

Development of Autoimmune Hypothyroidism after Interferon-beta 1a Treatment in Patient with Multiple Sclerosis: A Case Report

¹Md. Abdul Awal, ¹Md. Sunny Anam Chowdhury and ²Md. Hafizur Rahman

¹Institute of Nuclear Medicine and Allied Sciences, Bogra, ² Institute of Nuclear Medicine and Allied Sciences, Faridpur

Correspondence Address : Dr. Md. Sunny Anam Chowdhury, Institute of Nuclear Medicine and Allied sciences, Bogra. GPO Box # 61, Mohammad Ali Hospital Campus, Bogra. E-mail: drsunny43@gmail.com

ABSTRACT

Interferon beta therapy is a well-established treatment of patients suffering from multiple sclerosis, a demyelinating disease of the central nervous system. Since type I interferons have immunomodulatory properties, these cytokines may trigger several autoimmune disorders. In this case, we report the development of autoimmune hypothyroidism in a multiple sclerosis patients receiving interferon-β 1a.

Key Words: Interferon-β 1a, Multiple sclerosis, Autoimmune hypothyroidism.

INTRODUCTION

Interferon beta-1a (INF-β 1a), a cytokine in the interferon family, is widely used to treat the relapsing multiple sclerosis (MS), a demyelinating disease of the central nervous system, and a single demyelinating event with an active inflammatory process with high risk of developing clinically definite multiple sclerosis. The mechanism, how INF-β exerts its beneficial effects is still unknown. But, INF-β has a number of immunomodulatory effects. As a result development of other autoimmune diseases including autoimmune thyroid disease has been found in patients with MS (1-4). Alteration of thyroid function and autoimmunity has been reported in 5-12% of patients treated with interferon-α for various diseases (5,6). Similar effect was noticed in patients treated with both INF-β 1b and 1a, specially in those with preexisting autoimmunity (2,7,8). We report the development of autoimmune hypothyroidism by the course of INF-β 1a treatment of a patient with relapsing MS, who was euthyroid and negative for antithyroid antibodies-antithyroglobulin antibody (anti-Tg Ab) and

antithyroid peroxidase antibody (anti-TPO Ab) during pretherapy assessment.

CASE REPORT

A 52 years old man with relapsing MS for six months with optic neuritis was treated with 30 microgram (6 million IU) of interferon-beta 1a by intramuscular (IM) injection once a week along with intravenous corticosteroids injection one gm per day for five days followed by 80 mg per day for two weeks and finally the dose of the steroid was tapered and stopped by three months. His pretherapy body weight was 81 kg, free triiodothyronine (FT3) and free thyroxine (FT4) level were 7.8 p mol/L (normal range 2.8-9.5 p mol/L) and 13.2 p mol/L (normal range 9.5-25.5 p mol/L), thyroid stimulating hormone (TSH) level was 3.1 m IU/L (normal range 0.3-5.0 m IU/L) and normal antithyroid antibodies level (anti-Tg Ab – 14 IU/ml, normal range: <20 IU/ml and anti-TPO Ab 24 IU/ml, normal range: <35 IU/ml) After six months of therapy the patients was presented with weight gain (94 kg), puffy face and dry, coarse skin. Thyroid function test revealed decreased in serum T3, T4, free T3 and free T4 levels, which were 1.2 m mol/L (normal range 1.23-3.54 m mol/L), 09 m mol/L (normal range 54-173 m mol/L), 1.7 p mol/L and 1.0 p mol/L respectively. His serum TSH level rose to 27.7mIU/L. An elevated level of anti-TPO Ab (1200 IU/ml) and normal anti-Tg Ab (18 IU/ml) were found. The clinical features and biochemical results were reliable with hypothyroidism associated with autoimmune thyroiditis. He started

levothyroxine replacement therapy at the dose of 100 microgram daily and has continued the INF- β therapy.

