Central hypothyroidism and hypophysitis during treatment of chronic hepatitis C with pegylated interferon alpha and ribavirin

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Thyroid dysfunction is a known complication of interferon treatment in patients with hepatitis C virus (HCV) infection. Other uncommon endocrine complications have been reported during the treatment of viral hepatitis with IFN-\(\alpha\), such as hypopituitarism. A 54-year-old female patient with chronic hepatitis C began treatment with pegylated (PEG)-IFN-\(\alpha\) 2a 180 \(\mu\)g/week plus ribavirin 1000 mg/day. At week 20 of treatment, her routine laboratory control showed low levels of thyroid-stimulating hormone (TSH) and free serum thyroxine. This was confirmed at week 24, and other laboratory values showed low levels of adrenocorticotrophic hormone (ACTH). A T1-weighted magnetic resonance imaging scan demonstrated high intensity of the anterior pituitary gland and enhancement after intravenous administration of gadolinium. Hypophysitis with hypothalamic-pituitary dysfunction and secondary or central hypothyroidism was diagnosed on the basis of the clinical features, endocrinological assessment, immunological markers and imaging studies. Twenty-four weeks after stopping treatment, HCV RNA was negative by polymerase chain reaction and alanine aminotransferase values were below the upper limits of normal, and ACTH and thyroid values remained within the reference values. This is the first report of central hypothyroidism and hypophysitis during treatment with PEG-IFN-\(\alpha\) plus ribavirin, and may be included in the potential list of side effects of the combination treatment. Eur J Gastroenterol Hepatol 18:693–694 © 2006 Lippincott Williams & Wilkins.

Keywords: central hypothyroidism, chronic hepatitis C, hypophysitis, pegylated interferon alpha, ribavirin

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Received 29 October 2005 Accepted 20 January 2006

Introduction

Thyroid dysfunction is a known complication of interferon treatment in patients with hepatitis C virus (HCV) infection. The prevalence varies between 3.9 and 11.8%, and it is independent of the type of interferon used and the dosage [1–4]. Both hyperthyroidism and hypothyroidism have been reported, and can be symptomatic or subclinical. Recent reports suggested a correlation between increases in thyroid autoantibodies and the development of thyroid dysfunction during IFN-\(\alpha\) therapy. Other uncommon endocrine complications have been reported during the treatment of viral hepatitis with IFN-\(\alpha\), such as hypopituitarism [5,6]. Treatment with pegylated (PEG) interferon plus ribavirin is currently the standard of care in patients with HCV infection. The prevalence of thyroid disorders with this newer treatment is unknown. We report a case of central hypothyroidism and hypophysitis during treatment with PEG-IFN-\(\alpha\) and ribavirin.

Case report

A 54-year-old female patient with chronic hepatitis C was referred for treatment. She was infected by genotype 1a and had a viral load of 623 188 UI/ml (5.79 log). She had elevated alanine aminotransferase (ALT) levels and the liver biopsy showed mild damage (metavir A1 F1). Before treatment she had normal thyroid-stimulating hormone (TSH) and free serum thyroxine levels (Table 1). She was taking nifedipine for Raynaud’s syndrome. She began treatment with PEG-IFN-\(\alpha\) 2a 180 \(\mu\)g/week plus ribavirin 1000 mg/day. At week 20 of treatment, her routine laboratory control showed low levels of TSH and free serum thyroxine; this was confirmed at week 24 (Table 1). At this time, antithyroid peroxidase, antithyroglobulin and TSH receptor antibodies were negative. Other laboratory values showed low levels of adrenocorticotrophic hormone (ACTH) and normal levels of cortisol, T3, T4, follicle-stimulating hormone, luteinizing hormone and prolactin (Table 1). An \(^{131}\)I radionuclide scan showed a morphologically functionally normal thyroid gland. A T1-weighted magnetic resonance imaging scan demonstrated high intensity of the anterior pituitary gland and enhancement after intravenous administration of gadolinium. At week 24 HCV RNA was negative and ALT values were below the upper limits of normal; the patient refused to stop or reduce the dose of PEG-IFN-\(\alpha\). Laboratory work-up performed at week 28 showed normalization of ACTH and thyroid values (Table 1). Treatment continued and thyroid values remained between below and within the lower limits of normal.
The diagnosis is suggested by clinical features, endocrinological assessment, immunological markers and imaging studies. Our patient was asymptomatic; her routine laboratory controls during treatment with PEG-IFN-α showed thyroid values compatible with central hypothyroidism. Further studies revealed low levels of ACTH, suggesting hypothalamic–pituitary dysfunction. Magnetic resonance imaging showed signs of hypophysitis. We could not perform pituitary antibody tests, and although she has an autoimmune disease, Raynaud’s syndrome, this has not been reported to be related to lymphocytic hypophysitis or autoimmune hypophysitis [9]. Other markers of autoimmunity such as antinuclear antibodies, antismooth muscle antibody, antineutrophil cytoplasmic antibodies, etc., were negative.

The patient suffered transient or spontaneously resolved hypophysitis. We do not know if it can be classified as primary or autoimmune hypophysitis associated with PEG-IFN-α plus ribavirin, or secondary hypophysitis. This is the first report of central hypothyroidism and hypophysitis during treatment with PEG-IFN-α plus ribavirin, and may be included in the potential list of side-effects of the combination treatment.

Conflict of interest
None declared.

Authors’ contributions
The authors contributed equally to the preparation of this report.

References