CASE REPORT

Visual symptoms with Sofosbuvir in hepatitis C treatment — a case report from Pakistan

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Abstract

Hepatitis C virus infection is one of the main causes of chronic liver disease worldwide. The highly efficacious direct-acting antiviral (DAA) drugs licensed for therapy have revolutionised the treatment and are reported to have few side effects. Sofosbuvir is a pan-genotypic DAA that acts by inhibition of the hepatitis C NS5B polymerase. It has shown high efficacy in combination with several other drugs with low toxicity, a high resistance barrier, and minimal drug interactions with other hepatitis C DAA drugs. We describe a first of its kind case from Pakistan with visual disturbances caused by Sofosbuvir. A temporal relationship was observed between the treatment initiation and the onset of visual disturbances. The aim of this case report is to draw attention to the unanticipated side effects of this relatively new class of drug that have not been reported previously.

Keywords: Sofosbuvir, Hepatitis C, Colour vision, Pakistan.

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Introduction

Hepatitis C virus is a blood-borne viral infection that can cause acute and chronic liver disease. Deemed as a public health emergency at global level, it is also one of the major causes of hepatocellular carcinoma.[1] Introduction of highly effective, pan-genotypic oral, direct-acting antiviral (DAA) drugs (such as Sofosbuvir) has helped to overcome challenge of poor compliance and poor efficacy associated with the use of interferon-based therapy,[2] making them a widely used, viable treatment option.[3] Drug trials have reported headache, fatigue, and nausea as the most common adverse events associated with these regimens.[4]

We report a case of visual symptoms suspected to be associated with the use of Sofosbuvir in a middle-aged male patient with hepatitis C infection. Verbal informed consent of the patient has been taken for the publication of this case report; written consent could not be taken as the patient was lost to follow-up despite multiple attempts to reach him over phone.

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Case Report

A 39-year-old male patient was diagnosed as a case of genotype 3 chronic hepatitis C infection in December 2016, by a healthcare provider outside of our clinic (Figure 1). The patient belonged to the lower socioeconomic background and was employed as a firefighter. Upon diagnosis, he was prescribed Sofosbuvir and Ribavirin. After one week his treatment was discontinued due to the onset of chikungunya infection accompanied by visual symptoms. He reported having developed joint pain and fever with ocular symptoms described as night blindness, with green vision (chloropsia) at night. He did not visit an ophthalmologist as his symptoms resolved when hepatitis C treatment was discontinued. Information about developing vision disturbances with hepatitis C treatment was not reported to us by the patient until April 2017.

During his first visit to our family medicine clinic at The Indus Hospital, Korangi campus, Karachi, in January 2017, he was clinically stable, with no history of diabetes or hypertension. His blood workup revealed an APRI score of 1.1 with hypoalbuminaemia. In February 2017, he was initiated on a 24-week treatment regimen (Sofosbuvir 400mg daily, Ribavirin 1200mg daily (in divided doses) with folic acid 15mg per day), based on recommendations from national guidelines.[5]

In April 2017 (after week 5 of treatment) he started to develop visual symptoms. This was reported during an unscheduled clinic visit in the sixth week of treatment, following which the treatment was discontinued immediately. He was severely distressed due to night blindness and chloropsia after sunset, with difficulty in differentiating between contrasting colours, e.g. skin colour of a person. Other significant findings on clinical evaluation were abdominal distention, decreased urinary output with diarrhoea. However, he was alert, oriented with no motor or sensory deficits in the upper and lower

