge, there are almost no other reports of patients with severe hypothyroidism induced by isoflavone. The components of the substances suspected to be isoflavones disappeared or decreased along with the clinical impairment of our

patient. To the best of our knowledge, this is the first report of the presence of isoflavone in the serum of a patient with severe hypothyroidism.

Case presentation

A 72-year-old Japanese woman had been followed because of chronic lymphocytic thyroiditis caused by a goiter. She had an elevated thyroid-stimulating hormone (TSH) level (6.56 μ IU/ml), a high TPOAb level (> 600 IU/ml), and a high anti-Tg level (> 4000 IU/ml) but normal levels of free triiodothyronine (T3; 3.08 pg/ml) and thyroxine (T4; 1.18 ng/ml). Her past medical history included only hypertension. She did not have any fever or neck pain suggestive of subacute or painless thyroiditis during recent months, and she had not taken any medication that would reduce thyroid function. Her social, family, and environmental histories were also unrevealing.

Table 1 Patient's laboratory findings on admission

	Values	Normal ranges	Blood chemistry	Values	Normal ranges
Blood cell counts					
WBC, n/μ l	57×10^2	$40\text{--}90 \times 10^2$	TP, g/dl	8.3	6.7–8.3
RBC, n/μ l	389×10^4	$380\text{--}480 \times 10^4$	Alb, g/dl	4.0	3.9–4.9
Hb, g/dl	11.3	12.0–15.2	BUN, mg/dl	13.2	8.0–22.0
Hct, %	36.0	35–48	Cr, mg/dl	1.0	0.4–0.7
Plt, n/μ l	13.1×10^4	$14\text{--}34 \times 10^4$	UA, mg/dl	4.9	3.0–5.5
Serological tests					
Fe, μ g/dl	58	43–172	Na ⁺ , mEq/L	141	135–147
UIBC, μ g/dl	213	137–325	K ⁺ , mEq/L	3.5	3.5–5.0
TIBC, μ g/dl	271	251–398	Cl ⁻ , mEq/L	102	98–108
Ferritin, ng/ml	72.8	5–157	Ca ²⁺ , mg/dl	9.2	8.8–10.2
IgG, mg/dl	2231	1156	Pi, mg/dl	3.2	2.5–4.5
IgA, mg/dl	397	103	AST, U/L	41	13–33
IgM, mg/dl	128	125	ALT, U/L	28	6–27
NT-proBNP, pg/ml	49	< 125	γ -GTP, U/L	31	10–47
Urinalysis					
Protein	–	–	ALP, U/L	208	115–359
Occult blood test	–	–	LDH, U/L	330	119–229
Fecal occult blood test					
	–	–	T-Bil, mg/dl	0.6	0.2–1.2
			CPK, U/L	567	45–163
			T-cho, mg/dl	310	130–220
			TG, mg/dl	233	30–150
			HDL-cho, mg/dl	54	41.5–67.3
			LDL-cho, mg/dl	187	70–139
			Glu, mg/dl	85	70–110
			CRP, mg/dl	0.15	< 0.30

