KJO
pISSN: 1011-8942 eISSN: 2092-9382

Korean J Ophthalmol 2012;26(2):147-150
http://dx.doi.org/10.3341/kjo.2012.26.2.147

Case Report

Pegylated Interferon-Associated Severe Retinopathy in a Patient with Chronic Hepatitis

Hee Young Kang[1], Min Chul Shin[2]

[1]*Konyang University Kim's Eye Hospital, Seoul, Korea*
[2]*Department of Ophthalmology, Chuncheon Sacred Heart Hospital, Hallym University College of Medicine, Chuncheon, Korea*

This paper reports a case of pegylated interferon-associated retinopathy in a patient with chronic hepatitis C. A 32-year-old female with chronic hepatitis C undergoing pegylated interferon and ribavirin combination therapy complained of visual blurring. Features of interferon-associated retinopathy, including ocular complications such as cotton wool spots, retinal hemorrhages, macular edema, and branch retinal vein occlusion, were found in the fundus of both of her eyes. Pegylated interferon combination therapy was stopped, and the retinopathy of the patient was treated with intravitreal bevacizumab injections and panretinal photocoagulations. This case shows that pharmacokinetically improved pegylated interferon has ocular complications for patients with chronic hepatitis C. Accordingly, patients undergoing pegylated interferon treatment for hepatitis C need regular eye examinations for protection of their vision.

Key Words: Chronic hepatitis C, Interferon-associated retinopathy, Ocular vision, Pegyalted interferon

Interferon is a monotherapy or combination therapy antiviral drug for patients suffering from chronic hepatitis C. Certain ocular complications from interferon therapy have been reported, however, such as cotton wool spots [1-7], retinal hemorrhages [1-7], and optic neuropathy [8], among others. By pegylation of polyethylene glycol (PEG) to interferon, pharmacokinetially improved pegylated interferon has a larger molecular weight and a longer half life in the serum than non-pegylated interferon [3], which increases the efficacy of the drug for chronic hepatitis C patients. Non-pegylated interferon has a 12% to 16% clearance rate in the serum, whereas the 50% to 60% clearance rate of pegylated interferon makes it safer for long-term use by patients [3]. Even though pegyalted interferon is a more effective drug for chronic hepatitis C patients, to our knowledge there are no existing reports or studies about pegylated interferon-associated ocular complications such as interferon-associated retinopathy. To bring the issue to light, this study reports a case of pegylated interferon-associated acute and irreversible severe retinopathy in a patient with chronic hepatitis C.

Received: May 19, 2008 *Accepted*: August 4, 2010

Corresponding Author: Min Chul Shin, MD, PhD. Department of Ophthalmology, Chuncheon Sacred Heart Hospital, Hallym University College of Medicine, #77 Sakju-ro, Chuncheon 200-704, Korea. Tel: 82-33-240-5176, Fax: 82-33-241-8063, E-mail: mcshin@hallym.ac.kr

Case Report

A 32-year-old female was diagnosed with chronic hepatitis C (grade 3/4, stage 2/4, genotype 2a/c) in February of 2007. She underwent treatment with pegylated interferon-α2b 80 micrograms and ribavirin combination therapy for 5 months (from February of 2007 until July of 2007). She was also treated with subcutaneous insulin injections for a previous condition of pregnant diabetic mellitus diagnosed seven years before. She was first referred to ophthalmology in February of 2007 for a diabetic retinopathy examination. Her vision was 0.6 in both eyes, and intraocular pressure was 11 mmHg in the right eye and 12 mmHg in the left eye. Fundus examination found moderate nonproliferative diabetic retinopathy (NPDR) in the right eye and mild NPDR in the left eye. Accordingly, a follow-up visit to check her eyes was scheduled for six months later. She felt visual blurring two months later, and we referred to a past ophthalmologic exam in June of 2007. At that time, her best corrected visual acuity was 0.04 in both eyes.

