CASE REPORT

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Thyroid-associated Ophthalmopathy in a Chronic Hepatitis C Patient during IFN-α Therapy

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Case presentation

A 40-year-old man who had been admitted to Tehran Hepatitis Center, was treated with IFN-α and ribavirin for a diagnosis of chronic hepatitis C genotype b. He showed right globe exophthalmia one month after the beginning of IFN-α treatment (fig 1). In orbital CT (with contrast), hypertrophy of rectus muscles of orbit suggested thyroid-associated ophthalmopathy (TAO) (fig 2). Thyroid function tests before and after starting of IFN-α treatment were normal. The patient had neither a history of thyroid disease, nor any particular family history. In this case, steroid therapy improved the sign of TAO.

In this article we will review the most possible causes of thyroid abnormalities during IFN-α treatment and other related topics in a patient with chronic hepatitis C.

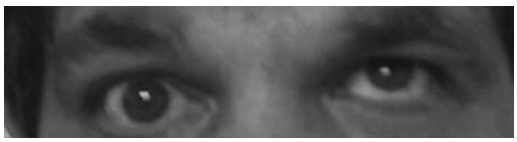

Fig 1. Right globe exophthalmia.

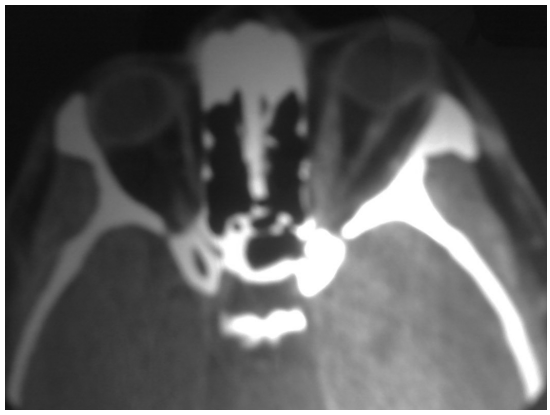

Fig 2. Hypertrophy of rectus muscles of orbit.

Discussion

IFN-α therapy for patients infected with chronic hepatitis C may exacerbate or induce thyroid disorders[(1)]. Production of autoantibodies is the main cause for occurrence of autoimmune diseases such as autoimmune thyroid disease (AITD) during IFN-α therapy[(2)].

It is not well known whether IFN-α initiates AITD or simply exacerbates it in individuals with subclinical AITD[(7)]. IFN-α associated AITD consists of autoimmune primary hypothyroidism, Graves'-like hyperthyroidism (GD), and destructive thyroiditis (DT)[(3)]. IFN-α induced Graves'-like disease is characterized by the following features: suppressed thyroid-stimulating hormone levels, normal or elevated free triidothyronin (FT3) and free thyroxin (FT4) values, the presence of thyroid peroxide antibodies, antithyroglobulin antibodies, and thyroid receptor antibodies and high radioactive iodine thyroid uptake[(4)]. Graves'-like disease has been observed both in the presence and in the absence of IFN-α chronic hepatitis C patients. Graves'-like disease developed during chronic hepatitis C without IFN-α is less clearly defined. However, data show a better course of Graves'-like with a more precocious and significantly higher number of recoveries in patients with IFN-α

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induced GD than in IFN-α unrelated disease[4].

HLA system examination is an important and promising diagnostic aspect that may be considered in order to evaluate the appearance of thyroid disorders during IFN-α therapy [1].

There are no significant differences in ultrastructure of orbital fibroblasts (OF) of TAO patients and that of normal subjects. OFs treated with the serum of TAO patients showed proliferation and increasing cytokine secretion [5].

IFN-α induced destructive thyroiditis (DT) is a mild disease because thyroid-destructive processes last for a short time and involve a small portion of the gland[6]. IFN-α induced DT is characterized by suppressed serum TSH levels, normal or elevated FT4 and FT3 concentrations, with presence or absence of thyroid peroxide antibodies and antithyroglobulin antibodies, the absence of thyroid receptor antibodies and radioactive iodine uptake suppressed or <5%[3]. Some studies showed fluctuating thyroid status (transient hypothyroid state followed by hyperthyroidism) during IFN-α therapy in chronic hepatitis C[8].

The transient hypothyroid state may be explained by two possible mechanisms. One may be due to the shift in the balance between the stimulating and blocking types of thyroid receptor antibodies (tRAb), and the other may be due to the complication of destructive thyroiditis that developed during IFN-α therapy [8]. Risk factors for developing thyroid dysfunction with IFN-α treatment are: female sex, underlying malignancy or HCV, higher doses of IFN-α for longer durations, presence of thyroid autoantibodies prior to or during treatment[9].

Type 2 immune response (Th2) is activated early and specifically in patients with IFN-autoimmune thyroiditis (AT) who remain euthyroid throughout the follow-up. Predominant in patients developing thyroid dysfunction, by contrast, is the type 1 immune response (Th1) that seems to occur earlier in innate than acquired immune system[10]. In other words the Th1 pattern of secreting inflammatory cytokines may contribute to pathogenesis of autoimmune thyroiditis [11].

Some studies also showed that cytolytic T cells with Th1 profile of cytokine production predominate in retro-orbital (RO) space infiltrates of Graves' ophthalmopathy (GO), a pattern quite similar to those previously described in thyroid infiltrates of Hashimoto's thyroiditis or Graves' disease [12]. There is not strong evidence for coexistence of depression and thyroid dysfunction secondary to IFN-α therapy in patients with chronic hepatitis C[13]. At present, the therapeutic approach in DT is IFN withdrawal and 1-2 months of steroid therapy. Nevertheless, some studies showed that the simple withdrawal of IFN therapy in patients with chronic hepatitis C, who had developed DT, appears to be effective in the treatment of thyroid disease[3].

It is recommended that in a patient with chronic hepatitis C, systemic thyroid assessment be performed before initiating IFN therapy, including clinical examination, and measurement of TSH, FT4, FT3, antithyroid peroxidase antibodies(Tpo Ab) during treatment, and a TSH assay every other month[6].

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