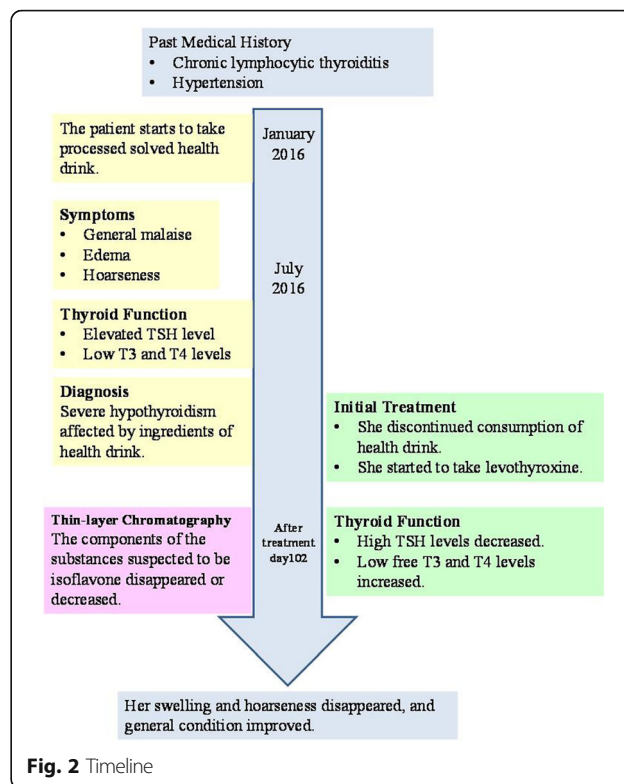
Abbreviations: Alb Albumin, ALP Alkaline phosphatase, ALT Alanine transaminase, AST Aspartate transaminase, BUN Blood urea nitrogen, Ca²⁺ Calcium, Cl⁻ Chloride, CPK Creatine phosphokinase, Cr Creatinine, CRP C-reactive protein, Fe Iron, γ -GTP γ -Glutamyltransferase, Glu Glucose, Hb Hemoglobin, Hct Hematocrit, HDL-cho High-density lipoprotein cholesterol, IgA Immunoglobulin A, IgG Immunoglobulin G, IgM Immunoglobulin M, K⁺ Potassium, LDH Lactate dehydrogenase, LDL-cho Low-density lipoprotein cholesterol, Na⁺ Sodium, NT-proBNP N-terminal pro-brain natriuretic peptide, Pi Inorganic phosphate, Plt Blood platelets, RBC Red blood cells, T-Bil Total bilirubin, T-cho Total cholesterol, TG Triglyceride, TIBC Total iron-binding capacity, TP Total protein, TSAT Transferrin saturation, UA Uric acid, UIBC Unsaturated iron-binding capacity, WBC White blood cell

The patient had been taking a processed, solved health drink (“barley young leaf”) in amounts of 9 g/day, which included soybean and kale powder extract, for 6 months. She had gradually developed general malaise, edema, and hoarseness. She presented to our hospital with sudden-onset elevated TSH (373.3 μ IU/ml) level and very low T3 (< 0.26 pg/ml) and T4 (0.10 ng/ml) levels. Her levels of total cholesterol, triglyceride, lactate dehydrogenase, aspartate transaminase, creatine phosphokinase, and immunoglobulin G were increased. These laboratory findings are shown in Table 1. Her goiter was swollen with mild hardness; her blood pressure at admission was 123/77 mmHg; her body temperature was 36.0 °C; and her pulse rate was 55 beats/minute. Computed tomography (Fig. 1) and thyroid ultrasound revealed bilateral thyroid enlargement. In addition, her uptake rate of 99m Tc-pertechnetate was reduced. On the basis of these findings, we diagnosed severe hypothyroidism affected by ingredients of the health drink. She discontinued consumption of the health drink immediately and began taking 12.5 μ g of levothyroxine. The amount of levothyroxine was gradually increased every 3 days up to 100 μ g. After oral administration of levothyroxine, her high TSH levels decreased gradually, and her low free T3 and T4 levels increased. Her swelling and hoarseness disappeared, and her general condition improved. Her free T3 and T4 levels did not decrease in the follow-up period of the subsequent 6 months. The time line of this patient’s clinical course is shown in Fig. 2. Her TSH, free T3, and T4 levels are shown in Table 2.

There are many risky foods lowering thyroid function, such as soybean and cruciferous vegetables, especially in a patient with chronic lymphocytic thyroiditis. Among these foods, some experimental



Fig. 1 Computed tomographic scan showing thyroid enlargement (arrowheads)



studies have shown that isoflavone reduces thyroid function [2, 3]. It was suspected that isoflavones might be the reason for our patient’s hypothyroidism. Therefore, we measured the presence of isoflavone in the patient’s frozen serum at 5 points from before admission to day 102 for further investigation. A blood sample was pretreated as described previously [4]. The sample was analyzed with thin-layer chromatography on precoated silica gel 60 F₂₅₄ or RP-18 WF₂₅₄ plates (Merck Millipore Corporation, Darmstadt, Germany), with detection achieved by spraying with iron(III) chloride solution. After she discontinued consuming the health drink, two components quickly disappeared, and the other three components gradually decreased (Fig. 3). On the basis of developing solvent composition and a positive ferric chloride reaction in thin-layer chromatography experiment, the five ingredients that disappeared or decreased were highly suspected to be soy isoflavones.

