

## SHORT COMMUNICATION

# Branch retinal artery occlusion combined with branch retinal vein occlusion in a patient with hepatitis C treated with interferon and ribavirin

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**PURPOSE.** *To report a case of a combined branch retinal artery and vein occlusion in a patient with hepatitis C treated with interferon and ribavirin.*

**METHODS.** *A 29-year-old man with a 1-week history of sudden visual field defect and decrease of central visual acuity was examined.*

**RESULTS.** *Ophthalmoscopy and fluorescein angiography demonstrated an ischemic whitening of the inferior hemi-retina involving part of the macular region, numerous intraretinal hemorrhages, and a significant delay in arterial and vein filling of the dye.*

**CONCLUSIONS.** *The findings of a retinopathy associated with interferon and ribavirin treatment of hepatitis C are important. The symptomatic permanent visual field defect and decrease of central visual acuity developing following a branch retinal artery and vein occlusion event emphasizes the need for careful and regular ocular monitoring of patients receiving interferon for hepatitis C. (Eur J Ophthalmol 2005; 15: 811-14)*

**KEY WORDS.** *Hepatitis C, Retina, Interferon, Ribavirin, Hemorrhage, Ischemia*

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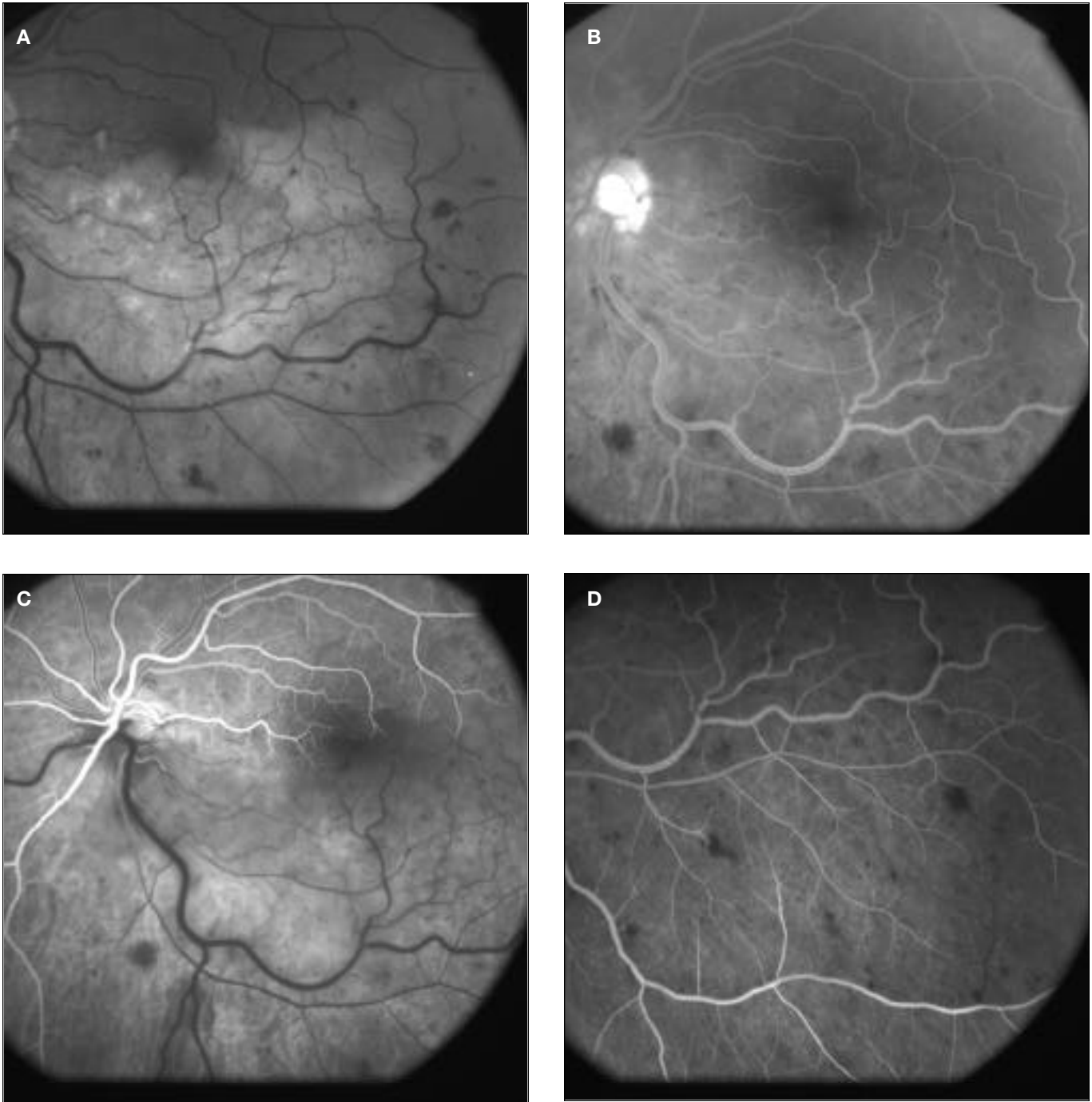
## INTRODUCTION

