A case of autoimmune polyglandular syndrome developed after interferon- α therapy

Treatment of chronic hepatitis C with interferon (IFN) alone or with ribavirin is recommended for patients with persistently high levels of serum aminotransferase and detectable viraemia [1].

Approximately 2–3% of patients develop isolated thyroid disease while on IFN, of whom about 20–30% have an isolated elevation of thyroid peroxidase (TPO) antibodies [2]. Additionally, a few cases of isolated Type 1 diabetes mellitus have been described during IFN treatment in genetically predisposed patients [3, 4]. Just two cases of IFN-related isolated hypopituitarism have been reported, one of which resolved after 11 months [5]. Autoimmune polyglandular syndrome (APS) associated with IFN- α treatment has not been described previously.

A 51-year-old woman suffering from chronic active hepatitis with detectable circulating hepatitis C virus-RNA (HCV-RNA) was examined. She had regular menstrual cycles. Thyroid function was normal and thyroid antibodies were undetectable. Therapy with IFN- α , 6 million units three times per week, was commenced and was continued for 6 months.

At 1 month, elevation of TPO antibodies occurred (250 IU mL⁻¹), with no thyroid functional disorder. Serum transaminase became normal and circulating HCV-RNA disappeared 3 months after beginning treatment.

At 4 months, she reported amenorrhoea and asthenia. At 12 months, the patient reported polydipsia, polyuria and weight loss for about 2 weeks. Severe hyperglycaemia was documented (approximately 44 mmol L⁻¹), so she was admitted to our unit. Ketoacidosis was detected, and promptly corrected. The following abnormalities were revealed: serum C-peptide 0.5 μ U mL⁻¹ (basal) and 0.8 μ U mL⁻¹ (6 min after 1 mg i.v. of glucagon); HbA_{1c} 10.6%; follicle stimulating hormone (FSH) 3.5 U L⁻¹; luteinizing hormone (LH) 2.5 U L⁻¹; basal serum cortisol and ACTH were 2.4 μ g dL⁻¹ (normal range 4.1–22.4) and 2.5 pg mL⁻¹ (normal range 6.1–55.0), respectively; pituitary gland autoantibodies by immunofluorescent assay (positive at 1 : 16 dilution); islet cell antibodies (ICA); glutamic acid decarboxylase antibodies (GADA); tyrosine phosphatase IA-2 antibodies (IA-2A) (positive at 38 JDF-U mL⁻¹, 33 IU mL⁻¹ and 48 IU mL⁻¹, respectively). Serum growth hormone, prolactin, aldosterone and parathyroid hormone were normal.

Serum cortisol rose to 23.2 μ g dL⁻¹ after corticotropin stimulation, suggesting recent onset of corticotropin defi-

ciency, whereas, LH and FSH did not rise after GnRH stimulation.

Magnetic resonance imaging showed a partial empty sell.

Retrospective evaluation of serum samples stored at –80 °C, collected for future viral investigation, showed that autoantibodies to pancreas and pituitary gland were undetectable before treatment with IFN was started.

Molecular typing of class II major histocompatibility complex alleles revealed homozygosity for the known Type 1 diabetes-associated DR3 (DQB1 *0201 and DQA1 *0501) haplotype, demonstrating a susceptible genetic background for autoimmune diseases.

At 16 months, the patient has normal thyroid function, liver function tests and absent blood HCV-RNA, but remains insulin dependent with amenorrhoea and adrenal insufficiency. ICA, GADA, IA-2A and pituitary gland antibodies remain positive (53 JDF-U mL⁻¹, 84 IU mL⁻¹, 44 IU mL⁻¹ and 1 : 16 dilution, respectively).

These findings suggested a type III APS, according to Neufeld's classification.

IFN- α enhances MHC expression and may cause both the onset of organo-specific autoantibodies, and the clinical manifestations of autoimmune diseases, as occurred in our patient. The absence of autoantibodies does not exclude humoral or clinical autoimmunity during or after treatment.

Therefore, we recommend strict clinical monitoring during, as well as after IFN- α treatment, in order to detect promptly any symptoms and signs of autoimmune disease. The clinical suspicion has to be confirmed by appropriate autoimmune and hormonal assays.

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Received 4 February 2003, accepted 18 March 2003

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