A Case Report of Seasonal Hyperacute Panuveitis Associated with Human Herpes Virus 7 and *Acinetobacter Baumannii*

Kharel Sitaula R,[1] Karki P,[1] Katuwal N,[2,3] Gurung H,[4] Shrestha E,[4] Shrestha A,[2,3] Shrestha A,[5] Sharma A,[1] Joshi SN,[1] Shrestha R,[2,3,6] Upadhyay MP[7]

[1]Department of Ophthalmology,
B. P. Koirala Lions Centre for Ophthalmic Studies,
Maharajgunj Medical Campus, Institute of Medicine,
Tribhuvan University, Kathmandu, Nepal.

[2]Center for Infectious Disease Research and Surveillance, Dhulikhel Hospital, Kathmandu University Hospital, Dhulikhel, Nepal.

[3]Molecular and Genome Sequencing Research Lab,
Dhulikhel Hospital Kathmandu University Hospital,
Dhulikhel, Nepal.

[4]Himalaya Eye Hospital, Pokhara, Nepal.

[5]Department of Opththalmology,
Dhulikhel Hospital, Kathmandu University Hospital,
Dhulikhel, Kavre.

[6]Department of Pharmacology,
Kathmandu University School of Medical Sciences,
Dhulikhel, Nepal.

[7]Children Hospital for Eye,
ENT and Rehabilitation Services,
BP Eye Foundation, Bhaktapur, Nepal.

Corresponding Author

Ranju Kharel Sitaula
Department of Ophthalmology,
B. P. Koirala Lions Centre for Ophthalmic Studies,
Maharajgunj Medical Campus, Institute of Medicine,
Tribhuvan University, Kathmandu, Nepal.
E-mail: helloranju50@gmail.com

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ABSTRACT

Seasonal Hyperacute Panuveitis (SHAPU) is a rapidly vision-threatening uveitis reported predominantly in Nepal, with uncertain aetiology and suspected association with white moths. We report a 36-year-old electrician who developed seasonal hyperacute panuveitis following accidental exposure to white moths while repairing a tube light. He presented with severe vision loss, corneal haze, anterior chamber inflammation, and vitritis. Vitreous cultures were negative for bacterial and fungal pathogens, but polymerase chain reaction detected Human Herpesvirus 7, requiring valganciclovir. Although the patient initially showed signs of recovery, surgery was required to treat secondary angle-closure glaucoma. Progressive endothelial cell loss and cataract formation were successfully managed with phacoemulsification and intraocular lens implantation. Metagenomic sequencing of vitreous samples later identified Acinetobacter baumannii, although no additional treatment was required. After two years of follow-up, vision remained stable. This case report highlights significance of molecular diagnostics in detecting uncommon bacterial and viral infections in seasonal hyperacute panuveitis and improving understanding of its complex aetiology.

KEY WORDS

Seasonal hyperacute panuveitis, White moth, Ocular foreign body, Corticosteroids, Cataract surgery

INTRODUCTION

Rapid vision loss is a common presenting symptom in the catastrophic ocular illness in Nepal-Seasonal Hyperacute Panuveitis (SHAPU).[1] Although the precise cause is still unknown, there is evidence that white moths are associated with its seasonal appearance.[2] Despite several attempts, the definitive cause of SHAPU remains a mystery. Hypothesis range from viral or bacterial infections to autoimmune reactions to a cytokine storm induced by an agent that the moths carry.[3] This case study describes a singular case of SHAPU in an electrician who had an accidental fall of a white moth in his eyes while at work. Prompt medical management, laser peripheral iridectomy, and later cataract surgery restored eyesight despite substantial visual impairment at the presentation time. The case report also highlights the detection of dual microbes-Human Herpes Virus HHV-7 and Acinetobacter baumannii in the vitreous fluid and begs concerns regarding their role in the pathogenesis and etiology of SHAPU.

CASE REPORT

A 36-year-old male, electrician by profession, presented to the emergency department in September of 2021 in Pokhara, Nepal, with a history of sudden fall of white

moths over his face from the tube light he was trying to repair as a part of his work.

He developed a foreign body sensation over his right eye and redness after 2 hours, for which he immediately visited the emergency unit at the tertiary level Eye Hospital in Pokhara. On examina-tion, his vision was 6/6, N6 in the right eye. The patient was diagnosed with mild SHAPU based on the SHAPU classification system. The other eye was completely normal. His right eye was irrigated with 100 ml of balanced salt solution; prophylactic topical antibiotics with topical cortico-steroid drops were prescribed, and he was advised to return in three days. However, his redness increased after two days, and his vision decreased. He was referred to our ophthalmology depart-ment which is a university hospital based tertiary eye care centre situated at Kathmandu, for further management.

