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Basedow Disease that Remained Asymptomatic with Iodine Gargle: A Case Report

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Abstract

According to past studies, excessive iodine intake affects thyroid function in a variety of ways. We encountered a female pediatric patient in whom hyperthyroidism symptoms may have been inhibited by daily gargling with iodine solution. This report describes the course of treatment with discussion of the relevant literature.

Keywords: Iodine; Gargle; Urinary iodine; Excessive iodine intake; Hyperthyroidism

Introduction

Thyroid hormones are synthesized from iodine. Adequate iodine intake helps maintain normal levels of thyroid hormones [1-4]. When iodine is lacking, the thyroid gland is stimulated by thyroid-stimulating hormone (TSH), in response to decreased synthesis of thyroid hormones. The thyroid gland then accumulates iodine and enlarges, thereby leading to colloid goiter development. Severe iodine deficiency induces hypothyroidism. In contrast, excessive iodine inhibits iodine organification in the thyroid, resulting in decreased thyroid hormone synthesis. This phenomenon is called the Wolff-Chaikoff effect [1,2] and does not generally last long because of the subsequent adaptation (escape) phenomenon, which prevents hypothyroidism [2,3]. Excessive iodine without inhibition of iodine organification will result in hyperthyroidism [2-4]. High iodine intake will also induce hyperthyroidism in iodine-deficient areas. This so-called Jod-Basedow effect has classically been reported as a type of hyperthyroidism related to iodine intake [5,6].

Iodine intake tends to be excessive in Japanese people because of the tradition of consuming iodine-rich seaweed products and Japan's geographical location surrounded by iodine-abundant ocean waters [7]. Frequent use of iodine gargle on top of these factors may raise susceptibility to iodine excess.

We incidentally identified thyroid dysfunction in a girl who had been using iodine gargle for several years. Hyperthyroidism (Basedow disease) then manifested clinically after she discontinued gargling. We report this case with a discussion of the relevant literature.

Case Presentation

A 7-year-old female.

Chief complaint: vomiting, diarrhea, malaise.

Current illness: Vomiting and diarrhea started the day prior to admission. The patient was brought to our clinic because she was unable to drink water and was producing very little urine. She was admitted to receive treatment for dehydration associated with gastroenteritis.

Past illness: N/A.

Family history: N/A.

Current findings and symptoms: blood pressure, 109/53; heart rate, 110bpm; height, 114cm; weight, 16.7kg; facial pallor; slight ocular depression; normal oral condition; no lymphadenopathy; no thyroid enlargement; normal respiratory sounds; systolic heart murmur, Levine grade II to III/VI; no hepatosplenomegaly; decreased bowel sounds; soft abdominal wall; no rash.

Laboratory tests: Table 1.

Clinical course (Figure 1): Fluid replacement was administered to correct the dehydration. We performed echocardiography to assess the systolic heart murmur, and her thyroid function

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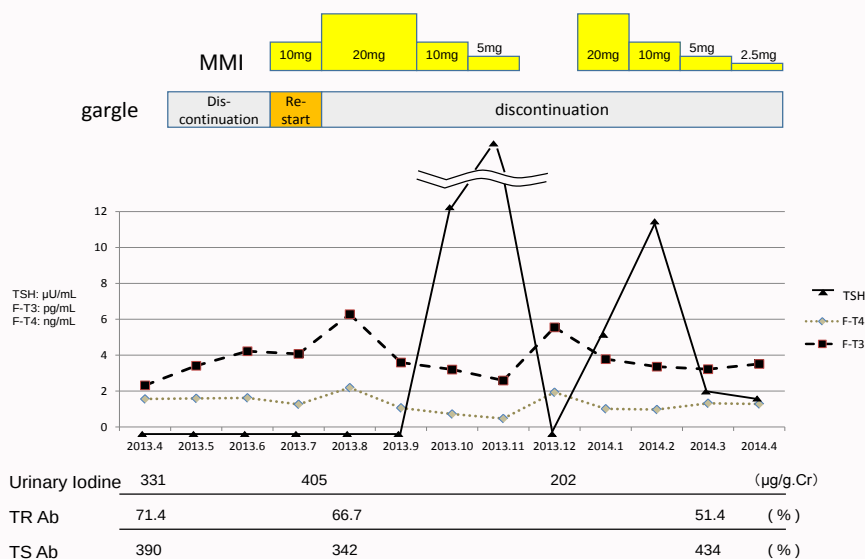


Figure: Clinical course.

was tested. Echocardiography revealed no apparent abnormalities. The heart murmur gradually diminished and then disappeared with correction of the dehydration. The thyroid function testing showed abnormally low TSH, despite normal F-T4 and F-T3 levels. A thorough interview revealed that the patient had been using Iodine Gargle Solution[®] (Lugol's solution) daily after coming home and before going to bed since she was 2 years old. The patient discontinued gargling, and F-T4 and F-T3 gradually increased. Basedow disease was diagnosed based on elevated thyroid stimulating and TSH receptor antibodies, as well as being negative for thyroglobulin antibody. At first Lugol's solution was used concomitantly with oral MMI 10mg, but the hyperthyroidism revealed by laboratory tests did not improve. The signs and symptoms of hyperthyroidism disappeared after discontinuation of the gargle and increasing the MMI dose to 20 mg. We then gradually tapered the MMI. The patient has since maintained euthyroid status.

