



Case report

A case of non-arteritic anterior ischemic optic neuropathy after completion of Harvoni therapy

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ABSTRACT

Purpose: To report the first reported case of non-arteritic anterior ischemic optic neuropathy (NAION) associated with the use of Harvoni (Gilead Sciences, Foster City, CA, USA), a newly approved treatment for Hepatitis C.

Observations: We report a case of NAION in a hepatitis C patient who completed Harvoni therapy just prior to presentation. Harvoni was suspected to be the causative agent given a lack of NAION risk factors in an otherwise healthy young patient.

Conclusions and importance: NAION is an acute, painless vision loss that typically affects adults over 50. The mechanism of NAION remains uncertain although numerous associations have been identified including certain medications. Harvoni, a combination drug of ledipasvir/sofosbuvir, is a recently FDA-approved treatment for Hepatitis C. To date, however, no ophthalmological side effects have been reported with its use. Continued surveillance of patients treated with Harvoni will be needed to determine if additional events are observed in the future.

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1. Introduction

Non-arteritic anterior ischemic optic neuropathy (NAION) causes acute, painless vision loss and is the most common acute optic neuropathy in patients over age 50. The mechanism of NAION remains uncertain, and numerous risk factors have been identified, including hypertension, hyperlipidemia, and obstructive sleep apnea.¹ Additionally, pharmaceutical agents including phosphodiesterase-5 inhibitors and interferons have been linked to NAION occurrence.^{2,3} Interferon therapy, however, has largely been replaced with newer hepatitis C treatment modalities. Harvoni (ledipasvir/sofosbuvir) is a combination of viral polymerase and protein function inhibitors which recently was FDA-approved for hepatitis C treatment. Although case reports regarding ophthalmological side effects, including NAION, exist for interferon therapy, to our knowledge, no such reports exist for Harvoni. We report a case of sudden vision loss in a hepatitis C patient within 3 days of completing therapy with Harvoni and ribavirin.

2. Case report

A 39-year-old Caucasian man presented with complaints of painless, progressive vision loss in his left eye over 24 hours. Past medical history was significant for hepatitis C secondary to blood transfusion and congenital heart disease status post heart surgery as a child. He completed a six month course of 90 mg/400 mg Harvoni daily and 500 mg ribavirin twice daily three days prior to the onset of his visual symptoms.

Visual acuity was 20/20 right eye and 20/30-1 left eye. His color vision appeared unaffected with a score of 10/10 in both eyes with Hardy-Rand-Rittler color plates. A 3+ afferent pupillary defect was noted in left eye. Fundus exam of the right eye revealed a 0.1 cup to disc with a “disc at risk” appearance. Left eye was remarkable for 360° hemorrhagic swelling of the optic disc with engorged venules (Fig. 1).

Initial labs were unremarkable with normal erythrocyte sedimentation rate and C-reactive protein (obtained because of the observed cotton wool spots). MRI brain/orbits and MR venography were unremarkable and showed no optic nerve enhancement or signs of demyelinating disease. Humphrey visual field examination was normal in the right eye and showed incomplete superior and inferior altitudinal defects in the left eye (Fig. 2).