He visited us on the 7th day of the onset of eye problems, and he had visual acuity of 5/60, N8 in the right eye, and 6/6, N6 in the left eye. Slit lamp examination revealed a hazy cornea with multi-ple Descemet folds (Fig. 1A) at the center and temporal quadrant. The anterior chamber had 4+ cells and 2+ flare. Iris had diffuse atrophy (Fig. 1A) with the mid-dilated pupil. The vitreous had 2+ cells and haze; however, the central and peripheral retina appeared normal through the hazy vitreous. The intraocular pressure was 23 mmHg and 18 mmHg in the right and left eye, respectively. Ultrasonography of the right eye supported the vitritis with a flat retina (Fig. 1B). We diagnosed him with a severe stage of SHAPU. The serological, CBC, ESR, HIV serology, syphilis tests (TPHA & VDRL) and RBS blood examinations performed at baseline were within normal limit.

The patient was immediately taken for a diagnostic vitreous tap, followed by intravitreal injections combining vancomycin (1mg/0.1ml), ceftazidime (2.25/0.10 mL), and dexamethasone (0.4gm/0.1ml), along with subconjunctival gentamycin (40mg/0.4ml) and dexamethasone (4mg/0.4ml).

The vitreous fluid did not yield any bacteria or fungi on culture. Real-time polymerase chain reaction (PCR) analysis revealed the herpes simplex virus (HSV) family. The PCR analysis could not detect the presence of HSV 1, 2, and Varicella Zoster virus, but surprisingly, it detected the pres-ence of Human Herpes Virus 7 (HHV-7). (Fig. 2 top). The residual samples were refrigerated at -40oC for future metagenomics next generation sequencing.

The patient was started on tablet valgancyclovir 900 mg twice daily. After two weeks, his visual acuity improved to 6/36, with N8 in the right eye. The cornea appeared relatively clear, but there were multiple areas of Descemet's fold. The anterior chamber reaction showed signs of resolution; the presence of seclusion pupillae and cataracts with diffuse iris atrophy was visible. The vitreous started clearing, and the retina was normal (Fig. 3A & 3B)

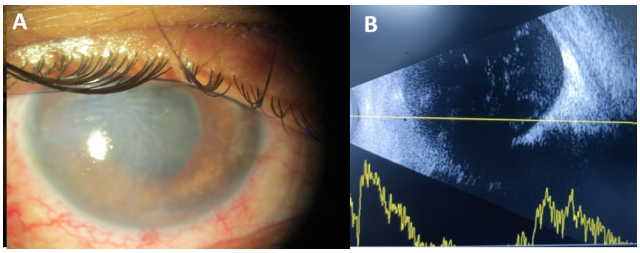

Figure 1. Clinical photograph of the right eye showing conjunctival congestion, corneal haze with multiple descemet's striaes and iris atrophy (A). The ultrasonography B+A scan revealed multiple hyperechoic shadows in the mid and posterior vitreous with intact retina (B).

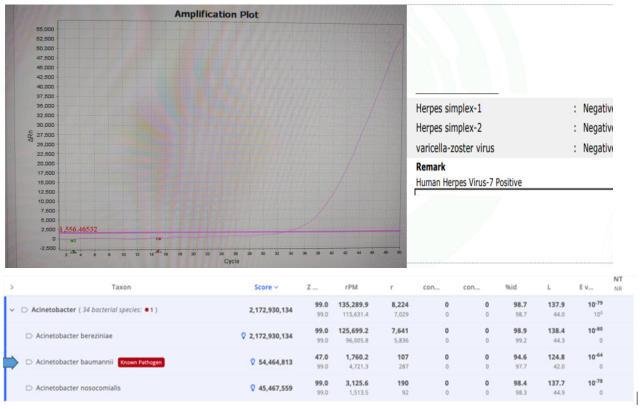

Figure 2. The real-time PCR amplification plot showing the detection of Human Herpes Virus- 7 (pink colour curve) with 36 as Ct value (Top). The figure below depicts hits from the heatmap from sequencing of RNA library of the vitreous samples showing the presence of Acinetobacter species using the threshold of NT rPM (nucleotide reads per million) <=10 and NT L (alignment length in base pairs: length of the aligned sequence) <=50 where the background model from healthy eye was the control sample (Bottom).

