Autoimmune Thyroid Dysfunction: A Possible Effect of Mangosteen

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When an otherwise healthy 55-year-old woman developed hyperthyroidism, a popular dietary supplement was implicated.

Herbal, hormonal, food, and vitamin supplements are widely available "over-the-counter" in stores and online. These products are not regulated by the FDA, however, and their efficacy and systemic effects are largely unknown. One such popular derivative is mangosteen, a drink derived from the tropical fruit *Garcinia mangostana* (called the "queen of fruits"). This fruit is native to Southeast Asia where it long has been used as a topical anti-inflammatory agent in the treatment of skin infections and wounds. More recently, it is increasingly being used systemically in managing dysentery, cystitis, and gonorrhea.[1]

In this article, I report the case of a woman who was referred to our endocrinology clinic after routine laboratory tests revealed that she had a suppressed level of thyroid stimulating hormone (TSH), characteristic of Graves disease. The relationship of abnormal thyroid function tests to ingestion of mangosteen juice suggested a possible association of mangosteen with autoimmune thyroid dysfunction. This effect has not yet been reported in the medical literature.

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INITIAL EXAM

An otherwise healthy, postmenopausal, 55-year-old woman presented to our endocrinology clinic on March 17, 2009, for evaluation of suppressed level of TSH discovered by her primary care provider through routine laboratory and follow-up testing. She had no family history of thyroid or autoimmune disease.

She reported that she took no prescription medications, but occasionally took naproxen for osteoarthritic pain, and supplemented her diet with calcium and a multivitamin. Five months prior to her first abnormal thyroid function test in late October 2008, she had started consuming 8 ounces of mangosteen juice blend daily to improve her cholesterol and general well-being, per the advice of a family member. Follow-up testing by her primary care provider, prior to referral, continued to show a pattern of suppressed TSH level and elevated levels of the free thyroid hormones thyroxine (T4) and triiodothyronine (T3).

The patient denied experiencing any symptoms of hyperthyroidism, such as anxiety, excessive sweating, weight loss, frequent bowel movements, or heart palpitations, and she had a normal systemic examination. Physical examination of her thyroid revealed it to be firm, nontender, and of a normal size and consistency. Following oral administration of 300 microcuries of iodine-123, however, the patient's uptake was 15.4% at 2 hours (normal, 3% to 8%) and 29.8% at 6 hours (normal, 3% to 17%), supporting a diagnosis of hyperthyroidism, possibly due to Graves disease.

TREATMENT COURSE

The patient's absence of symptoms and history of normal thyroid function prior to starting daily mangosteen ingestion suggested a possible association of her thyroid dysfunction with this ingredient. She was advised to stop taking the drink, and the thyroid function tests that followed showed immediate improvement. Free T4 and free T3 levels normalized within 6 weeks and TSH level normalized 6 months later (Table 1). The thyroid antibodies—including the TSH receptor antibodies, which had been elevated in March 2009—normalized within 3 months of mangosteen cessation (Table 2).

She continued to be asymptomatic and had a normal TSH level 1 year later. Her antithyroid peroxidase antibodies had improved initially and eventually normalized as well.

ABOUT THE CONDITION

Graves disease, the most common cause of hyperthyroidism, is an autoimmune disease in which thyroid-

Table 1. Patient's thyroid function tests from November 2007 through March 2010

Date	TSH (mIU/mL) (reference, 0.48–3.94)	Free T4 (ng/dL) (reference, 0.61–1.12)	Free T3 (pg/mL) (reference, 2.5–3.9)
11/05/07 (routine evaluation prior to first suspicious test)	0.755	1.34 [0.65–1.75]	N/A
10/29/08 (first abnormal test)	< 0.01	N/A	N/A
1/09/09 (follow-up by primary care provider)	< 0.01	1.65	N/A
3/05/09 (follow-up by primary care provider)	< 0.01	1.64	5.44
3/17/09 (test ordered at first endocrinology clinic visit)	< 0.01	1.41	5.02
Follow-up tests ordered by endocrinologist after patient stopped Mangosteen on 3/18/09			
4/28/09	< 0.01	0.94	3.42
10/27/09	0.952	0.8	N/A
12/21/09	1.032	0.73	N/A
3/23/10	1.22	N/A	N/A

