European Journal of Ophthalmology / Vol. 18 no. 2, 2008 / pp. 313-315

SHORT COMMUNICATION

Hepatitis C virus presumably associated bilateral consecutive anterior ischemic optic neuropathy

M. FODOR[1], V. NAGY[1], A. BERTA[1], I. TORNAI[2], G. PFLIEGLER[3]

[1]Department of Ophthalmology
[2]Division of Gastroenterology
[3]Division of Rare Diseases, Medical and Health Sciences Center, Faculty of Medicine, University of Debrecen, Debrecen - Hungary

PURPOSE. *To report a case of bilateral nonarteritic anterior ischemic optic neuropathy (NAION) in a hepatitis C (HCV) infected patient and demonstrate the relationship between HCV and the development of NAION.*

METHODS. *Case report.*

RESULTS. *A 43-year-old woman with chronic HCV infection and long-term euthyroid autoimmune thyroiditis suddenly lost vision in her right eye, and 6 months later in her left eye, due to NAION. Slightly elevated levels of aminotransferases suggested liver infection activity. Anti-HCV antibody was detected; the genotype of the virus was 1b and the viral RNA level was 1.8 x 106 IU/mL. Liver biopsy proved chronic active hepatitis (Ishak score grading: 7, staging: 2). Except for the elevated levels of antithyroid antibodies and a weak antinuclear factor, the detailed laboratory examinations (thrombophilia, cryoglobulin, anticardiolipin antibodies, co-infections) revealed no other abnormalities; a causative relationship between the underlying chronic hepatitis C and bilateral NAION therefore seems probable. The patient was treated with pegylated interferon and ribavirin for 1 year and a sustained viral remission could be achieved. Her vision has neither improved nor deteriorated further.*

CONCLUSIONS. *This appears to be the first reported case of bilateral NAION presumably caused by HCV infection. (Eur J Ophthalmol 2008; 18: 313-5)*

KEY WORDS. *Hepatitis C, Nonarteritic anterior ischemic optic neuropathy, Thrombophilia*

Accepted: September 17, 2007

INTRODUCTION

Hepatitis C virus (HCV) infection is manifested extrahepatically in about 50% of chronically infected patients. Dry eye syndrome, keratitis, nonarteritic anterior ischemic optic neuropathy (NAION), and ischemic retinopathy caused by HCV-induced vasculitis or interferon treatment are frequent; an association with Mooren ulcer is less equivocal (1-3). In HCV-associated NAION, cryoglobulin or anticardiolipin antibodies are always detected as putative pathogenic agents (4, 5).

Our purpose was to report a case in which the presumable relationship between HCV and the development of bilateral NAION can be demonstrated.

Case report

In September 2004, a 42-year-old woman had been admitted elsewhere with a sudden right visual loss. Her history included posttransfusion HCV positivity, acquired in 1990. In 1999, thyroglobulin (TG) and thyroperoxidase (TPO) autoantibodies developed, but the thyroid function

 1120-6721/313-03$25.00/0

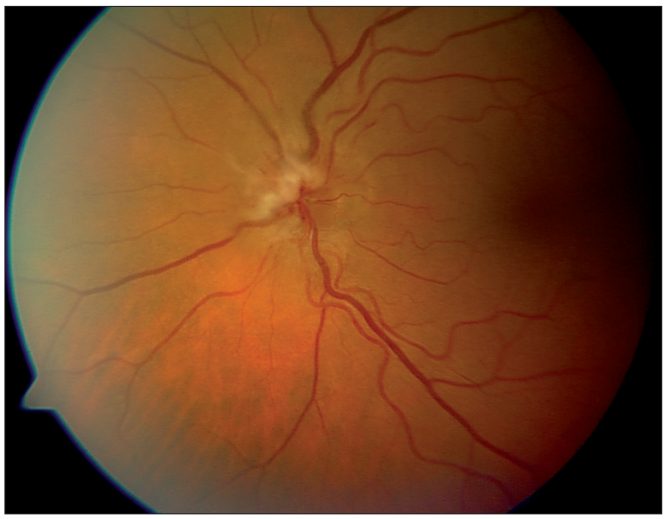

Fig. 1 - *Left eye with pale disc and hemorrhage after second attack.*

remained normal and no therapy was required. Best-corrected visual acuity (BCVA) was 20/80 in the right (RE) and 20/20 in the left eye (LE). A relative afferent pupillary defect was present in RE. Slit-lamp biomicroscopy revealed no differences and intraocular pressure was normal. Funduscopy in RE showed a swollen, pale disc with surrounding radial hemorrhages. Visual field tests demonstrated inferonasal nerve fiber bundle defects. Fluorescein angiography indicated sectorial defects on the optic disc in the early arterial phase, but hyperfluorescent filling developed in the end stage, with choroidal and retinal perfusion delay, without retinal pathology. There was evidence of right NAION. Intravenous methylprednisolone (1 mg/kg/day) and pentoxifylline (600 mg/day) were administrated for 7 days, with subsequent oral therapy (stepwise steroid reduction), but without any clinical improvement.

In March 2005, the patient presented with a sudden left visual disturbance. BCVA was 20/80 in RE and 20/25 in LE. The left optic disc swelling and peripapillary hemorrhage were consistent with a diagnosis of second-eye NAION (Fig. 1) without ischemic retinopathy. Visual field tests showed superior, mild nerve fiber bundle defects. The previous therapy was supplemented with hemodilution (6% hydroxy-ethylamyl-starch), oral vitamin C, and subcutaneous low molecular weight heparin (nadroparine, in prophylactic dose); then she was discharged on oral prednisolone, pentoxifylline, and aspirin therapy.

