



Neuroretinitis with secondary retinal venous stasis in a patient with Schistosomiasis

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ARTICLE INFO

Keywords:

Neuroretinitis
Vein occlusion
Schistosomiasis

ABSTRACT

Purpose: Schistosomiasis, one of the most important parasitic diseases in humans, is caused by the trematode parasites. Common manifestations include gastrointestinal and genitourinary symptoms while ophthalmologic involvement is rare. Here we report a case of retinal vein occlusion and neuroretinitis secondary to a schistosomiasis infection.

Observations: A healthy 23-year-old man presented with headache and decreased vision in his right eye. Ophthalmic examination revealed a swollen disc, engorged retinal veins with retinal hemorrhages in all quadrants and macular edema with hard exudates ('macular star'). Fluorescein Angiography demonstrated a hot disk and an irregular pattern of filling defects along a major retinal vein. Further questioning revealed that a few months earlier, the patient had returned from an endemic area and was found seropositive for schistosomiasis.

Conclusion: In this case of neuroretinitis and secondary retinal venous stasis, the presumed underlying mechanism is associated with embolization of Schistosoma eggs or deposition of immune complexes. Although ophthalmic manifestations of schistosomiasis are rare, awareness should be maintained especially among world-travelers with unusual ocular findings.

1. Introduction

Schistosomiasis, also known as Bilharzia, is a parasitic disease caused by the trematode parasites of the genus *Schistosoma*. It is one of the most important parasitic diseases.^{1,2} There are differences in the geographical distribution of the 3 species which account for most of the disease burden in humans: *Schistosoma mansoni* and *Schistosoma haematobium* are found in the sub-Saharan Africa and the Middle East, while *Schistosoma japonicum* is found in China, Indonesia and parts of southeast Asia.³ Nevertheless, ongoing climate changes are introducing the parasites as well as their vector snails into currently non-endemic areas.⁴ Infection occurs in fresh water contaminated with cercariae, which are released from snails acting as intermediate hosts. Humans, the definitive hosts, are infected by penetration of cercariae through the skin and subsequent transformation into schistosomula, an immature form of the larva, which enter capillaries and lymphatic vessels.⁵ The adult parasite forms, which live within the veins, continually produce eggs that shed into the environment through feces or urine. Yet, egg migration into the end-organ lumen is a complex process, and the majority of eggs fail to reach the intestine or bladder and remain permanently

embedded in host tissues.⁶ Schistosomiasis morbidity is caused primarily by an excessive inflammatory response to the parasites, notably to the trapped eggs.⁷

Acute schistosomiasis is seen in people who are infected for the first time and can manifest as fever, malaise, myalgia, fatigue, cough, diarrhea and hematuria, depending on the *Schistosoma* species.⁸ In states of chronic infection, the host's immune response to the eggs can result in a granulomatous reaction at the sites of maximal egg deposition leaving fibrotic plaques in host tissues which cause chronic morbidity.^{9,10} Fibrosis most commonly affects the gastrointestinal tract and liver, resulting in a life-threatening hepatosplenic disease.¹¹

The reported prevalence of neurologic involvement in schistosomiasis is 3–5% (*S. japonicum*) but it is presumably underdiagnosed.¹² In post mortem studies, ectopic migration of eggs to the central nervous system (CNS) is described in up to 13% of the patients but can for itself remain asymptomatic or results in various neurological symptoms.^{13,14} The mechanism of egg deposition outside the gastrointestinal and urinary systems is unknown and may reflect either aberrant migration of worms close to the CNS and in situ oviposition or embolization of eggs from the portal system.¹⁵

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<https://doi.org/10.1016/j.ajoc.2022.101355>

Received 9 May 2021; Received in revised form 9 August 2021; Accepted 22 January 2022

Available online 29 January 2022

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There are only a few case reports describing ophthalmic involvement in schistosomiasis. Sporadic evidence of *Schistosoma* infections describes diverse ocular manifestations. These include conjunctivitis, periorbital edema, myositis of the extra ocular muscles,¹⁶ macular edema,¹⁷ retinal pigment epithelium inflammation,¹⁸ choroiditis¹⁹ and optic nerve atrophy.²⁰

Here we report a case of retinal involvement in patient with schistosomiasis to raise awareness to the potentially devastating ocular morbidity in schistosomiasis.