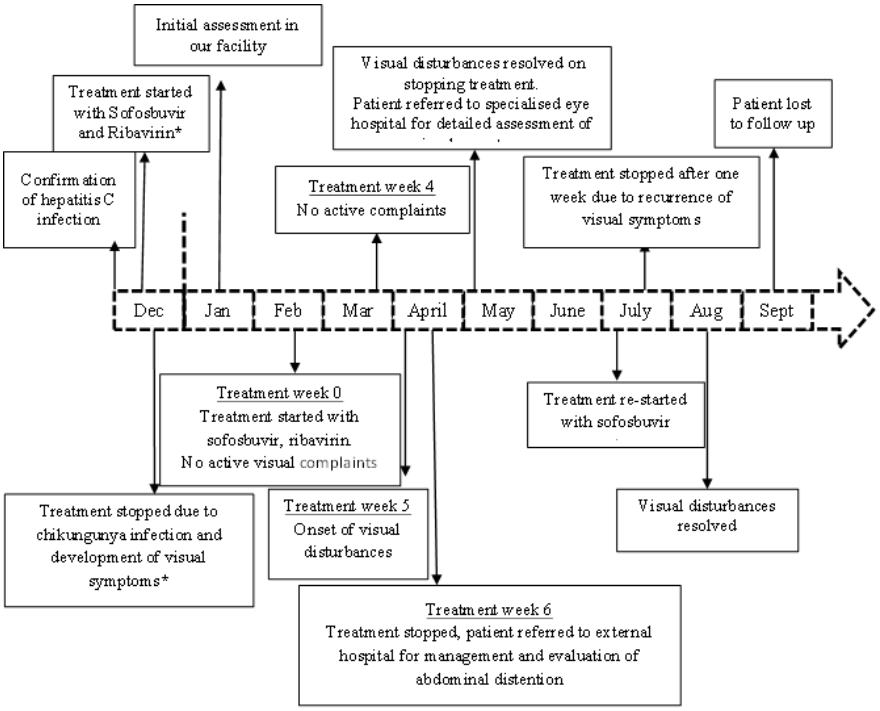

Figure: Timeline of patient's clinic visits, treatment initiation with the onset of visual symptoms
*Patient encounter at the primary care clinic outside our hospital.

limbs. There was no history of loss of consciousness, headache, diplopia, watery eyes, loss of peripheral vision or floaters. Personal history was insignificant for trauma or use of illicit drugs, whereas family history was unremarkable for colour blindness or night blindness.

With a provisional diagnosis of spontaneous bacterial peritonitis, he was referred to another hospital for further evaluation and inpatient care. Telephonic follow-up by our clinical team to monitor the status of visual symptoms revealed improvement in his complaints of night blindness and chloropsia on discontinuation of the treatment.

He returned to our family medicine clinic after four weeks (May 2017) of discontinuing the treatment. Even though no active vision disturbances were reported, he was referred to a specialised eye hospital for detailed assessment and clearance to restart hepatitis C treatment. The following ocular investigations were reported to have inconclusive results: visual acuity, colour perception (Ishihara), electrophysiology, visual field analysis, optical coherence tomography, intravenous fluorescein angiography, and fundus photography. Permission to publish images could not be obtained from the patient.

After 12 weeks of being off treatment, therapy was re-initiated as monotherapy with Sofosbuvir in July 2017. This was decided after consultation with gastroenterology, ophthalmology team and the patient. Within a week of restarting Sofosbuvir, the patient's visual symptoms returned, stopping the treatment altogether. Improvement of ocular symptoms was reported upon discontinuation of treatment assessed by the clinical team over phone; however, the patient was lost to follow-up despite multiple attempts to reach him via various means.

Discussion

Highly efficacious Sofosbuvir-based regimens are an emerging therapy to tackle hepatitis C epidemic. Drug trials conducted on predominantly Caucasian participants demonstrate these regimens to be well tolerated with minor side effects.[4,6] Even though our patient's first episode of visual symptoms coincided with the onset of chikungunya infection, temporal association of symptoms with treatment of hepatitis C infection points towards a drug-related aetiology. Therefore, careful clinical use and monitoring of Sofosbuvir-based regimens is essential. Any adverse effect should be documented and reported. This will provide data on side effects amongst different ethnic subsets.

There have been isolated reports of ocular symptoms such as the onset of uveitis, retinopathy, changes in ocular surface, and impairment of tear function in patients using Sofosbuvir. However, none of these studies report disturbance in colour vision.[7-9] These reports are predominantly amongst males, hence more data can reflect on the association with gender differences.

Limitations

In addition to limitations inherent in drawing conclusions from a single case, we were unable to rule out other causes due to lack of extensive laboratory workup during active phase of complaints. Similarly, external referral to specialised eye hospital led to time lag in symptoms and assessment. Additionally, lack of available data and specialist advice on how to continue treatment in patients with such side effects, dose-related response was not assessed.

Conclusion

With this report, we aim to highlight the unanticipated side effects associated with new drugs, such as Sofosbuvir, for ophthalmologists, gastroenterologists, primary care physicians and public healthcare specialists. We propose gathering further evidence about possible ocular adverse events associated with use of Sofosbuvir.

Disclaimer: Dr. Aliya Hasnain and Dr. Sabeen Shah are currently affiliated with Department of Medicine and Department of Family Medicine, Aga Khan University, Karachi, respectively.

Conflict of Interest: None to declare.

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