His antiviral medications were maintained once daily. However, after two months, he presented with sudden pain and redness in the same eye associated with headache. He had an edematous cornea with a shallow anterior chamber suggestive of secondary angle closure glaucoma with pu-pillary block. (Fig. 3C) Antiglaucoma agents (timolol maleate 0.5%, brimonidine 0.2%) were given through topical and acetazolamide tablets 500mg by oral route, and the next day, he underwent surgical peripheral iridectomy with anterior chamber reformation and an air bubble was left in situ to maintain the anterior chamber contour (Fig. 3D).

At his next visit in 6 months, his BCVA was 1/60 due to the cataract progression (Fig. 3E). We planned for the cataract surgery, but on specular microscopy, his endothelial count was grossly reduced to 1059 cells/mm^2 with 57% hexagonocity in the right eye, while the left eye had 2704 cells/mm^2 cell count with 64% hexagonocity (Fig. 3F). He underwent phacoemulsification with posterior chamber foldable intraocular lens implantation under topical anesthesia with additional special precaution with cohesive viscoelastic to protect the endothelium. After a month of cataract (Fig. 3G), his BCVA was 6/12 in the right eye, there was clarity in the media and fundus appeared normal.

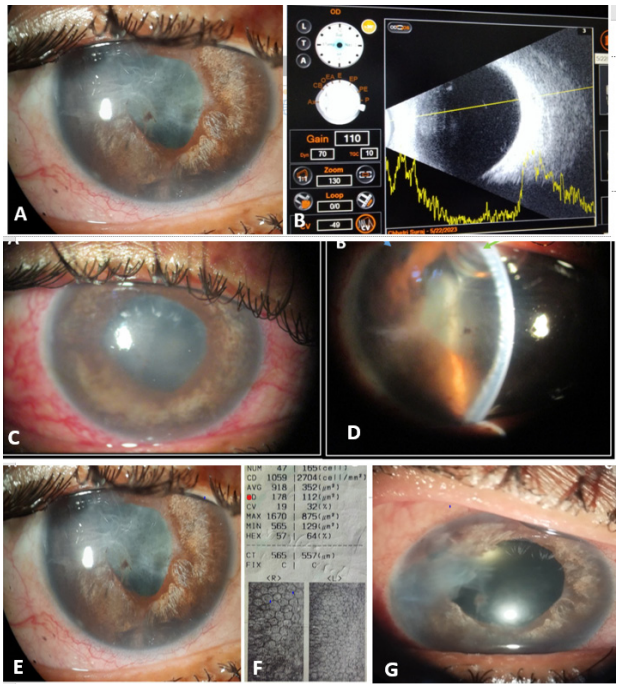

Figure 3. The clinical photograph of the right eye showing the presence of multiple descemet's folds in the cornea, diffuse iris atrophy, 360°synechiae, and cataractous lens (A) and the ultrasonography scan showing the residual hyperechoic shadows in the mid and posterior vitreous cavity with flat retina (B). Picture C is the diffuse view clinical photography showing circumcorneal congestion with the hazy cornea, a fixed mid-dilated pupil with synechia and a shallow anterior chamber (C). Picture D is the slit view photography with intact peripheral iridectomy and air bubble in situ (green arrow) after surgical iridectomy and anterior chamber formation (D). Picture E is the clinical photography of cataractous lens, iris atrophy with corneal opacities before surgery (E); Specular microscopy with low endothelial count of 1059 cells/mm2 (F); After phacoemulsification with posterior chamber intraocular lens and central clear cornea (G).

His preserved vitreous sample (around 150ul) was sent to Center for Infectious Disease Research and Surveillance, Dhulikhel Hospital Kathmandu University Hospital, Dhulikhel, Nepal for metagenomic next gereration sequencing. Nucleic acid was extracted from the ocular fluid. This was followed by library prepartion (along with negative controls) and sequencing in Illumina iSeq100. The evaluation of genomic data, in Chan Zuckerberg ID (now SeqToID) detected Acinetobacter baumannii (Fig. 2, bottom). This evaluation used background model from the ocular samples of healthy controls.

No additional treatment was opted for this bacteria. The patient has been under regular follow-up for the past two years, and his vision and endothelial counts are maintained at 6/12 and 1059 cells/mm^2, respectively.

DISCUSSION

This case is the first of its kind and presents many unique features. The first report of SHAPU related to a professional hazard, where an electrician had direct contact with the white moth while repairing the tube light, followed by immediate development of the symptoms. This scenario suggests using protective glasses for electricians working in the SHAPU endemic zones. The second uniqueness is the report of the clinical course of a SHAPU case with the longest follow-up, thus offering important information about the condition's long-term complications and outcome.