2. Case report

2.1. Symptoms and ophthalmologic examination

A 23-year-old man was referred due to complaints of blurred vision in his right eye accompanied by periocular discomfort and headache. Symptoms had commenced with headaches 7 days prior to his admission and have gradually progressed. He had no previous vision problems in either eye. He was otherwise healthy, with no known chronic conditions and no regular medications.

Best-corrected visual acuity (BCVA) was 6/15 in his right eye (OD) and 6/6 in his left eye (OS). A maculo-vesicular rash was noted on his forehead and right periocular area. Relative afferent pupillary defect was weakly positive in the right eye. In each eye, the anterior segment was unremarkable with no signs of inflammation, and the intraocular pressure (IOP) was normal. Ophthalmoscopic examination of the right eye (Fig. 1) showed largely clear vitreous except for few small snowballs in the inferior vitreous and subtle peripapillary opacities. The optic nerve head was swollen 360° with adjacent cotton wool spots and retinal hemorrhages. Retinal veins in all four quadrants were mildly dilated. There was macular edema with a perifoveal star configuration of exudates. Ophthalmoscopic examination of the left eye was normal.

2.2. Ocular imaging and visual field test

Spectral domain optical coherence tomography (SD-OCT) demonstrated small hyperreflective foci in the vitreous cavity and confirmed the presence of intra-retinal and subretinal fluid predominantly in the nasal part of the macula (Fig. 2, C-D).

Fluorescein angiography (FA) demonstrated dilated veins in all four quadrants in the right eye. Of note, an irregular filling pattern was observed in the inferior retinal vein persisting through late phases, and there was late optic disc leakage (Fig. 3).

Humphrey visual field test (SITA FAST 24-2) demonstrated blind spot enlargement and a temporal arcuate scotoma with VFI 84% in the right eye. Normal test results with VFI 99% were obtained from the left eye.

2.3. Systemic workup

Brain computed tomography (CT) was normal. Brain MRI with

gadolinium contrast demonstrated pathological enhancement of the right intra-orbital optic nerve. Chest X-ray demonstrated multiple various-sized round opaque lesions in both lungs, which were verified on CT demonstrating focal ground-glass opacities with bilateral involvement. Such CT finding can be due to a wide etiology including opportunistic and non-opportunistic infections, chronic interstitial disease and acute alveolar disease. In this case, findings were interpreted as atypical lung infection (Fig. 4).

2.4. Laboratory tests

Complete blood count was within normal range excluding isolated eosinophilia of 1300 cells/microliter. Blood chemistry values were within normal range. Blood sedimentation rate was 13 mm/hour. Blood cultures were negative for bacteria and parasites, and so were microscopic examinations of stool for ova and parasites. Negative results were obtained from a wide infectious disease panel, including HIV, bartonella, syphilis, toxoplasma, toxocara, strongyloides, leptospirosis and filaria. There was no evidence of recent infection with herpes simplex type 1 and 2, Epstein-Barr virus, cytomegalovirus, varicella zoster or West Nile virus. RT-PCR from 24-h urine collection for schistosomiasis was negative.

2.5. Further medical history

Due to suspicion of a systemic infection, detailed history of relevant risk factors was taken. This revealed that the patient had volunteered in agricultural work at Dire Dawa, Ethiopia one year prior to his clinical presentation, when he had suffered from fever and rash. He was then diagnosed with Dengue fever, which resolved without complications. Later on, the patient traveled to northern-central Ethiopia and Uganda with friends, of whom 3 individuals were infected by schistosomiasis. This prompted serologic testing for schistosomiasis after his return to Israel, which was positive. He was subsequently treated with a single dose of 2,400mg of oral praziquantel, administered 2 months before his admission to our department.

Based on the previous positive serology for schistosomiasis, ipsilateral cutaneous manifestations, chest CT findings and lack of evidence supporting other causative infections, a high suspicion for schistosomiasis with an atypical ocular manifestation was raised.