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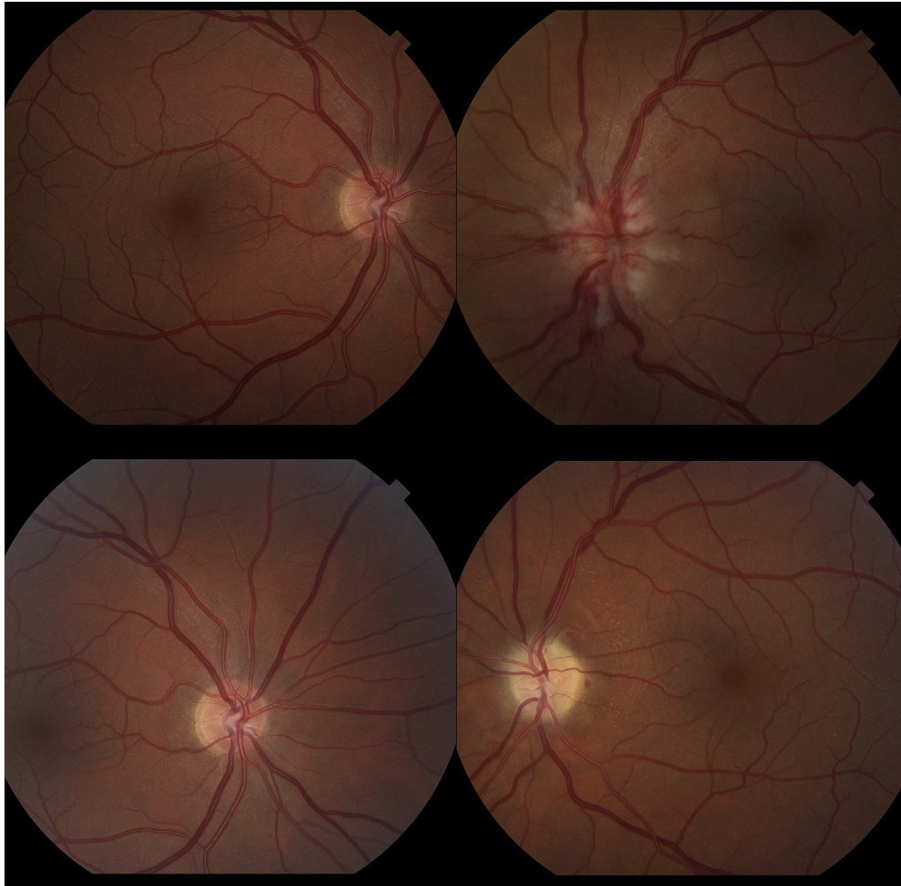


Fig. 1. – Fundus Photos at Presentation and Two Month Follow-up. Fundus photo at two weeks (top) showing “disc at risk” right eye and hemorrhagic swelling of optic disc left eye with cotton wool spots at the disk and retinal venular engorgement. Fundus photo at two months (bottom) showing “disc at risk” right eye and marked pallor of optic disc left eye.

Two months later, central visual acuity, color vision, and perimetry were unchanged. Fundus exam showed resolution of left optic disc swelling with diffuse pallor. His overall health remained excellent.

3. Discussion

We describe a patient with unilateral, painless, acute vision loss with visual field deficits and optic disc swelling. Given the lack of visual field recovery, marked disc pallor at follow-up, and disc at risk appearance of the fellow eye, we made a diagnosis of non-arteritic anterior ischemic optic neuropathy. It appeared unlikely to be Hepatitis C-related optic neuritis as viral RNA levels had remained negligible prior to and after presentation. It also appeared unlikely to be optic neuritis in general given the lack of optic nerve enhancement on MRI, lack of pain with eye movement, lack of visual field recovery, and onset of pallor. Of note, our patient had no history of vascular risk factors, obstructive sleep apnea or use of erectile dysfunction drugs. In this otherwise healthy young male patient with no known risk factors, we felt the history of recent completion of Harvoni and ribavirin therapy may have played a causative role.

The mechanism by which Harvoni might increase the risk for NAION is not known, but vasculopathic and other adverse effects of other antiretroviral agents (as in HAART therapy for HIV) could be informative. Protease inhibitors such as ritonavir have been implicated in the development of atherosclerosis, and reverse transcriptase inhibitors reduce mitochondrial function.⁴ While neither ledipasvir, a general inhibitor of viral function through

interaction with viral NS5A, nor sofosbuvir, an RNA polymerase inhibitor, are known to have similar side effects, the adverse effects of antiretroviral treatment for HIV was not recognized until several years later. Vasculopathic diseases such as hypertension and atherosclerosis are known risk factors for NAION, and mitochondrial dysfunction could worsen optic nerve damage and lessen RGC survival once the ischemia starts.

It is unlikely that ribavirin, an antiviral nucleoside analog, plays a role in NAION, given its longstanding use with no reported ocular side effects other than conjunctivitis.⁵ The reported cases of NAION with ribavirin were when it was used in combination with interferon, which alone has been associated with NAION.³ There are two reported cases of NAION occurring in HCV patients with no other risk factors.^{6,7} Our patient, however, had just completed his six month course of anti-viral treatment prior to his NAION presentation, making HCV infection an unlikely causative agent.

