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REFRACTORY HYPOTHYROIDISM POST-CHOLECYSTECTOMY SUCCESSFULLY TREATED WITH SOFTGEL CAPSULE THYROXINE

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INTRODUCTION
Refractory hypothyroidism has been increasingly identified globally and its management can be challenging. Primary hypothyroidism is considered refractory when there is persistent elevation of TSH despite escalating doses of levothyroxine >1.9 µg/kg/day. Physicians should rule out non-compliance and pursue further evaluation to identify aetiologies for increased dose requirements.

CASE
We present a case of a 44-year-old female with Hashimoto's thyroiditis well-replaced with levothyroxine 100 µg/day (1.6 µg/kg/day). After cholecystectomy, her TSH was persistently high despite increasing levothyroxine to 500 µg/day, good compliance and no concurrent drug interference. She developed progressive hypothyroid symptoms with elevated TSH levels >100 mIU/L. Thyroxine absorption test confirmed poor enteral absorption. Extensive evaluation failed to reveal any evidence of malabsorption where her esophagogastroduodenoscopy finding shows mild antral erosion. Further tests excluded H. pylori infection, coeliac disease and exocrine pancreatic insufficiency. She was hospitalized multiple times for severe symptomatic hypothyroidism and responded well with intravenous thyroxine. After extensive diagnostic measures, she was started on levothyroxine 300 µg/day in soft gel capsules. Her TSH and FT4 normalized following 8 weeks of treatment.

CONCLUSION
Various gastrointestinal disorders that lead to malabsorption or loss of intestinal secretions may result in higher requirements of levothyroxine. Our case highlights the malabsorption of oral levothyroxine in tablets after cholecystectomy. Hypothesized causes include intestinal malabsorption of levothyroxine due to reduction in bile salts after cholecystectomy and altered intestinal microbiota. An empirical switch to soft gel capsule formulation may resolve this treatment-refractory issue. This formulation has been shown to have the most consistent dissolution pattern, resulting in a more reliable bioavailability than the tablet form.

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INCREASED LEVOTHYROXINE REQUIREMENT IN A PATIENT WITH NEPHROTIC SYNDROME

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INTRODUCTION/BACKGROUND
In hypothyroid patients, there are no studies that exemplify the need for levothyroxine adjustment in patients with coexisting nephrotic syndrome.

CASE
This case report highlights the degree of levothyroxine adjustment that may be required.

A 36-year-old Malay male with post-radioioidine hypothyroidism presented in October 2022 with bilateral lower limb swelling, abdominal distention and a 10-kg weight gain over the preceding 3 months. He received RAI twice (October 2020 and February 2021) for relapsed Graves' disease. He had been on a levothyroxine replacement dose of 700 µg/week (1.12 µg/kg/day). Tests revealed low albumin (16 g/L), elevated urine protein:creatinine index (PCI) (341 mg/mmol), elevated TSH (148 mU/L), normal T4 (11 pmol/L) and significant hypercholesterolaemia. Following nephrology consultation and renal biopsy showing minimal change disease, the diagnosis of nephrotic syndrome was made. Nephrotic syndrome has been rarely reported in association with Graves' disease. Reports show membranous glomerulonephritis rather than minimal change disease. In nephrotic syndrome, there is increased permeability of the glomerular basement membrane to large molecules. Thyroxine replacement was deemed inadequate as a consequence of thyroid-binding globulin wasting. Levothyroxine dose was increased to 1150 mcg/week (1.93 µg/kg/day) initially. He had good clinical response to high-dose steroid, and this was gradually tapered over several months. At the time of publication (May 2023), his urine PCI improved to 68.47 mg/mmol. Prednisolone requirement had been reduced to 10 mg/day, along with levothyroxine dose at 850 µg/wk (1.4 µg/kg/day).

CONCLUSION
This case highlights the importance of recognising the increased levothyroxine requirement in patients with nephrotic syndrome. Although rare, the association between autoimmune thyroid disease and nephrotic syndrome should be recognised.