2.6. Treatment and follow up

The patient was treated with oral praziquantel 2400 mg/d for 2 days and oral prednisone 60 mg/day for 2 weeks with slow tapering. During the treatment course, visual acuity gradually improved to 6/7.5 and absorption of retinal edema was seen after 1 week (Fig. 5a). Further improvement was noticed after 3 weeks with visual acuity of 6/6.5 and resolution of the retinal fluids on repeat OCT imaging (Fig. 5b). The patient remained stable at all follow-ups for at least 2 years after his first presentation. The left eye remained uninvolved.

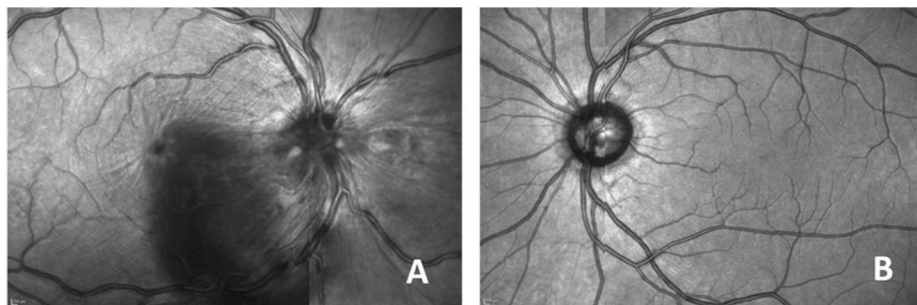


Fig. 1. Infrared fundus photographs at presentation. Note the blurred disc borders, macular folds implying macular edema, and mild vein engorgement in the right eye (A) comparing to the left eye (B).

