

A case of *H. pylori* infection presenting as refractory hypothyroidism

Pragya Gupta, Johns T. Johnson, Sudarsanababu Lalitha Soumya,
Kripa Elizabeth Cherian, Nitin Kapoor, Thomas Vizhalil Paul

Department of Endocrinology, Diabetes and Metabolism, Christian Medical College and Hospital, Vellore, Tamil Nadu, India

ABSTRACT

We present the case of a 45-year-old lady with long standing hypothyroidism who was euthyroid on replacement for many years, but stopped responding even to supraphysiological doses of LT₄ since the last five years. She complained of abdominal discomfort, bloating, and nausea. She did not have diarrhea or weight loss. Levothyroxine absorption test was done which was suggestive of malabsorption and she was started on triple therapy for *H. pylori* eradication after confirmation of diagnosis. After 10 days of treatment initiation, she developed symptoms of thyrotoxicosis with her supraphysiological dose of LT₄, which was then tapered to a lower dose. Euthyroid state was ultimately achieved with lower doses of LT₄ replacement.

Keywords: *H. pylori* infection, levothyroxine absorption test, refractory hypothyroidism

Introduction

Levothyroxine (LT₄) replacement is the treatment of choice for hypothyroidism and is usually required lifelong. The therapeutic efficacy of LT₄ is confounded by many factors, most of which interfere with its absorption. Identification and treatment of these causes may prevent repeated dose adjustments, repeated testing, and adverse effects associated with intermittent supraphysiological dose of LT₄. Hypothyroidism is a common endocrine dysfunction that is managed to a large extent by physicians involved in primary care and family medicine. It is easily treatable, as drug doses remain stable with monitoring of thyroid functions performed annually. Occasionally however, cases of refractory hypothyroidism may be encountered in clinical practice. While the common approach to management of these refractory cases would be an increase in drug dose,

there are rare situations where inadequate control might result from malabsorption of levothyroxine due to various causes.^[1] A mere escalation of the dose of levothyroxine may not be appropriate in such instances, and an underlying cause of potential malabsorption of drug should be actively sought, especially when the patient reports good compliance to the drug.

Case

A 45-year-old lady, known to have autoimmune hypothyroidism for 15 years, was referred by her primary care physician for recent onset of refractory hypothyroidism. For the initial 10 years, she had been euthyroid on replacement with weight-based doses of LT₄, but for the past five years her TSH remained elevated despite her receiving supraphysiological doses of LT₄ supplementation [Table 1]. At presentation, she was on 400 mcg of LT₄ (6.7 mcg/kg/day) since four months. She complained of easy fatigability and constipation. She also had intermittent palpitations. There was no history of weight gain or loss and menstrual cycles were regular. There was no history suggestive of malabsorptive disorders or other major

Address for correspondence: Dr. Kripa Elizabeth Cherian, Department of Endocrinology, Diabetes and Metabolism, Christian Medical College and Hospital, Vellore - 632004, Tamil Nadu, India.
E-mail: kripaec@gmail.com

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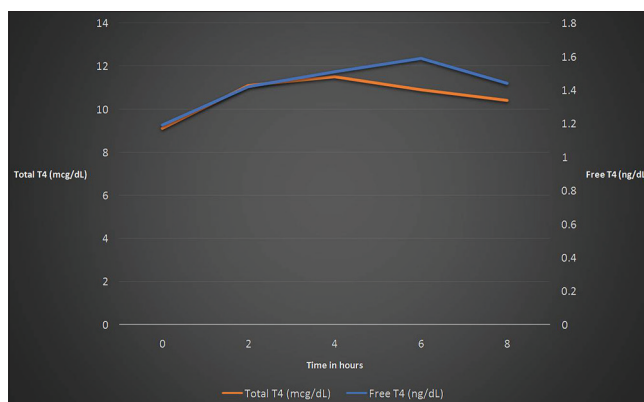
Table 1: Thyroid function tests and dose of LT4 before and after treatment of *H. pylori* infection

Timeline	Daily LT4 dose (mcg/day)	TSH (mIU/mL)	T4 (µg/dL)	FT4 (ng/dL)
Normal dose range	1.6-1.8 mcg/kg/day	0.3-4.2	4.5-12.0	0.8-2.0
Treatment and evaluation at hometown				
June 2018	175	60.8	NA	NA
April 2019	225	14.1	NA	NA
September 2019	300	18.2	NA	NA
November 2019	500	10.3	NA	NA
Further management at the author's centre				
January 2020	400	9.2		
On completion of <i>H. pylori</i> treatment	400	0.038	20.2	3.04
After 6 weeks of treatment completion	200	0.08	10.30	1.09

