INTRAMUSCULAR LEVOTHYROXINE AS OUTPATIENT MANAGEMENT OF REFRACTORY HYPOTHYROIDISM

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Introduction

Oral levothyroxine (LT4) supplementation is usually sufficient therapy for hypothyroidism. However, oral replacement may be ineffective in cases of poor intestinal absorption. In such cases, other formulations of LT4 replacement may be more effective in restoring euthyroidism.

We present a patient with refractory hypothyroidism who now requires intramuscular (IM) LT4 maintenance therapy as an outpatient.

Date	4/1/19	5/28/19	6/21/19*	7/8/19	12/16/19
TSH level (mcUnits/mL)	0.643	94.700	152.700	1.771	0.402

*Figure 1. TSH values for our patient prior to initiation of IV and IM levothyroxine with subsequent resolution after initiating therapy. *The day of hospital admission, showing hypothyroidism which subsequently no rmalized after initiation of IV LT4, followed by the transition to IM formulation of LT4 as an outpatient*

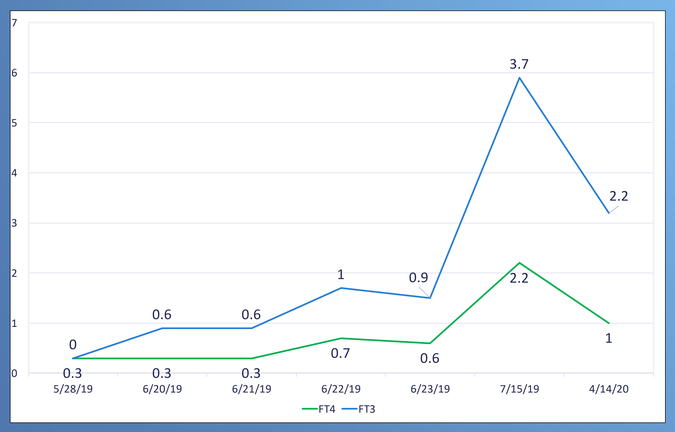

Figure 2. Free T3 and free T4 levels prior to initiation of IV and IM levothyroxine with achievement of normal levels after initiating IM therapy. The patient has maintained generally normal levels on a combination of oral and intramuscular levothyroxine during follow-up visits, including as recently as April 2020.

Case Description

A 60-year-old woman with Hashimoto's disease, on oral LT4 since being diagnosed at age nine, was admitted for evaluation of refractory hypothyroidism. Approximately two months earlier, she developed worsening symptoms of hypothyroidism (severe fatigue, 45 lb weight gain, hair loss). Evaluation revealed significantly elevated TSH (94.7 mcUnits/mL) and decreased free T4 levels (0.3 ng/dL). She reported strict medication adherence and adequate LT4 intake. There was initial concern for drug-related LT4 malabsorption, as she had recently started taking sucralfate. However, TSH levels continued rising after stopping sucralfate. Her generic LT4 dose was uptitrated without improvement. Other oral formulations, including trade name Synthroid and liquid LT4, were also ineffective. Evaluation for Celiac disease was negative. Upon admission to the hospital, TSH level was 152.7 mcUnits/mL. She was initially challenged with 300mcg PO LT4, with persistently low free T4/T3 levels. Repeat PO challenge yielded similar results. GI was consulted to further evaluate for malabsorption. Endoscopy revealed moderately severe gastritis. Tissue biopsies were negative for H.pylori or sprue. She then received two days of daily intravenous levothyroxine with improvement in free T4/T3 levels and clinical status before being discharged home. As an outpatient, she was transitioned to 200 micrograms of IM LT4 bi-weekly. Dosage and injection frequency were titrated over the next few months with eventual normalization of TSH and free T4/T3 levels (Fig. 1-2).

The patient continues to receive weekly injections of IM LT4 (which are being slowly tapered down) with reintroduction of PO LT4 to maintain a euthyroid state. Due to practical difficulties with adhering to the frequent injection schedule and high cost, the ultimate plan is to transition back to PO LT4 and stop the IM formulation.

Discussion

Patients who are unable to achieve euthyroidism with oral LT4 replacement should be evaluated for causes of malabsorption. These patients may need intravenous or intramuscular formulations of LT4.

This case highlights the importance of recognizing refractory hypothyroidism and initiating timely evaluation of causes of malabsorption, as well as initiation of parenteral hormone replacement and continuation on an outpatient basis. Our patient's presentation was particularly challenging, since a malabsorption cause was not identified. The case also raises important questions regarding the bioavailability of IM LT4, the financial burden of parenteral formulations, and inconvenience for the patient with scheduling frequent injections. There is also an absence of any guidelines on an effective transition plan from the IM to PO formulation.

References

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