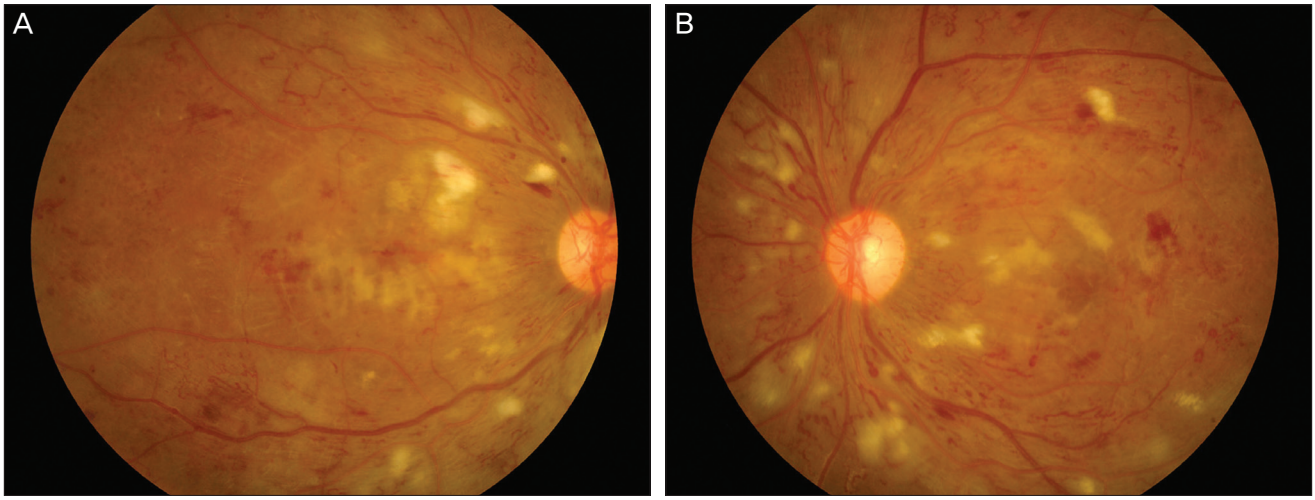

Fig. 1. Retinal hemorrhages, cotton wool spots, macular edema, and new vessels were found in both of the patient's eyes.

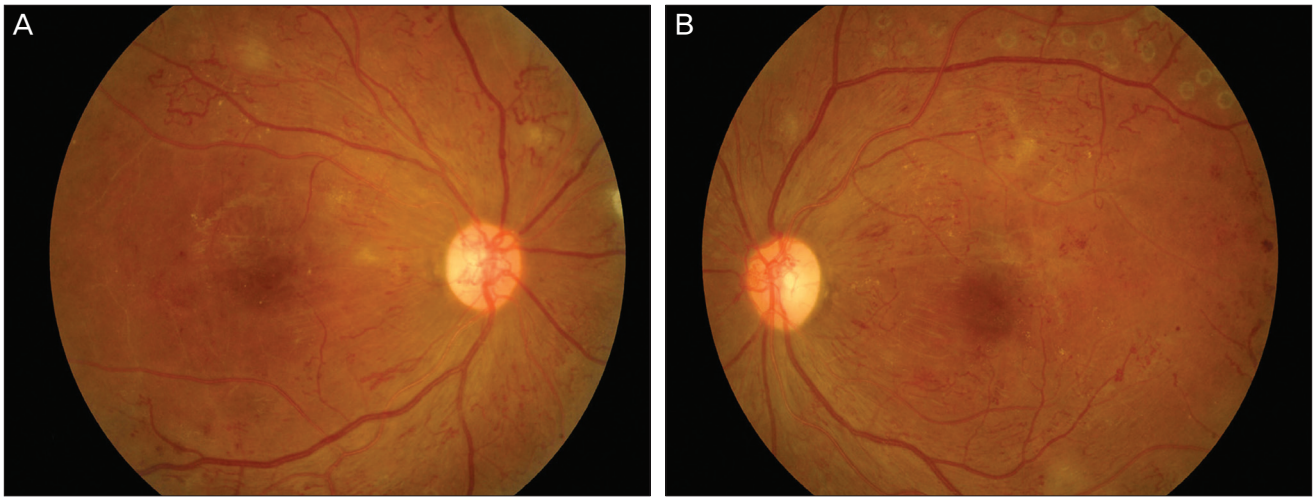

Fig. 2. (A,B) After intravitreal bevacizumab injections and panretinal photocoagulations, the cotton wool spots and retinal hemorrhages regressed, but the new vessels remained.

Previous fundoscopy revealed retinal hemorrhages, cotton wool spots, macular edema, and new vessels elsewhere (NVE) in both eyes (Fig. 1). The pegylated interferon and ribavirin combination therapy was stopped, and the patient was treated with intravitreal 0.05 mL bevacizumab (Avastin) injections. Panretinal photocoagulations were added.

