CASE REPORT

Retinopathy: An Overlooked Adverse Effect of Interferon-beta Treatment of Multiple Sclerosis

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Abstract

Interferon (IFN), which is an established maintaining therapy for multiple sclerosis (MS), has been reported various adverse effects. This paper describes a case of IFN-associated retinopathy, representing an overlooked adverse effect in MS. A 46-year-old woman with diabetes mellitus was diagnosed with MS and treated with IFNβ-1b for three years. She displayed sudden defect of the visual field and ocular fundi showed retinal cotton wool spots indicating IFN-retinopathy, which resolved rapidly after IFN was discontinued. To evaluate the prevalence of retinopathy in MS, we performed fundoscopic examination on twenty MS patients treated with IFNβ-1b in our hospital. However, none of the patients displayed retinopathy. Only four other cases of IFN- retinopathy in MS have been reported in the literature. Therefore, IFN-retinopathy may be uncommon in MS, but neurologist should be mindful of this adverse effect and regularly check the fundus, particularly in patients with possible risk factor, diabetes mellitus. (Keio J Med 58 (1) : 54–56, March 2009)

***Keywords*: multiple sclerosis, interferon, retinopathy, adverse effect**

Introduction

In multiple sclerosis (MS), many clinical trials have demonstrated ameliorating effects of interferon (IFN) on disease activity, and recombinant IFNβ is now the mainstay of maintenance therapy for MS in many countries. To date, a variety of adverse effects of IFN use have been described, and flu-like symptoms, inflamed injection sites, and depression are widelyknown as frequent adverse effects in MS.[1]

Herein we report a case of IFN-associated retinopathy in a patient with MS receiving subcutaneous IFNβ-1b treatment and reviewed the clinical properties of this adverse effect in MS.

Case Report

A 46-year-old woman, who was diagnosed with relapsing-remitting MS in May 2003, had experienced relapse 4 times, with mild spastic paraparesis and sensory disturbance of the limbs. Subcutaneous IFNβ-1b was started at eight million units 3 times/week in June 2003. The patient also had diabetes mellitus and hypertension and had been under medication with voglibose, amlodipine besilate and candesartan cilexetil since 2004. In May 2006, she suddenly displayed defect of the visual field in the right eye. CSF examination and MRI did not reveal any evidence of relapse, and ocular fundi showed several retinal cotton wool spots (**Fig. 1a**). As the retinal lesion was suspected to represent IFN retinopathy, administration of IFNβ-1b was suspended. Visual disturbance gradually improved and retinal lesions had disappeared by 5 weeks after cessation of the drug (**Fig. 1b**). We thus concluded that IFN was a cause of retinopathy in this patient. To evaluate the prevalence of retinopathy in MS, we subsequently performed fundoscopic examination in all other MS patients (N=20) treated with IFN at our hospital. All patients (mean age, 43.0±13.0 years) were receiving

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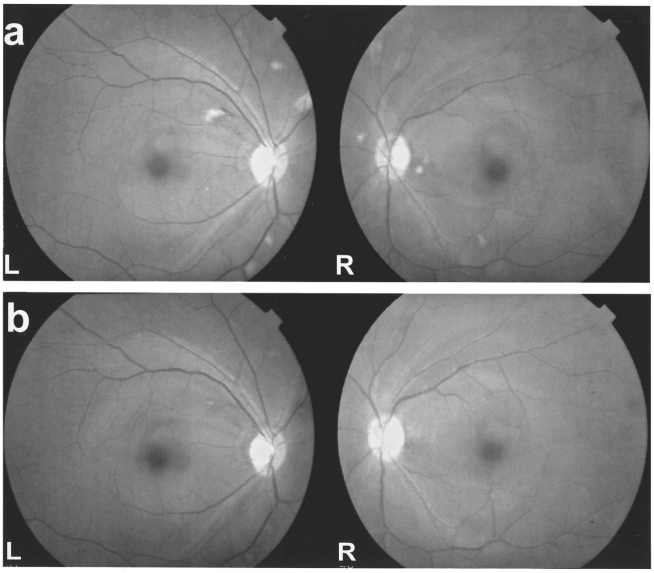

Fig. 1 Fundoscopic examination. a) Ocular fundi show several cotton spots in May 2006. b) Cotton spots have largely recovered by 2 months after discontinuation of IFN in June 2006.

eight million units of IFNβ-1b three times/week. Mean duration of disease was 100.7±104.4 months and mean period of IFNβ-1b administration was 37.1±23.0 months. In our study series, no other patients exhibited retinopathy.

Discussion

This is the first neurological report to describe clinical findings of retinopathy in an MS patient during IFN treatment. Moreover, we also examined the frequency of IFN retinopathy in MS in a retrospective hospital-based analysis. Ophthalmological complications related to IFN administration were first described in 1990 by Ikebe *et al*. in Japan and, since the introduction of IFN therapy for viral hepatitis, retinopathy has been identified as an important adverse effect of IFN therapy for this disease.[1] Incidence varies according to country and study design, with a high frequency of >50% reported in Japan,[1] suggesting that patients should be carefully monitored by ophthalmological assessment during treatment for viral hepatitis. Retinopathy reportedly develops between 2 weeks to 5 months after initiation of IFN therapy, and prevalence may depend on dosage of IFN received. Signs of retinopathy are cotton-wool spots and associated ischemic signs, such as papilledema, retinal artery occlusion and retinal vein thrombosis.[2] Risk factors remain unclear. Many authors believe that diabetes mellitus is a strong risk factor, and arterial hypertension and old age are also suspected as possible risk factors.[1]

Consensus is lacking regarding treatment for IFN retinopathy. As described in previous studies of viral hepatitis, most cases of IFN retinopathy are asymptomatic, and spontaneously improve over a period of several weeks, despite continued full-dose IFN treatment.[2] Continuing IFN without reducing dosage is thus more often chosen to avoid secondary aggravation due to cessation of treatment. Indeed, regression of retinopathy has been described after completing IFN treatment for hepatitis.[1] However, in some cases, severe retinal lesions are reportedly responsible for significant decreases in visual acuity. Some authors thus recommend continuing treatment with reduced IFN dosages.

To date, only four other cases of IFN-associated retinopathy in MS have been reported by ophthalmologists.[3–6] First case continued IFN therapy under strict monitoring of ophthalmologic condition, and showed no serious visual deterioration.[3] In contrast, IFN was discontinued for cases in Spain and the United States and changed to other maintenance treatment with glatiramer acetate, and then the retinopathy were reportedly improved.[4,5] IFN therapy was discontinued for the most recent case, reported from Japan, and retinopathy subsided without specific therapy.[6] In the present case, treatment was stopped because the patient reported serious visual disturbance with several risk factors for retinopathy, diabetes mellitus and arterial hypertension. Unfortunately, because glatiramer acetate is not available in Japan, we could not use that for her. The patient is still not receiving IFN therapy and has shown no serious relapse or neurological aggravation for 6 months.

Visual disturbance is one of the most common symptoms in MS patients. Based on our study series, IFN retinopathy may be an uncommon but potentially serious adverse effect in MS patients. Our examination of twenty MS patients identified no other cases with retinopathy. Although further large-scale studies are necessary, prevalence of retinopathy seems to be much lower in MS than in viral hepatitis. We speculate that this low occurrence could be attributed to lower patient ages and lower IFN dosage for MS. However, because diabetes mellitus is suggested as a strong risk factor for this adverse effect, neurologists should thus be aware of this adverse effect due to IFN and regularly perform retinal examinations, particularly for patients with risk factors for retinopathy, diabetes mellitus or arterial hypertension.

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