NA: Not available

co-morbidities. However, she had symptoms of gastritis in the form of nausea, heartburn, and bloating, but had never received treatment for the same. She denied missing her medication and intake of other drugs known to impair levothyroxine absorption. She was fairly compliant with LT4, which she admitted to taking on an empty stomach, one hour before breakfast. Her brother and sister also had hypothyroidism, which was well controlled on regular doses of levothyroxine. On examination, her weight was 60 kg, body mass index (BMI) was 28.2 kg/m², blood pressure was 130/70 mm of Hg, and pulse rate was 82 beats per min. Biochemical evaluation revealed elevated TSH [Table 1]. Her symptoms were suggestive of fluctuating levels of circulating T4 (total thyroxine), which is seen mostly in cases of nonadherence. However, in view of symptoms of gastritis, we proceeded with levothyroxine absorption test to distinguish between malabsorption of drug and noncompliance to therapy. She was loaded with 1000 mcg of levothyroxine after an overnight fast of eight hours following which levels of T4 and fT4 (free thyroxine concentration) was monitored 2 hourly for 8 hours [Figure 1].

Levothyroxine absorption test showed suboptimal absorption (28.8%) suggestive of malabsorption. Upon ingestion, Levothyroxine is absorbed at the level of jejunum and ileum.^[2] Its absorption is influenced by many factors including gastric acidity, meals, caffeinated drinks, drugs, and malabsorptive disorders. Usually, 62–82% of the ingested LT4 is absorbed and maximum absorption is seen between the first and third hours.^[3] In view of her symptoms of gastritis, she underwent an upper gastro-intestinal endoscopy which confirmed the diagnosis of gastritis secondary to *H. pylori* infection. She was initiated on triple therapy for *H. pylori* eradication. She received 14 days of amoxicillin, clarithromycin, and pantoprazole. After completion of her treatment course, thyroid function tests (TFT) were repeated which was suggestive of thyrotoxicosis [Table 1]. She also complained of increased intensity of palpitations, tremors, and decreased sleep. Her levothyroxine dose was reduced to 200 mcg/day and she was advised to review after a month. On follow up, the thyrotoxic symptoms had resolved, although her TSH was still suppressed. The levothyroxine dose was further reduced to 150 mcg and she was asked to review after a month.

**Figure 1: Levothyroxine absorption test**

Discussion

Refractory hypothyroidism is a commonly encountered problem in the peripheral setting among patients presenting to primary care physicians. In most circumstances, the dose of levothyroxine is gradually increased to ensure euthyroid status in all of such patients. Often, compliance to medication and continued adherence to therapy is not inquired of the patient. In patients with hypothyroidism refractory to a levothyroxine dosage greater than 1.9 mcg/kg/day, further increment in the dose may not always be the most appropriate approach.^[4] In this situation after ensuring adequate adherence to therapy, factors interfering with drug absorption and/or increased drug metabolism should be sought.^[5] *H. Pylori* infection is a frequent cause of malabsorption which often goes undiagnosed and untreated.^[6] In patients with refractory hypothyroidism, unawareness of this condition may lead to repeated dose adjustments, unwarranted testing, unnecessary investigations, referral, and/or treatment failure. Also, prolonged exposure to supratherapeutic doses may result in adverse effects related to the bone and cardiovascular system. In patients with hypothyroidism, on high doses of replacement presenting with dyspeptic symptoms, testing for *H. pylori* should be considered. However, in peripheral and primary care settings where testing may not be feasible, empirical treatment of *H. pylori* infection, and the subsequent decrease in levothyroxine requirement may confirm the diagnosis.

Keypoints

- Hypothyroidism is commonly encountered in primary care settings. Most often, it is easily treatable, with the patient being on stable doses of levothyroxine. Thyroid function tests are usually monitored annually.
- The presence of *H. pylori* gastritis is an important cause for an inadequate response to levothyroxine therapy in hypothyroidism and should be sought for clinical practice when deemed relevant.
- The eradication of *H. pylori* in individuals on high doses of levothyroxine may result in thyrotoxicosis, and hence warrants close monitoring for the same.^[4]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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