Moreover, this is the first report of SHAPU induced by HHV-7 and goes beyond the previously identified viral triggers.[4,5] There are minimal reports on HHV-6 and 7 induced uveitis, and majority are from Japan.[6-8] High copy numbers of HHV-6 DNA (ranging from 4.0 X 103 to 5.1 X 106 copies/mL) have been reported in 2% (7/350) patients with uveitis, implying the possibility of viral reactivation or replication in the eye.[6,7] There was a report on the detection of HHV-6B and HHV-7 associated choroiditis, but the patient was under acute myelogenous leukemia-induced immunosuppression, next reported case was of a unilateral granulomatous severe panuveitis by HHV-6A had a concomitant toxocara infection.[7,8] In fact, HHV-6A/B and HHV-7 both are members of the Roseolovirus genus within the Betaherpesvirinae subfamily; among them, HHV-6A and HHV-7 are acquired later through asymptomatic infection and can maintain lifelong latency in lymphocytes and monocytes.[7,8] HHV-7 can reactivate and are known as significant opportunistic pathogens in immunocompromised individuals. In fact, latent HHV infection is ubiquitous, with 95% seroprevalence in most communities. Conditions like stresses such as immunosuppressive illnesses can reactivate the dormant virus. However, our patient was neither immunocompromised nor had any features of uveitis recurrence. However, the corneal edema, Descemet's fold, iris atrophy, and raised IOP favors the viral etiology of uveitis in our case.

This report's next distinctive feature is identifying Acinetobacter baumannii by metagenomics sequencing, where the ocular cultures from SHAPU cases have never before yielded the recovery of Acinetobacter baumannii. However, other Acinetobacter species have been documented in SHAPU cases. A. baumannii's significance is unknown, and it is thought to be a passing colonizer rather than a pathogen that causes illness. A. baumannii is an infrequent cause of endophthalmitis, more commonly community-acquired or nosocomial infection, with poor visual and anatomical outcomes. Cultures of Acinetobacter species have been established from the damp skin of human subjects in good health; patients in hospitals and long-term care institutions have higher rates of skin colonization and more significant colonization of the respiratory and gastrointestinal tracts. There are only two papers on A. baumannii endophthalmitis, of which the first paper 2 cases, one involving endogenous endophthalmitis obtained in the community and the other involving postoperative endophthalmitis acquired in a hospital.[9] The second paper describes a case series of four patients with the detection of A. baumannii from the vitreous in three cases of postoperative endophthalmitis and 1 case of post-traumatic endophthalmitis, all with visually poor

prognosis. However, our case was a healthy person with no community or nosocomial infection background, which adds concern on detecting this bacteria from his vitreous sample.

In the past, there were few reports of culture-based identifications of individual bacteria (Streptococcus pneumonia, Staphylococcus aureus, Acinetobacter, and viruses (Varicella Zoster virus, Adenovirus).[1,4,5,10] But for the first time, we report the possible ramifications of the simultaneous discovery of HHV-7 and Acinetobacter baumannii, leading to severe ocular inflammation after moth contact in a SHAPU patient. Identifying these microorganisms is crucial for understanding SHAPU pathophysiology and developing effective management strategies. While concerns exist about the coincidental nature of their presence, analyzing the relationship between viral and bacterial findings in the context of SHAPU will provide valuable insights. Identifying these microorganisms will facilitate targeted treatment strategies, such as using agents HHV-7 and Acinetobacter baumanni, leading to better outcomes in SHAPU cases.

The discovery of HHV-7 and Acinetobacter baumanni in SHAPU patients' ocular samples is groundbreaking. However, it's essential to consider other potential explanations for their presence. Hence, this case report serves as a reminder that seemingly innocuous events, such as coming into contact with a white moth, can result in severe ocular inflammation. Early recognition and prompt ophthalmic intervention are essential for optimal outcomes and preventing vision loss.

Identifying HHV-7 and Acinetobacter baumannii provides new insights on the potential etiology of SHAPU and suggests possible infectious pathways. However, it is crucial to consistently identify these organisms in future SHAPU cases to confirm their true role as the causative agents. Furthermore, in-depth research is imperative to establish the relationship between infection, immune response, and genetic predisposition in SHAPU, regardless of the presence of specific microorganisms. Additionally, this case report also suggests that moths may transmit microbes or directly cause rapid intraocular inflammation, but a clear causal link with SHAPU has not been demonstrated and thus, there is need of future studies to reach a definitive conclusion.

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