The result of routine laboratory tests, total blood cell count, erythrocyte sedimentation rate, CRP, lipids, and kidney functions were in the normal ranges, except for slightly elevated transaminase levels (ALAT: 34–63 IU/mL; normal: <40 IU/mL). Screening for hereditary (protein S, C, antithrombin, FV Leiden mutation, FII polymorphism, lipoprotein-a, vWFAg, and FVIIIC) and acquired thrombophilia (antiphospholipid antibodies, lupus anticoagulant, cryoglobulin, and homocysteine) furnished normal results. Platelet function and plasma viscosity were normal. Serologic tests for syphilis, HIV, CMV, EBV, toxocara, and toxoplasma infection were negative. Weak ANA positivity, a somewhat elevated immunocomplex level (442–358; normal <250), and high antithyroid antibody counts (anti-TPO: >3000, anti-TG: 356.3 IU/mL) with a normal thyroid function had been detected years earlier and were not correlated with the vascular events. Brain and orbit MRI were normal. Carotid and transcranial ultrasonographic and echocardiographic recordings excluded an embolic origin.

Chronic HCV infection was confirmed by the presence of anti-HCV antibody and a high titer (1.8×10^6 IU/mL) of HCV-RNA (genotype 1b) in the blood. Liver biopsy proved chronic active hepatitis (Ishak score grading: 7, staging: 2). Pegylated interferon and ribavirin therapy was administered, which resulted in sustained viral remission, i.e., 6 months after the end of treatment HCV-RNA remained negative. BCVA is 20/80 in RE and 20/20 in LE, with bilateral optic disc pallor and visual field defects.

DISCUSSION

We report a case of consecutive bilateral NAION as the only extrahepatic complication of chronic HCV infection. Since immunologic, thrombophilic, infective, and other well-known causes of NAION (1, 5) could be excluded, and our patient had no signs of vasculitis or cryoglobulinemia, a direct, and so far unknown effect of virus antigens seems plausible. In Mooren ulcer, cryoglobulin could likewise not be detected (2). Ischemic optic neuropathy related to chronic HCV infection is usually due to the presence of cryoglobulin (4), or anticardiolipin antibodies (5).

Propst et al found no correlation between HCV-RNA levels and episodes of papillitis, suggesting that not the virus alone, but rather cryoglobulin is responsible for this complication (4). However, in his patient the HCV-RNA levels were higher when paraplegia developed, pointing to the pathogenic role of the virus antigens themselves. In our

case, the virus titer was very high at the onset of the second eye NAION. Although no previous titers were available it is known that virus titer is relatively stable in HCV.

There are no guidelines as to how to treat or prevent HCV-related optic neuropathy. In our case, pentoxifylline could not prevent the second attack, and therefore antiplatelet therapy was also started subsequently. Since the virus titer was high at the onset and active disease was proved histologically, the initiation of antiviral therapy appeared to be reasonable, despite anecdotal reports of its possible effect per se in inducing NAION (1). However, in those cases the patients also had hepatitis C and other risk factors (1), and accordingly the pathogenic role of these underlying conditions cannot be completely excluded. In our case, NAION developed prior to therapy and no further deterioration occurred during treatment. The observation that Mooren ulcer improved in response to antiviral therapy might be of some relevance (2). The presence of antithyroid antibodies does not necessarily imply a cause-and-effect relationship between chronic HCV infection and NAION, since they were detected years earlier and remained at the same level, and no correlation was found with the vascular events. The finding that our patient had HCV genotype 1b is of special importance. In HCV infection with 1b genotype 32% of the cases have HCV-associated retinopathy versus 0% with 1a genotype (3). The immune response and target organ might be highly type-specific. Whether reduction of the virus titer has any beneficial effect in preventing NAION cannot be answered at present.

In the event of a sudden visual loss of unknown origin, the exclusion of chronic HCV infection appears desirable, together with close ophthalmic follow-up of patients with HCV genotype 1b infection.

Proprietary interest: None.

Reprint requests to:
Mariann Fodor, MD
Department of Ophthalmology
Medical and Health Sciences Center
Faculty of Medicine
University of Debrecen
Nagyerdei krt. 98
4012 Debrecen, Hungary
mfodor@dote.hu

REFERENCES

1. Vardizer Y, Linhart Y, Loewenstein A, et al. Interferon-α-associated bilateral simultaneous ischemic optic neuropathy. J Neuro-Ophthalmol 2003; 23: 256-9.
2. Wilson SE, Lee WM, Murakami C, et al. Mooren-type hepatitis C virus-associated corneal ulceration. Ophthalmology 1994; 101; 736-45.
3. Schulman JA, Liang C, Kooragayala LM, et al. Posterior segment complications in patients with hepatitis C treated with interferon and ribavirin. Ophthalmology 2003; 110: 437-42.
4. Propst T, Propst A, Nachbauer K, et al. Papillitis and vasculitis of the arteria spinalis anterior as complications of hepatitis C reinfection after liver transplantation. Transpl Int 1997; 10: 234-7.
5. Sinnreich M, Rossillion B, Landis T, et al. Bilateral optic ischemic neuropathy related to chronic hepatitis C-associated anticardiolipin antibodies. Eur Neurol 2003; 49: 243-5.