Discussion

Isoflavone, one of the isoflavonoids, is associated with breast cancer, prostate cancer, cerebral infarction, and myocardial infarction [5–7]. Moreover, some researchers have reported that soy isoflavone might reduce thyroid function by suppressing thyroid peroxidase [2, 3]. In our patient, the components of

Table 2 Patient's clinical course based on laboratory findings after discharge

	Before treatment	Day 11	Day 33	Day 61	Day 102	Normal range
TSH, μ U/ml	373.7	341.3	40.66	6.12	11.68	0.50–5.00
ft3, pg/ml	< 0.26	0.55	2.47	2.69	2.58	2.30–4.00
ft4, ng/ml	0.1	0.28	1.41	1.56	1.45	0.90–1.70

Abbreviations: ft3 Free triiodothyronine, ft4 Thyroxine, TSH Thyroid-stimulating hormone

the substances suspected to be isoflavones had disappeared or decreased along with her clinical impairment. To the best of our knowledge, this is the first case report in which the presence of isoflavone has been examined in the serum of a patient with severe hypothyroidism. This point is unique; to the best of our knowledge, there have been almost no other reports in which the presence of isoflavone has been examined in patient serum. The other following two mechanisms of hypothyroidism by soybean are considered: (1) An alcohol-soluble component in soybean inhibits iodide uptake [8], and (2) phytic acid salt in soybean chelates the essential minerals, especially zinc, for thyroid hormone production [9, 10]. Our patient presented with severe hypothyroidism after 6 months of regular consumption of a health drink. Because the thyroid contains several months' storage of thyroid hormone [11], overt hypothyroidism might present late. It is necessary to investigate further the detailed mechanisms of hypothyroidism caused by soy isoflavones.

Conclusions

This case emphasizes that consuming health drinks that include soy isoflavone powder extract can lead to severe hypothyroidism.

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Availability of data and materials

All data generated or analyzed for this report are included in this published article.

Authors' contributions

YN, IO, MF, and MI conceived of and designed the laboratory measurements. YN, IO, MF, and MI analyzed the data. YN wrote the first draft of the manuscript. IO critically revised the manuscript. YG, MT, TO, NS, YK, and HG jointly developed the structure and arguments for the paper. IO and YK made critical revisions and approved the final version of the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

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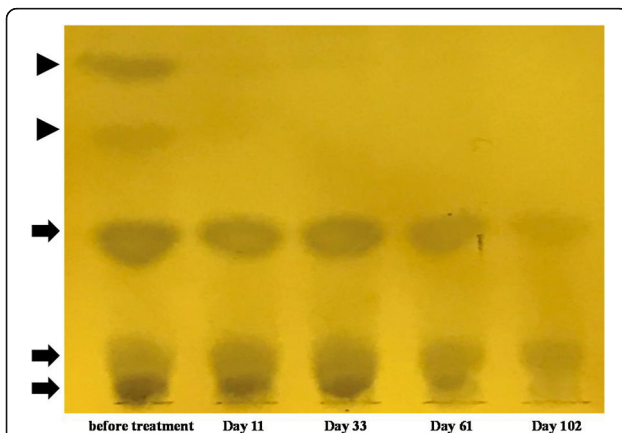


Fig. 3 Results of the thin-layer chromatography. After discontinuing health drink, two components (arrow heads) quickly disappeared and the other three components (arrows) gradually decreased. From the composition of the developing solvent and the positive findings of ferric chloride, these ingredients were speculated highly likely for soy isoflavone

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