After completion of treatment, the patient's retinal hemorrhages, cotton wool spots, and macular edema improved (Fig. 2). The retinal non-perfusion areas (Figs. 3 and 4) and the best corrected visual acuity of the patient did not improve. As of June, we began regular ophthalmic examination of her eyes every other week.

Discussion

Standard interferon therapy in chronic hepatitis C patients causes various ocular complications, including branch retinal vein occlusion [2], subconjunctival hemorrhages [5], visual blurring, papilledema [8], neovascular glaucoma, and retinal detachment [9], among others. The most common among the ocular complications are retinopathy-parapapillary retinal hemorrhages at the posterior pole, and cotton wool spots [1,2,4]. These features of retinopathy occur in approximately 18% to 86% of alpha interferon-treated chronic hepatitis C patients [1]. A study by Jain et al. [4] has reported that these features of retinopathy may occur between 4 to 12 weeks after the start of interferon and ribavirin combination therapy, and will regress within 4 to 12 weeks after therapy stops. The pathogenesis of these features of retinopathy is unknown, however, the hypothesis that interferon interferes with retinal microcirculations is persuasive [7]. In this respect, interferon treat-

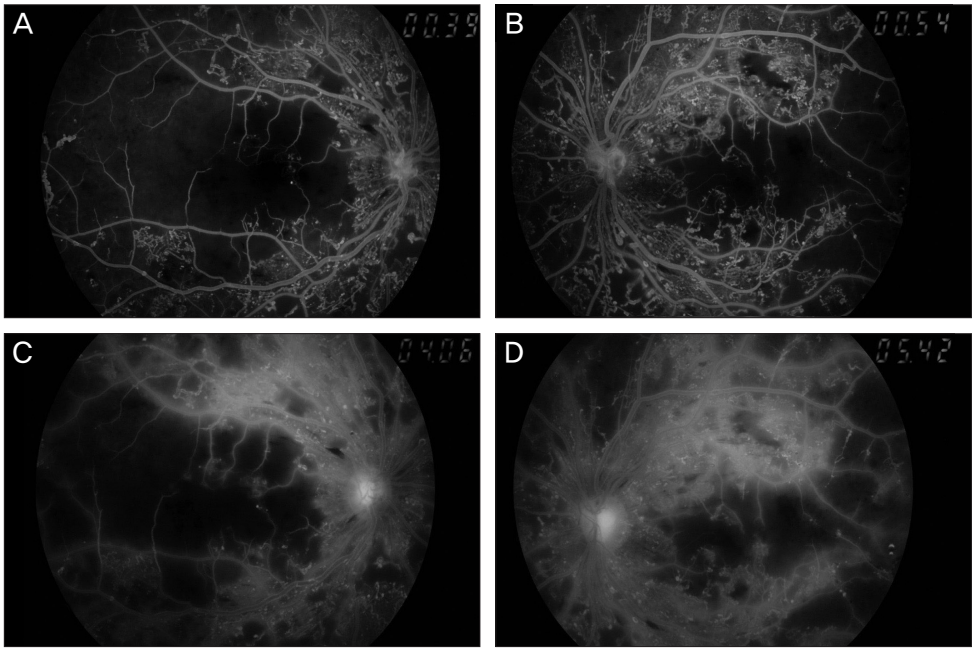

Fig. 3. At the late arteriovenous phase (A,B), many microaneurys and new vessels were found. At the mid-venous phase, non-perfusion was more severe in the left eye (D) than in the right eye (C).

