Cholestyramine for thyrotoxicosis?

This case demonstrates the value of cholestyramine when traditional first-line antithyroid drugs and radioactive iodine are not options.

CASE A 44-year-old Korean woman who was receiving pegylated interferon (IFN) and ribavirin for chronic hepatitis C infection came into our facility with complaints of gradual onset of fatigue, unintentional weight loss of 15 pounds within a month, palpitations, and heat intolerance. She said her symptoms had worsened a week earlier, after she’d undergone an abdominal computed tomography scan with intravenous contrast.

Her physical exam revealed a blood pressure of 90/60 mm Hg, heart rate of 120 beats per minute, body mass index (BMI) of 17 kg/m², and visibly symmetric thyroid enlargement without any nodules, tenderness, or bruits. Despite her low systolic reading, she was asymptomatic and not septic or in thyroid storm. Laboratory data showed pancytopenia with a white blood cell count of 700/mCL (absolute neutrophil count, 189), hemoglobin of 9.6 g/L, platelet count of 96,000 cell/mCL, elevated free thyroxine (T4) of 5.7 ng/dL (normal, 0.6-1.6 ng/dL), total triiodothyronine (T3) of 301 ng/dL (normal, 90-180 ng/dL), and suppressed thyroid-stimulating hormone (TSH) of 0.01 mcU/mL (normal, 0.27-4.20 mcU/mL). The thyroid peroxidase antibody level was elevated at 9420 u/mL (normal, <35 u/mL), with a normal level of thyroid-stimulating immunoglobulin. Neither of these latter tests was obtained before IFN treatment. The patient had no history of thyroid dysfunction.

We discontinued the patient’s pegylated IFN and ribavirin. Antithyroid medication and beta-blockade were contraindicated due to pancytopenia and hypotension, respectively. Given her recent iodine exposure from contrast media, radioactive iodine treatment would be ineffective. We started the patient on cholestyramine 4 g orally 3 times a day and she improved rapidly. Her thyroid function normalized after 2.5 weeks of treatment.

After 6 weeks, when her TSH increased to 13 mcU/mL, we discontinued cholestyramine. Two weeks later, her TSH was >50 mcU/mL and we started the patient on levothyroxine replacement.

Discussion
The association between IFN-alpha and thyroid disease was recognized as early as 1985. Between 5% and 10% of patients receiving IFN-alpha therapy may develop clinical thyroid disease, including painless thyroiditis, Hashimoto’s thyroiditis, and Graves’ disease, although a recent prospective study in Australia showed a thyroid disease prevalence of just 1% up to 6 months after treatment with IFN-alpha and ribavirin. The cause of our patient’s thyrotoxicosis. IFN-alpha therapy likely caused our patient’s thyrotoxicosis, but iodide-induced hyperthyroidism may occur after use of iodinated contrast media. Prompt treatment of thyrotoxicosis with beta-blockers, antithyroid drugs, or radioiodine is necessary to reduce morbidity and the risk of developing thyroid storm, a condition associated with significant mortality.
Cholestyramine, a bile salt sequestrant, has been used chiefly to lower cholesterol since the 1960s.6,7 However, studies also found that cholestyramine’s ionic exchange properties could decrease excessive thyroid hormone levels by enhancing hormone clearance from the enterohepatic circulation and thereby increase hormone fecal excretion.6,7 In one study, radioactive iodine was given to patients simultaneously receiving levothyroxine for thyroid hormone deficiency and cholestyramine for hyperlipidemia.6 Results included increased stool radioactivity, decreased urine radioactivity, and decreased thyroid uptake consistent with enhanced clearance of thyroid hormones.6 The study also showed that 50 mg of cholestyramine can bind about 3000 mcg of T4.6

**Cholestyramine as adjunctive therapy** has rapidly decreased thyroid hormone levels compared with standard therapy alone, maintaining its effect for about 4 weeks.2,5,8,9 Complete normalization of free T4 and free T3 levels and notable symptom improvement have occurred within one week of instituting cholestyramine therapy.5 The optimal dosage is 4 g cholestyramine orally, 2 to 4 times daily for 4 weeks.2,5,8,9 Primary adverse effects of cholestyramine are constipation and abdominal discomfort. In contrast to methimazole or propylthiouracil, which only treat conditions of excess thyroid hormone production, cholestyramine is effective for any condition with excessive thyroid hormone levels—eg, subacute thyroiditis, Jod-Baslow phenomenon, and factitious thyroid hormone disorder.

**Resolution.** In our patient, the clinical picture was consistent with an autoimmune form of thyrotoxicosis induced by IFN therapy and possibly exacerbated by iodine exposure. In the absence of a thyroid scan at the time of thyrotoxicosis, we cannot exclude destructive thyroiditis; in fact, the ensuing hypothyroidism strengthens this possibility. Nevertheless, we believe that the oral administration of cholestyramine as monotherapy contributed to the resolution of our patient’s thyrotoxic symptoms when first-line medications were contraindicated.

### References