We present this case of NAION after completion of Harvoni to alert the medical community of this potential causative relationship, as Harvoni has been FDA-approved for hepatitis C for only one year. Continued surveillance of patients treated with Harvoni will be needed to determine if additional events are observed in the future.

Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

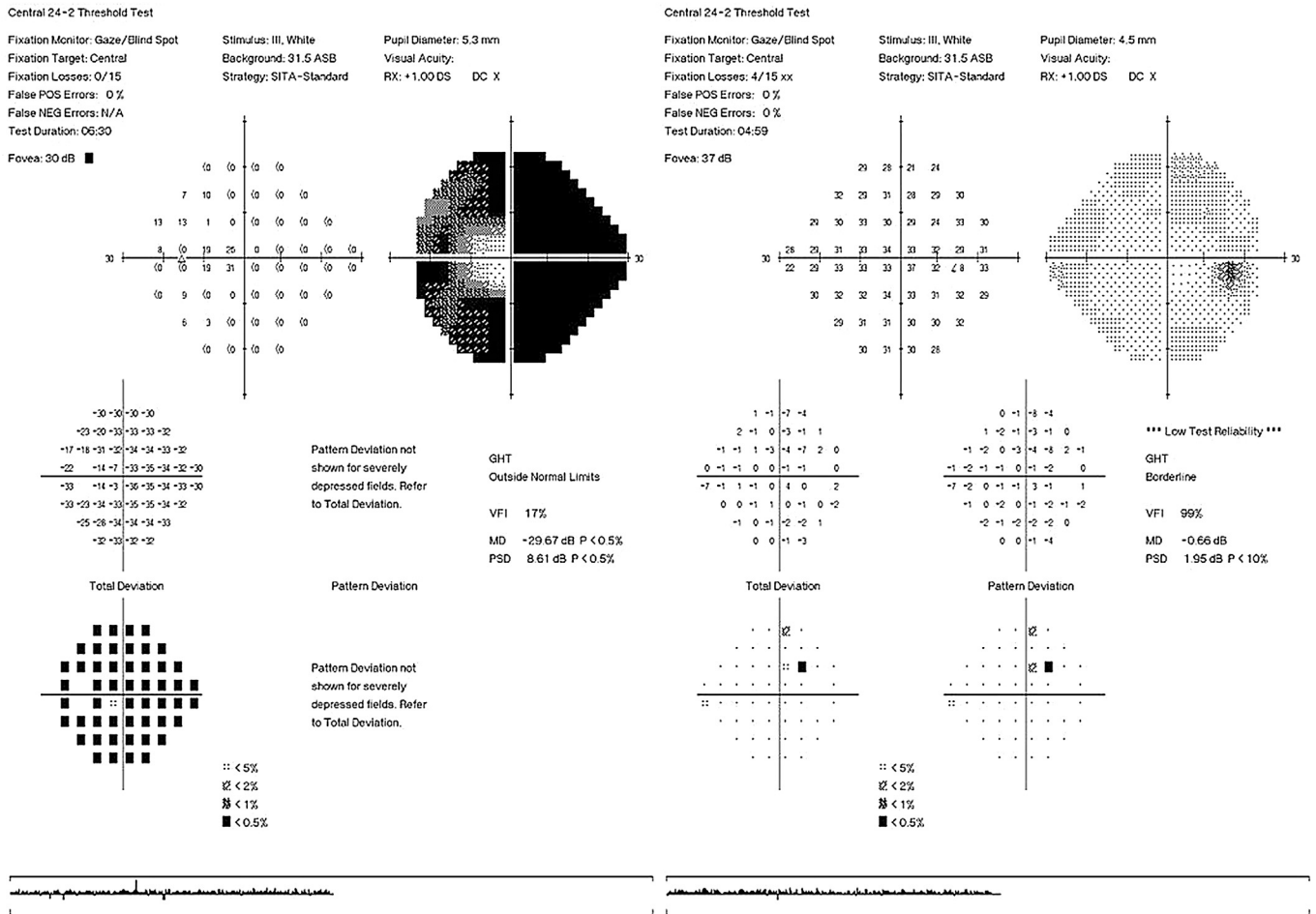


Fig. 2. – Humphrey Visual Field at Presentation. Humphrey visual field shows unremarkable right eye and global constriction left eye.

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Conflict of interest

All authors (NM, PSS) have no financial disclosures.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

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