Thyrotoxicosis induced by alpha interferon therapy for hepatitis C

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CASE REPORT

A man aged 41 years was referred in 1995 for investigation of longstanding gastrointestinal symptoms. He was found to have an alanine transferase activity of 244 iu/litre and to be hepatitis C positive, both by antibody testing and polymerase chain reaction. He was human immunodeficiency virus negative. He was later confirmed to have cirrhosis on liver biopsy and was started on interferon-alpha (IFN-α) 3 MU three times weekly. Past medical history included irritable bowel syndrome, appendicectomy and intussuception. His surgery may have been accompanied by blood transfusion. He drank moderately, occasionally smoked marijuana and had a past history of injection drug use. His wife was also known to be hepatitis C positive following multiple blood transfusions. He had a positive family history of thyroid disease. His thyroid function tests before starting IFN-α showed free thyroxine (T_4) 15.6 pmol/litre (normal range 9.6–26.5 pmol/litre) and thyroid-stimulating hormone (TSH) 0.2 mu/litre (normal range 0.6–4.8 mU/litre). Thyroid antibodies were not measured.

Two months after starting IFN-α he had a flare up of his irritable bowel, and a month later developed flu-like symptoms. This was followed by weight loss, palpitations and diarrhoea. Three months after commencement of IFN-α his free T_4 was 58.6 pmol/litre and TSH 0.1mU/litre, confirming thyrotoxicosis, and he had a weakly positive thyroperoxidase antibody. Interferon was discontinued but despite this his thyroid function tests worsened (free T_4 >126 pmol/litre and TSH <0.01mU/litre). He was therefore started on carbimazole, followed by propylthiouracil but developed arthalgia and rash on both treatments. He was subsequently treated with radioactive iodine and remained both clinically and biochemically euthyroid for 2 months after which time he became temporarily hypothyroid. He remained euthyroid having been off T_4 replacement for about 2 years. His latest free T_4 is 13 pmol/litre and TSH 14 mU/litre and he has since recommenced T_4 replacement. His chronic hepatitis C did not respond to a 3-month course of IFN-α.

INTRODUCTION

Various disorders of thyroid function are known to occur with interferon treatment, especially in patients with chronic hepatitis C. Although uncommon, they are by no means rare. This article reports a case of thyrotoxicosis caused by such a treatment and reviews the literature on thyroid dysfunction induced by interferon therapy.

DISCUSSION

Thyroid dysfunction is a recognized complication of interferon (IFN)-alpha therapy, especially when administered for chronic hepatitis C infection. Fentiman et al (1985) originally reported development of hypothyroidism in patients on IFN treatment. Preziati et al reported that after 12 months of IFN treatment, 20% of their viral hepatitis patients developed permanent hypothyroidism, and 8.6% became thyrotoxic (Preziati et al, 1995). Although underlying autoimmune thyroid disease predisposes patients to IFN-induced thyroid dysfunction, most affected patients become thyrotoxic or hypothyroid without pre-existing circulating thyroperoxidase antibody (Roti et al, 1996) and in the absence of other autoimmune diseases.

The exact mechanism of IFN-alpha induced thyroid dysfunction is unclear. Proposed theories include increase in MHC class I antigen expression in thyrocytes with suppression of expression of class II antigen (Roti et al, 1996), immunomodulatory effect inducing antibody production in susceptible patients (Imagawa et al, 1995) and de novo destructive changes in the intact thyroid gland (Amenomori et al, 1998).

IFN-alpha induced thyrotoxicosis in this patient may be the result of a silent or destructive thyroiditis with transiently positive thyroperoxidase antibody or indeed the result of the antibody inducing immunomodulatory behaviour of IFN-alpha in a susceptible individual. Thus, before starting treatment with IFN-alpha, thyroid function should be evaluated and regularly monitored during therapy. It might also be prudent to measure thyroid antibody status before starting interferon treatment.

Patients with thyroid antibodies and pre-existing thyroid dysfunction should be carefully monitored for the development of thyroid problems (Weissel et al, 1995). As increasing numbers of clinicians are involved in treating patients with this condition, it is important to be aware of this potential problem induced by interferon therapy. HM

Amenomori M, Mori T, Fukuda Y et al (1998) Incidence and characteristics of thyroid dysfunction following interferon therapy in patients with chronic hepatitis C. *Intern Med* **37**(3): 246–52

Fentiman IS, Thomas BS, Balkwill SR et al (1985) Primary hypothyroidism associated with interferon therapy of breast cancer. *Lancet* **i:** 1166

Imagawa A, Itoh N, Hanafusa T et al (1995) Autoimmune endocrine disease induced by interferon-alpha therapy for chronic active type C hepatitis. *J Clin Endocrinol Metab* **80**(3): 922–66

Preziati D, La Rosa L, Covini G et al (1995) Autoimmunity and thyroid function in patients with chronic active hepatitis treated with recombinant interferon alpha-2a. *Eur J Endocrinol* **132:** 587–93

Roti E, Minelli R, Giuberti T et al (1996) Multiple changes in thyroid function with chronic active HCV hepatitis treated with recombinant interferon alpha. *Am J Med* **172:** 482–7

Weissel M, Templ E, Gisslinger H (1995) Interferon-alpha induced disorders of thyroid function. A retrospective analysis of the literature and personal experiences. *Acta Med Austriaca* **22**(1-2): 1–5

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