Discussion

Excessive iodine intake strongly affects thyroid function. Iodine excess inhibits iodine organification in the thyroid gland and decreases thyroid hormone synthesis. However, the adaptation (escape) phenomenon subsequently occurs to prevent hypothyroidism. Careful monitoring is essential for patients with potential Hashimoto's thyroiditis, pregnant women, and infants because hypothyroidism associated with iodine excess is relatively common. On the other hand, iodine excess with uninhibited iodine organification leads to hyperthyroidism [2,4].

How much iodine is consumed by people in Japan, one of the areas having among the highest iodine intakes in the world? The Ministry of Health, Labour and Welfare (MHLW) defines dietary reference intakes (DRIs) for Japanese people every 5 years. According to the DRIs for 2015 and available on the MHLW website, the recommended iodine intake for adults is 130 $\mu\text{g/day}$, with a maximum of 3mg/day. For children under 7 years of age, the recommended iodine intake is 50 to 75 $\mu\text{g/day}$, with a maximum in the range of 250 to 500 $\mu\text{g/day}$. Our present patient had been gargling with Lugol's solution, which contains 7.8mg of iodine per drop, at least 5 times a day. Had the patient put 5 drops in a cup of water to gargle, her daily iodine intake

Table 1:

	⁽¹⁾ 2013-14	⁽²⁾ 2013-15	⁽³⁾ 2013-19	
WBC	6220	6290		/ μL
RBC	445	446		104/ μL
Hb	11.9	13		g/dl
Ht	36.1	38.6		%
Plt	20.1	23.4		104/ μL
AST	34	23		IU/L
ALT	44	11		IU/L
LDH	182	221		IU/L
TC	139	188		mg/dl
CPK	32	-		IU/L
BUN	13	10		mg/dl
Cr	0.23	0.41		mg/dl
TSH	<0.005	<0.005	0.085	$\mu\text{U/ml}$ (0.35-4.94)*
F-T3	2.32	4.22	3.59	pg/ml (1.71-3.71)*
F-T4	1.56	1.62	1.06	ng/dl (0.7-1.48)*
TRAb	71.4	-	66.7	% (≤ 15)*
TSAbs	360	-	342	% (≤ 180)*
Anti TPO antibody	20	-		IU/ml (<0.3)*
Anti thyroglobulin antibody	11	-		IU/ml (<0.3)*
Urinary Iodine /g.Cr	331			$\mu\text{g/g.Cr}$

(¹) at the first visit; (²) after discontinuation of gargling; (³) after administration of MMI. (*) standard value.

would have been 195mg. Not all of the iodine in the gargle solution is absorbed systemically, however. Oral absorption varies among substances. Iodine intake can be estimated by measuring urinary iodine. According to the World Health Organization's reference standard for urinary iodine in children age 6 years and older [8], the risk of thyroid disease should be of concern at $\geq 300\mu\text{g/g}$ of creatinine (Cr). Urinary iodine in Japanese children was reported to vary greatly among study populations, and no reference standard has yet been defined for children. However, urinary iodine level above 300 $\mu\text{g/g Cr}$

is also considered to be high in Japan [7]. In our present patient, two tests of early-morning urinary iodine yielded high values: 331 and 405 $\mu\text{g/gCr}$. After the patient discontinued gargling, urinary iodine decreased to $<250\mu\text{g/g Cr}$. Given that her diet and habitual gargling had been stable, she had clearly been ingesting an excess of iodine. Her urinary iodine had been elevated for at least 5 years. Since daily urine output correlates strongly with the iodine/Cr ratio in early-morning urine [9], we evaluated this patient using early-morning urine.

Was the hyperthyroidism in this patient caused by excessive iodine intake? Excessive iodine intake induces hyperthyroidism in iodine-deficient areas [2-6], while inducing hypothyroidism in iodine-sufficient areas [2-4]. If the autoregulation mechanism inhibiting iodine organification is absent, however, the production of thyroid hormones with iodine will continue. Hyperthyroidism may occur if iodine production continues despite the inhibitory action of TSH [2]. In such cases, thyroid function may normalize if excessive iodine intake is stopped. However, excess thyroid hormones accumulated in the thyroid gland may suddenly all be released at one time [2,10,11]. According to Galofre and colleagues, excessive iodine may induce autoimmune thyroid disease via an unknown mechanism [4]. Our patient first had low TSH and a normal thyroid hormone level. After discontinuing the iodine gargle, her TSH was unchanged but thyroid hormone levels remained abnormally elevated. These levels remained abnormally high even after resumption of gargling. Since the patient was antithyroid autoantibody positive, excessive iodine intake may have been coincidental with the onset of hyperthyroidism inhibiting iodine organification, thereby decreasing thyroid hormone synthesis. Such a mechanism could explain the clinical course of this patient, in which hyperthyroidism manifested after the discontinuation of excessive iodine intake and loss of the inhibition of thyroid hormone synthesis.

Conclusion

We incidentally identified thyroid dysfunction in a girl who had been using iodine gargle for several years. Iodine gargling may induce thyroid dysfunction and thus temporarily inhibit the progression of hyperthyroidism.

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