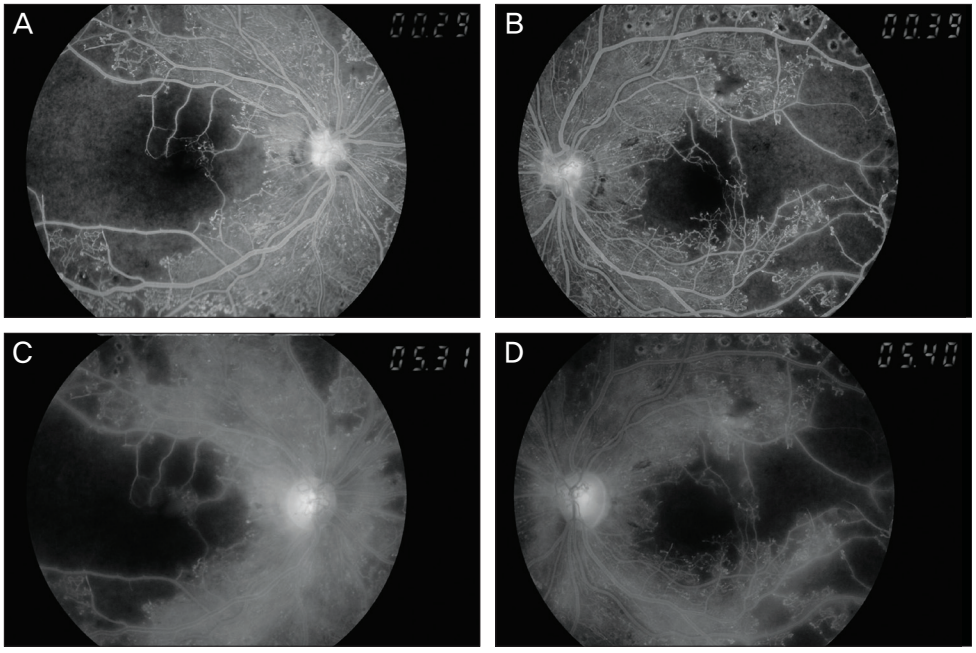

Fig. 4. At the late arteriovenous phase (A,B) and mid-venous phase (C,D), new vessels and non-perfused areas progressed.

ment for patients with abnormal microcirculation diseases, such as diabetic mellitus or hypertension, has a very high risk of causing interferon-associated ocular complications [6,7].

The patient in this case, due to previous diagnosis of diabetic mellitus, belonged to a high-risk group for interferon-associated ocular complications. The patient presented with retinal hemorrhages, cotton wool spots, macular edema, and retinal ischemic changes in both of her eyes. These ocular complications progress more acutely and severely than the progression of complications in a state of pre-pegylated interferon treatment, and the patient's vision decreased irreversibly.

Usually, interferon-treated patients have reversible interferon-associated retinopathy [1-7]. Cases of severe, irreversible visual impairment are very rare [10]. Chronic hepatitis C patients must undergo examination of their eyes before interferon treatment begins, and they must follow up with a second exam within three months of starting treatment. Particularly for high-risk patients with hyper-

tension or diabetes mellitus, not only are regular follow-up examinations very important, but also stopping the interferon treatment at the right time is critical. This report shows that patients treated with pegylated interferon combined with ribavirin may have irreversible and severe ocular complications. This study proposes that chronic hepatitis C patients treated with pharmacokinetically improved pegylated interferon must also be managed with regular and exact ophthalmic examinations on an ongoing basis.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

References

1. Hayasaka S, Nagaki Y, Matsumoto M, Sato S. Interferon associated retinopathy. *Br J Ophthalmol* 1998;82:323-5.
2. Goncalves LL, Farias AQ, Gonçalves PL, et al. Branch retinal vein thrombosis and visual loss probably associated with pegylated interferon therapy of chronic hepatitis C. *World J Gastroenterol* 2006;12:4602-3.
3. Malik NN, Sheth HG, Ackerman N, et al. A prospective study of change in visual function in patients treated with pegylated interferon alpha for hepatitis C in the UK. *Br J Ophthalmol* 2008;92:256-8.
4. Jain K, Lam WC, Waheeb S, et al. Retinopathy in chronic hepatitis C patients during interferon treatment with ribavirin. *Br J Ophthalmol* 2001;85:1171-3.
5. Hayasaka S, Fujii M, Yamamoto Y, et al. Retinopathy and subconjunctival haemorrhage in patients with chronic viral hepatitis receiving interferon alfa. *Br J Ophthalmol* 1995;79:150-2.
6. Okuse C, Yotsuyanagi H, Nagase Y, et al. Risk factors for retinopathy associated with interferon alpha-2b and ribavirin combination therapy in patients with chronic hepatitis C. *World J Gastroenterol* 2006;12:3756-9.
7. Nagaoka T, Sato E, Takahashi A, et al. Retinal circulatory changes associated with interferon-induced retinopathy in patients with hepatitis C. *Invest Ophthalmol Vis Sci* 2007;48:368-75.
8. Manesis EK, Petrou C, Brouzas D, Hadziyannis S. Optic tract neuropathy complicating low-dose interferon treatment. *J Hepatol* 1994;21:474-7.
9. Ayaki M. Development of neovascular glaucoma in the course of interferon alfa therapy for hepatitis type C. *Br J Ophthalmol* 1994;78:238.
10. Tu KL, Bowyer J, Schofield K, Harding S. Severe interferon associated retinopathy. *Br J Ophthalmol* 2003;87:247-8.