DISCUSSION

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system. It damages both oligodendroglia and axons and may cause paralysis, sensory disturbances, incoordination, visual impairment, and alterations in autonomic and sexual function (9). MS is often associated with autoimmune diseases as there is increased frequency of elevated autoantibodies including antithyroid antibodies (10). It is reported that about 4-22% thyroid autoimmunity to be present with MS (8, 11). Our patient had relapsing MS for six months with optic neuritis (confirmed by MRI) in the form of visual disturbance as dimness, blurring of vision. But, he had no thyroid dysfunction or thyroid autoimmunity before treatment.

Interferon (INF), one of the members of intracellular messengers known as cytokines, possess antiviral, antiproliferative, anti-tumor & immunomodulatory properties. Treatment of MS with INF- β began in the late 1970s. INF- β 1a and INF- β 1b are frequently used in MS. INF- β 1a has identical sequences to human INF- β (3). Interferon-alpha (INF- α), which is used to treat various diseases causes development of thyroid disorders (hypo- or hyperthyroidism) with or without thyroid autoimmunity in 5-12% of the patients. Interestingly, presence of antithyroid antibodies before treatment with INF- α is noticed as a predisposing factor to develop autoimmune hypothyroidism during treatment (5,6). Similar effects were found in patients treated with interferon-beta. A study showed after one year treatment with INF- β 1b in 31 MS patients, 33% of the patients developed thyroid dysfunction (10% hyperthyroidism and 23% hypothyroidism). Thyroid autoimmunity was developed in 19% patient (2).

Another multicenter prospective study showed, the frequency of clinical and subclinical thyroid dysfunction during INF- β was 8.3% and thyroid

autoimmunity was found in 13% of the patients and all the patients with persistent autoimmune thyroid dysfunction during therapy had a family history of thyroid disease or an elevated antithyroid antibody level before therapy (7). Another long-term follow-up study of 106 MS patients undergoing INF- β 1a or 1b therapy stated- thyroid dysfunction developed in 24% patient, without significant difference between INF- β 1a and 1b treatment groups. Hypothyroidism found in 19% patients receiving INF- β 1b and in 20% of INF- β 1a group. Hyperthyroidism, which was always transient, developed in 4.9% of patients (five patients) and only one of the five patients was treated with INF- β 1a. Thyroid autoimmunity developed in 22.7% (22 patients) of patients, without significant difference between INF- β 1a and 1b treatment groups. Ten patients developed positive serum Tg-Ab titre, nine TPO-Ab titre, two both and one TR-Ab (anti TSH-receptor antibody) titre. Incident autoimmunity was transient in 13 of 22 patients (59.1%), with no significant difference between INF- β -1a and 1b treatment groups. Twelve patients with incident autoimmunity remained euthyroid. Ten patients developed thyroid dysfunction (three hyperthyroidism, seven hypothyroidism). Both thyroid dysfunction and autoimmunity developed mainly within the first year of treatment, without significant differences between INF- β 1a and 1b (8). In our case, we found the patient treated with INF- β 1a developed thyroid dysfunction in the form of clinically featured hypothyroidism with the complaints of weight gain, puffiness of face and dry-coarse skin and biochemical evidence of low serum T3, T4, FT3, FT4 & high TSH levels, associated with thyroid autoimmunity with the evidence of elevated anti-TPO Ab level within six months of treatment.

The mechanism of thyroid dysfunction or autoimmunity by interferon is still unknown. Few author suggested INF- α to stimulate the production of thyroid-inhibitory cytokines and/or activation of

cytotoxic lymphocytes in thyroid gland and cause thyroid dysfunction (12-13). INF- α may also suppress the expression of major histocompatibility complex (MHC) class II antigens in thyroid cells (14). Another group of researchers showed that in vitro INF- α and INF- β inhibited organification of radioiodine in human thyroid cells (15), which may be most-likely explanation of developing hypothyroidism specially who develop hypothyroidism without thyroid autoimmunity.