Chronic hepatitis C affects an estimated 3.5 million people in the United States (1). The only treatments for chronic hepatitis C approved by the US Food and Drug Administration are interferon-alpha monotherapy, interferon plus ribavirin, pegylated (PEG) interferon, or PEG interferon plus ribavirin. Systemic complications associated with the use of interferon include flulike symptoms consisting of myalgia, mild fever and chills, rashes, hypotension, peripheral neuropathy, and thrombocytopenia (2). Hemolytic anemia is the most common side effect of ribavirin (3). Conjunctivitis is the only reported ocular side effect for ribavirin. This reaction has been reported only with the aerosolized administration of the drug and most likely represents topical contamination of the conjunctiva (4). In contrast, reports have documented ocular complications

after the use of interferon (5-12). Ocular complications reported include ischemic optic neuropathy (5, 6), subconjunctival hemorrhage (7), trichomegaly (8), ischemic retinopathy manifested as cotton-wool spots and retinal hemorrhage (7-13), combined choroidal and retinal perfusion deficits (14), and cystoid macular edema (15). We report a case of a branch retinal artery occlusion associated with a branch retinal vein occlusion in a patient with chronic hepatitis C treated with interferon plus ribavirin.

## Case report

A 29-year-old man was referred to our clinic because of a history of sudden and painless loss of the superior retinal hemifield in his left eye about 1 week previously. Visual acuity was 20/20 in the right eye and 20/32 in the left eye. Biomicroscopic examination of the anterior segment



**Fig. 1 - (A)** Red-free photograph shows retinal whitening and multiple diffuse intraretinal hemorrhages. **(B)** Early phase fluorescein angiography shows delayed filling of the inferior branch of the central retinal artery and vein. **(C)** Late phase fluorescein angiography shows a pinpoint staining of the vein wall. **(D)** Peripheral retinal image shows mild ischemic capillaropathy.

was unremarkable bilaterally. Intraocular pressure was 12 mmHg in the right eye and 14 mmHg in the left eye. Fundus examination was unremarkable in the right eye. Fundus examination in the left eye revealed a whitening of the inferior and temporal quadrant of the retina sparing most

of the macular region. There were numerous intraretinal hemorrhages located in the inferior retina both nasally and temporally. Fluorescein angiography disclosed a significant delay in the filling of several arteriolar vessels inferiorly to the papilla and of the inferior branch of

the central retinal vein, which appeared dilated. Late during the fluorescein angiography there was a pinpoint staining of the vein wall. Systemic examination did not disclose any risk factors (arterial hypertension, smoking habit, fat plasma levels, coagulation parameters) for retinal vessel occlusion disease.

## DISCUSSION

Hepatitis C is the leading cause of chronic liver disease and the most common chronic bloodborne infectious disease in the United States (3). Chronic hepatitis C accounts for 8000 to 10,000 deaths annually and is the leading indication for liver transplantation in the United States (2). Recently a prospective noncomparative case series of 42 patients with hepatitis C treated by interferon plus ribavirin (16) showed that 70% developed retinopathy, which consisted of cotton-wool spots, hemorrhages, and microvascular abnormalities, which were transient in all patients. Moreover, authors hypothesized that the incidence of retinopathy may be falsely low, because the cotton-wool spots were transient and patients were not examined until they had been taking interferon for several months. There is the general impression that this kind of retinopathy seems to be secondary to ischemic changes. To our knowledge, however, this is the first case describing a nontransient ischemic retinopathy caused by a combined retinal artery and vein occlusion. The etiology of the retinopathy remains obscure, but several hypothesis have been proposed. Guyer et al (10) speculated that the deposition of immune complexes followed by lymphocyte infiltration in retinal capillaries may account for the ischemic changes observed in patients on interferon therapy. Nishiwaki et al (17, 18) suggested that activated leukocytes and the highly toxic substances generated resulted in the capillary infarction observed in interferon-associated retinopathy. Other authors (19, 20) demonstrated that patients receiving interferon therapy for hepatitis C had high

circulating levels of plasma activated complement (5), which is a potent intravascular aggregator of platelets. Japanese authors (21) documented idiopathic retinopathy in about 30% of untreated patients with hepatitis C and observed that there was a worsening of the retinopathy after interferon therapy. In untreated patients with hepatitis C retinopathy usually shows a higher incidence of retinal hemorrhages compared to treated patients, in whom cotton-wool spots are more frequent. A possible explanation for the high incidence of retinopathy in untreated Japanese patients with hepatitis C and the absence of retinopathy in untreated non-Japanese patients with hepatitis C might be explained by genomic variability in HCV. However, infection with HCV can be associated with a hypercoagulable state and with a variety of hematologic and immunologic abnormalities (22-24). Individuals with these abnormalities might be predisposed to develop ischemic retinopathy when placed on interferon therapy. Patients with hepatitis C treated with interferon and ribavirin on this regimen have a high risk of developing ischemic retinal changes and need a careful and frequent ocular follow-up. In our report, the symptomatic permanent visual field defect and decrease of central visual acuity developing following a branch retinal artery and vein occlusion event emphasizes the need for careful and regular ocular monitoring of patients receiving interferon for hepatitis C.

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