Autoimmune hypothyroidism associated with interferon beta-1b treatment in two patients with multiple sclerosis

Interferon ß-1b reduces the frequency and severity of relapses of relapsing-remitting multiple sclerosis (MS) and slows the progression of disability in secondary progressive MS. It has a number of immunomodulatory effects but the mechanism of its beneficial effect in MS is unclear. In contrast to its beneficial effect in MS, interferon ß-1b has recently been reported to enhance other autoimmune diseases in patients with MS, including autoimmune thyroid disease.[1-3] We report the development of autoimmune hypothyroidism in two MS patients receiving interferon ß-1b therapy.

A 44-year-old woman with relapsing-remitting MS for six months was commenced on interferon ß-1b therapy, eight million units subcutaneously every second day. Thyroid function tests performed immediately before the commencement of interferon ß-1b showed a normal free T4 level of 11 pmol/L (normal range [NR] 9-23) and a normal thyrotropin level of 3.1 mU/L (NR 0.4-5.0). Five months after the commencement of interferon ß-1b, thyroid function tests were performed because of palpitations and revealed an elevated thyrotropin level of 10 mU/L, a highly elevated level of antithyroid microsomal antibodies (titre 6400) and a normal antithyroglobulin antibody level. These results indicated hypothyroidism due to Hashimoto's thyroiditis, although she had no clinical features of hypothyroidism. She was commenced on L-thyroxine 100 µg daily. She has continued on interferon ß-1b therapy, and her thyroid function has remained adequate on replacement therapy.

A 37-year-old woman with relapsing-remitting MS for 13 years was commenced on interferon ß-1b therapy, eight million units subcutaneously every second day. Three months later, she noted weight gain but had no other symptoms of hypothyroidism. Thyroid function tests revealed an elevated thyrotropin level of 80 mU/L, a highly elevated level of antithyroid microsomal antibodies (titre 6400) and a normal antithyroglobulin antibody level. These results were consistent with hypothyroidism due to Hashimoto's thyroiditis. She was commenced on L-thyroxine 100 µg daily. She has remained on interferon ß-1b therapy, and her thyroid function has been adequate on replacement therapy.

Interferon ß-1b therapy for MS. Recent reports have documented the occurrence of autoimmune hyperthyroidism or hypothyroidism[1-3] and increased autoantibody levels[2,3] in association with this treatment for MS. Another type 1 interferon, interferon α, which is widely used to treat chronic viral hepatitis, has been reported to induce autoimmune disease, including hypothyroidism.[4]

Autoimmune thyroid disease, as well as other autoimmune diseases, can occur in MS patients not receiving interferon ß therapy,[5] but it is unclear whether the occurrence of these diseases is increased in MS patients. Some studies have found an increased occurrence of autoimmune diseases but others have not. It is established that patients with MS have an increased frequency of elevated autoantibodies, including antithyroid antibodies,[6] indicating that patients with MS are predisposed to autoimmunity in general. Thus it is possible that interferon ß-1b unmasks or triggers autoimmune diseases on the background of such a predisposition. It would be anticipated that interferon ß-1a would have a similar effect. Interestingly, the presence of antithyroid antibodies prior to treatment with interferon α predisposes patients with chronic viral hepatitis to the development of autoimmune hypothyroidism during treatment.[7] Durelli and colleagues[3] found that all three patients with persistent autoimmune thyroid dysfunction arising during interferon ß-1b therapy for MS had a family history of thyroid disease or had elevated antithyroid antibodies prior to therapy. Recently it has been shown that interferon α and interferon ß inhibit B cell receptor-mediated apoptosis,[8] which may account for the increased autoantibodies and autoimmune disease in patients treated with these interferons.

Physicians should be alerted to the possibility of altered thyroid function in MS patients receiving interferon ß-1b and should perform thyroid function tests in patients with suggestive symptoms. In view of the beneficial effect of interferon ß-1b in MS, we decided to continue our patients on interferon ß-1b therapy while treating the hypothyroidism with L-thyroxine. ■

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