Since few researchers have mentioned the autoimmunity and thyroid dysfunction during INF- β therapy are transient and almost always reversible (7), considering the beneficial effect of interferon-beta 1a in MS, we decided to continue the therapy of our patient while combating his hypothyroidism problem with levothyroxine replacement.

CONCLUSION

Physicians should be alert regarding the development of thyroid dysfunction in MS patients receiving INF- β therapy. Proper clinical assessment, biochemical check up of thyroid hormones and antibodies every three months could be sufficient during the course of treatment.

REFERENCES

- McDonald ND, Pender MP. Autoimmune hypothyroidism with interferon beta-1b treatment in two patients with multiple sclerosis. *Aust NZ J Med* 2000;30:278-79
- Monzani F, Caraccio N, Mucchi G, Lombardo F, Moscato G, Casolaro A et al. Effect of 1-year treatment with interferon- β 1b on thyroid function and autoimmunity in patients with multiple sclerosis. *European J Endocrinol* 1999;141:325-31.
- Rog DJ, Mottershead JP. The role of interferon beta in multiple sclerosis management. *Future Prescriber* 2008;7(3):15-19.
- Surks MI, Sievert R. Drugs and Thyroid Function. *N Engl J of Med* 1995; 333(25):1688-94.
- Ronnblohm LE, Alm GV, Oberg KE. Autoimmunity after alpha interferon therapy for malignant carcinoid tumors. *Annals of Internal Medicine* 1991; 115:178-183.
- Dumoulin FL, Leifeld L, Sauerbruch T, Spengler U. Autoimmunity induced by interferon-alpha therapy for chronic viral hepatitis. *Biomed Pharmacother* 1999;53:242-54.
- Durelli L, Ferrero B, Oggero A, Verdun E, Ghezzi A, Montanari E et al. Thyroid function and autoimmunity during interferon β -1b treatment: A multicentre prospective study. *J of Clin Endocrinol & Metab* 2001;86(8): 3525-32.
- Caraccio N, Dardano A, Manfredonia F, Manca L, Pasquali L, Iudice A et al. Long-term follow-up of 106 multiple sclerosis patients undergoing interferon- β 1a or 1b therapy: predictive factors of thyroid disease development and duration. *J of Clin Endocrinol & Metab* 2005; 90(7): 4133-37.
- Paty DW, Ebers GC. Multiple Sclerosis. *Contemporary Neurology Series* 1998; 50:Chapter 4 – Diagnosis.
- Spadaro M, Amendolea MA, Mazzuconi MG et al. Autoimmunity in multiple sclerosis: study of a wide spectrum of autoantibodies. *Mult Scler* 1999;5:121-5.
- Monzani F, Caraccio N, Dardano A, Ferrannini E. Thyroid autoimmunity and dysfunction associated with type I interferon therapy. *Clin Exp Med* 2004;3:199-210.
- Nagayama Y, Izumi M, Ashizawa K, Kiriya T, Yokoyama N, Morita S et al. Inhibitory effect of interferon- γ on the response of human thyrocytes to thyrotropin (TSH) stimulation: relationship between the response to TSH and the expression of DR antigens. *J of Clin Endocrinol and Metab* 1987; 64: 949-53.
- Volpe R. Immunology of human thyroid disease. Editor. Volpe R. *Autoimmune Disease of the Endocrine System*. Florida, PA: CRC Press 1990.173-239.
- Guerin V, Todd I, Hammond LJ, Bottazzo GF. Suppression of HLA class II expression on thyrocytes by interferon-alpha 1. *Clin Exp Immunol* 1990; 79: 341-45.
- Yamazaki K, Kanaji Y, Shizume K, Yamakawa Y, Demura H, Kanaji Y et al. Reversible inhibition by interferons alpha and beta of ^{125}I incorporation and thyroid hormone release by human thyroid follicles in vitro. *J of Clin Endocrinol and Metab* 1993; 77: 1439-41.