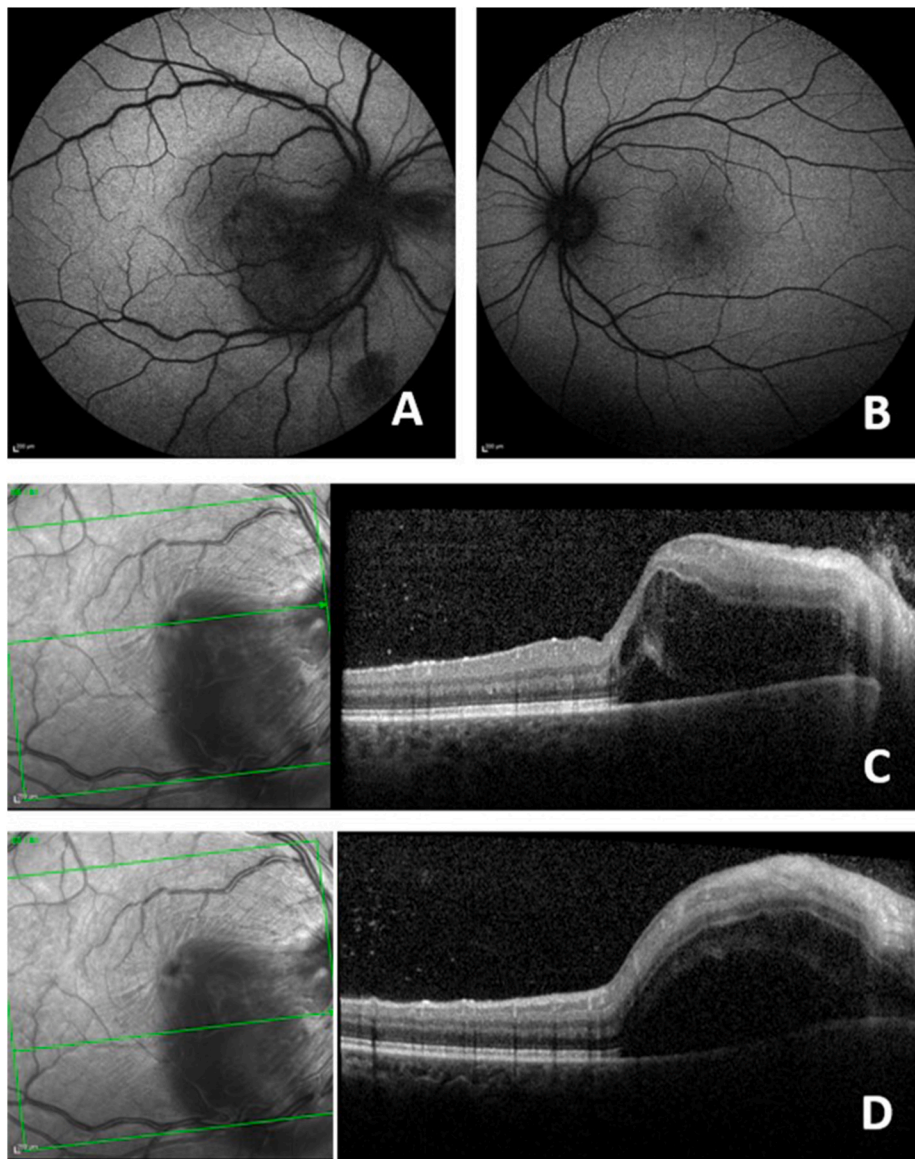


Fig. 2. Fundus Autofluorescence and spectral domain optical coherence tomography (SD-OCT) at presentation. Fundus Autofluorescence demonstrates blurred disc borders, hypoautofluorescence in the macula, and mild vein engorgement in the right eye (A) comparing to the left eye (B). SD-OCT of the right eye demonstrates vitreous hyperreflective foci, cystoid macular edema predominantly in nasal part of the macula with foveal involvement, and subretinal fluid (C,D).

3. Discussion

We report a unique presentation of ocular Schistosomiasis that involved unilateral swollen disc, cystoid macular edema, mild venous engorgement in all quadrants with an irregular intraluminal filling and a pathological enhancement of the right intra-orbital optic nerve on brain MRI with gadolinium. This study joins the scarce literature reporting on ophthalmic presentations of schistosomiasis. Ocular pathology caused by schistosoma is usually a diagnosis by exclusion, and only rarely, in postmortem or on enucleated eyes, the diagnosis can be confirmed by histopathology. Therefore, the underlying pathophysiologic mechanisms that lead to schistosoma ocular manifestations are yet to be determined. One suggested option involves retinal embolization by the parasite eggs present in the systemic circulation. Alternatively, immune complex depositions in response to the egg antigens could be another trigger for the ocular manifestations. A few models have been developed in order to investigate this issue. In one model,²¹ hamsters infected with *Schistosoma mansoni* cercariae were sacrificed at different periods post infection. Neither eggs nor granulomata were detected in eye sections.

In contrast, deposition of *S. mansoni* antigen in ocular tissues was revealed in 35% of the infected hamsters, mainly involving the sub-epithelial conjunctiva, subchoroidal compartment and sclera. Histologic examination of the retina revealed edema and loosening of the innermost layers, and later on a hyperplastic reaction, formation of retinal folds and destruction of the retinal architecture.²¹ Interestingly, in a different experiment with a murine neuroschistosomiasis mansoni model,²² the authors did find *S. mansoni* eggs and granulomas in the bulbar conjunctiva, lacrimal gland, choroid and corneoscleral limbus of infected mice.

The combination of findings in the case reported here, including retinal venous engorgement in four quadrants with irregular intraluminal filling alongside leakage from the optic disc, exudates, papillomacular-bundle involvement and retinal edema, forms a clinical picture consistent with retinal venous stasis that overlaps with neuroretinitis. We presume this overlapping presentation arises from the proximity of the neurological and venous structures at the lamina cribrosa. Theoretically, any disorder with an inflammatory component in this anatomical location, whether due to schistosoma ova or immune