N/A = not available; T3 = triiodothyronine; T4 = thyroxine; TSH = thyroid stimulating hormone.

stimulating immunoglobulins bind to and activate thyrotropin receptors, causing the thyroid gland to enlarge and increase the synthesis of thyroid hormone. Other causes of hyperthyroidism include toxic nodule, multinodular goiter, subacute thyroiditis, silent (lymphocytic) thyroiditis, struma ovarii, and exogenous exposure to iodine (for example, radio contrast media, thyroxine, kelp, or other preparations containing iodine). In thyroiditis and conditions related to iodine exposure, the radioiodine uptake is suppressed, whereas, in Graves disease and nodular goiter, the radioiodine uptake is elevated. With excess iodine intake or exposure, serum thyroglobulin is suppressed, while in thyroiditis, Graves disease, and nodular goiter, the thyroglobulin levels rise, as was the case in this patient.

This patient's thyroid function tests suggested hyperthyroidism, possibly due to Graves disease, because, initially, thyroid receptor and peroxidase antibodies were present and radioactive iodine uptake was elevated. Thyroid receptor and peroxidase antibodies eventually normalized when the patient stopped drinking mangosteen. Because little was known about the juice, an association was inferred based on the temporal relationship between the start of consumption and the first abnormal laboratory results.

Many tropical plants have biological effects with potential therapeutic applications. Products derived from *G mangostana* are widely distributed throughout the world, including within the United States. Its pericarp is a rich source of prenylated xanthones, which are known to possess antioxidant, antitumoral, antiallergic, antibacterial, and antimycobacterial properties. The most studied of the xanthones are alpha-, beta-, and gamma-mangostins; garcinone E; 8-deoxygartanin; and gartanin.[2] These act mainly through the production and release of nitric oxide and prostaglandin E2, but also modestly affect the release of tumor necrosis factor and interleukin-4.[3,4] People with cancer are advised to exercise caution in consuming such

Table 2. Patient's thyroid antibody tests from March 5 through June 2009

Test (unit) (reference values)	3/05/09 (tests ordered before first endocrinology clinic visit)	3/17/09 (tests ordered at first endocrinology clinic visit)	4/28/09 (6 weeks after patient stopped mangosteen on 3/18/09)	June 2009 (3 months after stopping mangosteen)
TG (ng/mL) (reference, 0.5–55)	105	N/A	N/A	N/A
AntiTG (IU/mL) (reference, 0–40)	22	24	< 20	< 20
TPO (IU/mL) (reference, 10–34)	65	72	N/A	N/A
T3 uptake (%) (reference, 24–39)	41	N/A	N/A	N/A
TRAB (U/L) (reference, 0–1.0)	N/A	1.3	0.8	0.77
AntiTPO (IU/mL) (reference, 0–34)	N/A	N/A	85	65

AntiTG = antithyroglobulin antibody; AntiTPO = antithyroid peroxidase antibody; N/A = not available; T3 = triiodothyronine; TG = thyroglobulin; TPO = thyroid peroxidase antibody; TRAB = thyroid receptor antibody.

products because, potentially, they can interact with cancer treatments and affect blood sugar levels.[5] In 1 reported case, consumption of mangosteen juice caused lactic acidosis.[6]

Many Web sites include anecdotal reports of patients being able to decrease their thyroid medications through the use of mangosteen. These findings have not, however, been authenticated through clinical studies. Although mangosteen's effects on the thyroid have not been determined through scientific trials, the present case illustrates its possible association with autoimmune thyroid disease.

IN SUMMARY

This case suggests that, through unknown mechanisms, mangosteen ingestion may trigger autoimmune hyperthyroidism. Prospective, placebo-controlled, clinical trials would be required to establish such a correlation. Clinicians, therefore, should monitor patients who consume mangosteen.

The patient described in this report had evidence of hyperthyroidism in the absence of any commonly associated etiology, which prompted an inquiry into herbal products the patient may have been consuming. The patient recently had introduced the botanical product mangosteen into her diet. Mangosteen had not previously been reported to cause Graves disease. This case report highlights the importance of simply following up on patient evaluations and laboratory tests after suspect products are excluded from the diet in order to ensure normalization of functions. This strategy may avoid unnecessary treatment.

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