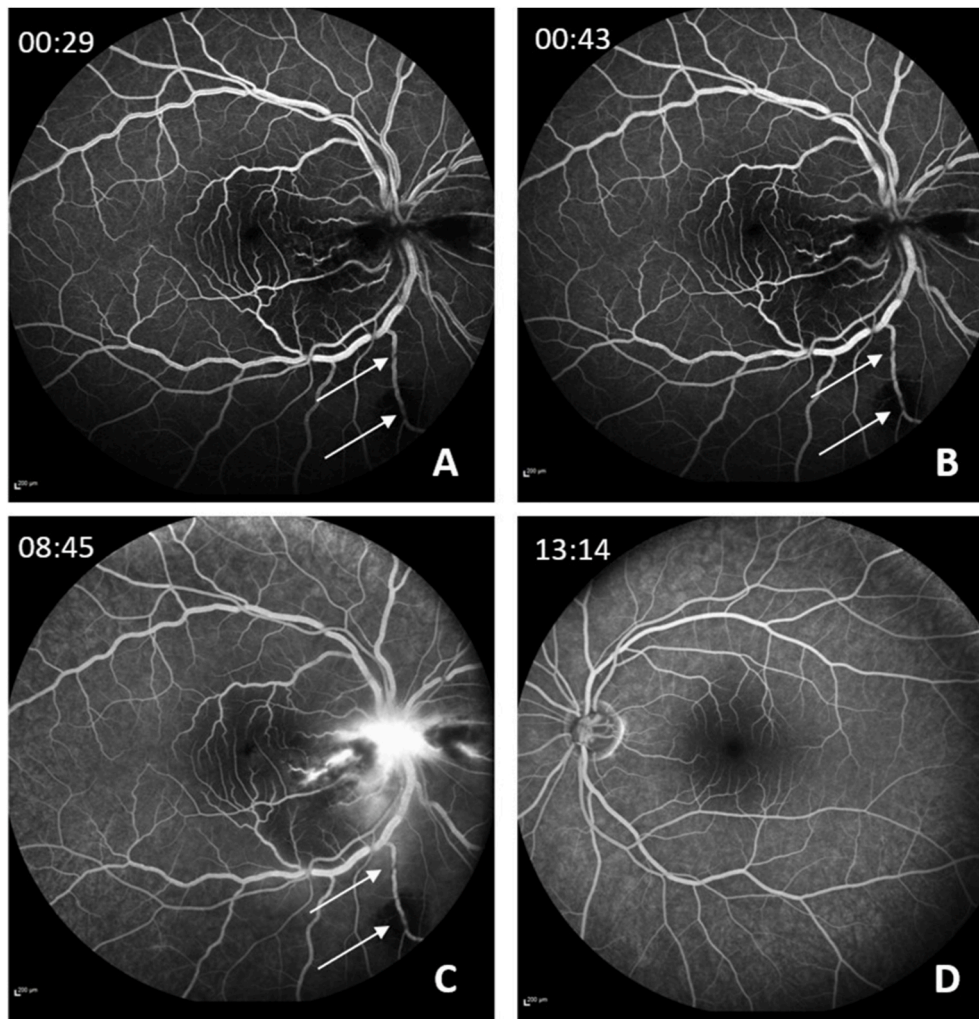


Fig. 3. Fluorescein angiography (FA). Upper left- time of photo taken (seconds). FA of the right eye (A–B) demonstrates hypofluorescent areas near the disc corresponding to cotton wool spots, hemorrhages and vein engorgement in four quadrants, comparing to the left eye (D). Later (C), leakage from the right optic disc is demonstrated. Arrows indicate irregular filling defects in a retinal vein.

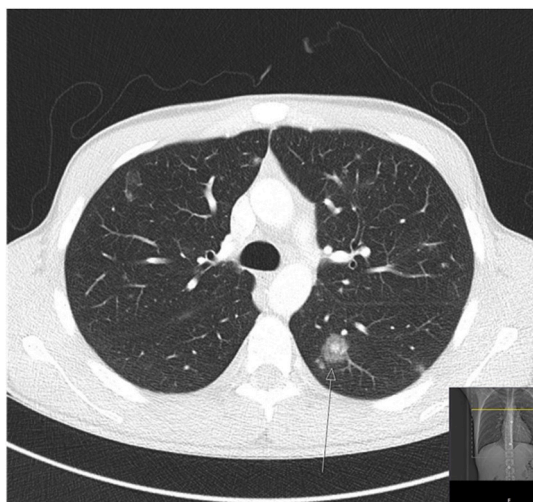


Fig. 4. Chest computed tomography (CT). A pattern of focal ground-glass opacities with bilateral involvement was demonstrated by chest CT, the largest of 1.7 cm (arrow).

complex deposition, could lead to such a clinical picture.

Ocular schistosomiasis may be either rare or underdiagnosed. The main concern in endemic areas is prevention and treatment of the systemic disease, including its life threatening complications. Therefore, the prevalence of ocular manifestation may be much higher than reported in the literature. We suggest that a high index of suspicion in patients with unusual ophthalmic findings who live or have traveled to endemic areas remains important, since schistosoma may have a sight threatening potential but which may be easily treated.

Conflicts of interest

No conflict of interest exists.

Funding

No funding was received for this work.

Intellectual property

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have

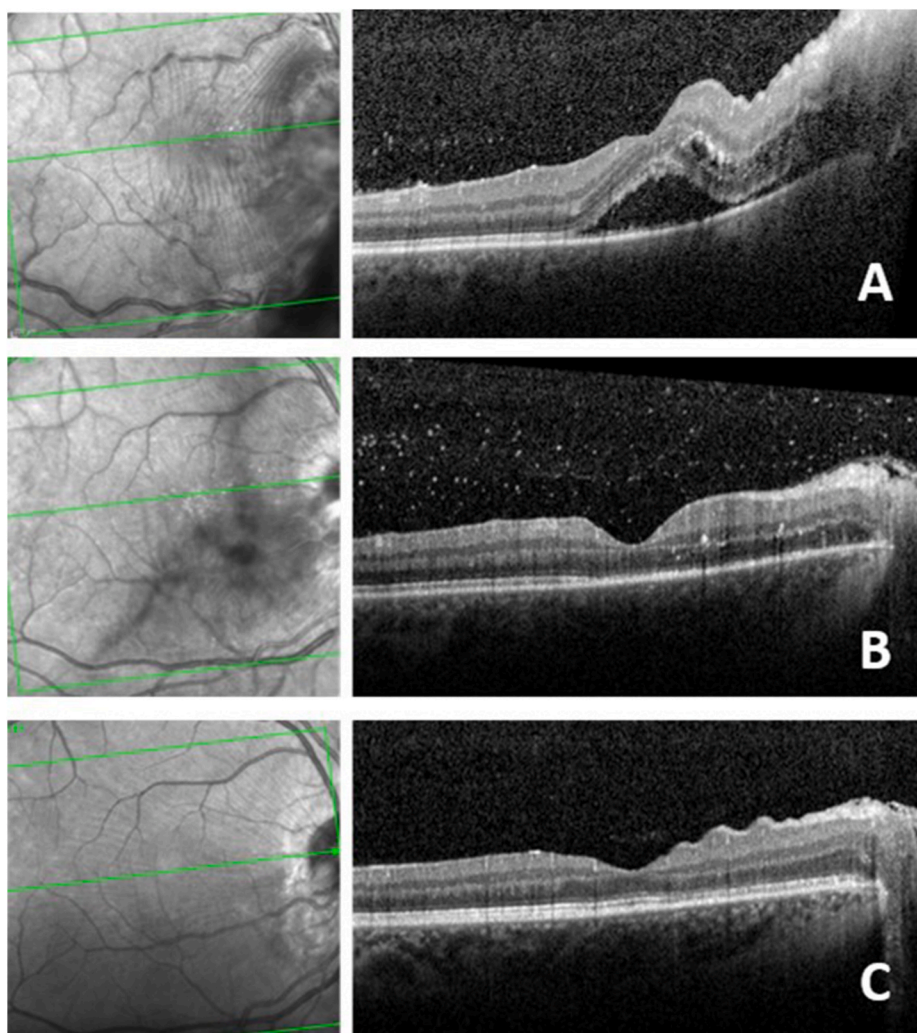


Fig. 5. SD-OCT following treatment. Right eye SD-OCT 1 week (A), 3 weeks (B) and 8 weeks (C) after treatment. Note the decreased vitreal inflammatory activity and absorption of macular edema and subretinal fluids.

followed the regulations of our institutions concerning intellectual property.

Research ethics

Written consent to publish potentially identifying information, such as details or the case and photographs, was obtained from the patient.

Authorship

All listed authors meet the ICMJE criteria. We attest that all authors contributed significantly to the creation of this manuscript, each having fulfilled criteria as established by the ICMJE.

We confirm that the manuscript has been read and approved by all named authors.

We confirm that the order of authors listed in the manuscript has been approved by all named authors.

Contact with the editorial office

The Corresponding Author declared on the title page of the manuscript is:

Patient consent

Consent to publish this case report has been obtained from the patient in writing.

Funding

No funding or grant support.

Authorship

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

Declaration of competing interest

The following authors have no financial disclosures: H.P, Y.V.A, E.N.

Acknowledgements

None.

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