Tubercular panophthalmitis in a patient with human immunodeficiency virus infection: Proven clinicopathologically and by molecular diagnostic tests

Suchitra Pradeep, Divya Thatikonda, Nivedita Nair, S Sudharshan, Chetan Rao[1], Jyotirmay Biswas

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Department of Uvea, Sankara Nethralaya, [1]Department of Vitreo-retina, Sankara Nethralaya, Chennai, Tamil Nadu, India

Correspondence to: Dr. Jyotirmay Biswas, Sankara Nethralaya, Sankara Nethralaya, 41, College Road, Nungambakkam, Chennai, Tamil Nadu, India. E-mail: drjb@snmail.org

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Ocular tuberculosis (OTB) in patients with human immunodeficiency virus (HIV) commonly presents as choroidal tubercles or granuloma. We report a rare presentation of OTB with hypopyon granulomatous uveitis in a patient with HIV on highly active antiretroviral therapy (HAART). Aqueous humor polymerase chain reaction (PCR) was positive for *Mycobacterium tuberculosis* (MTB). Antitubercular therapy (ATT) was initiated despite which it progressed to scleral abscess and panophthalmitis. Enucleation with ball implantation was done. Histopathology revealed caseating granuloma with numerous

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acid-fast bacilli (AFB) and real-time PCR showed increased copies of MTB genome. After a full course of ATT, he had stable ocular and systemic condition at final follow-up.

Key words: Human immunodeficiency virus, ocular tuberculosis, panophthalmitis, paradoxical worsening, real-time polymerase chain reaction

Tuberculosis (TB) is the commonest systemic opportunistic infection in patients with human immunodeficiency virus (HIV), which affects lungs and other extrapulmonary sites including eyes.[1] Ocular TB (OTB) in patients with HIV can have varied manifestations but commonly presents as choroidal tubercles or granuloma. Aggravation of the ocular inflammation in patients with OTB can either be due to worsening of infection, immune recovery uveitis (IRU), and/or paradoxical worsening.[2,3]

We report a case of OTB in a young HIV positive male on highly active antiretroviral therapy (HAART) who presented with hypopyon granulomatous panuveitis without any other active systemic opportunistic infection (OI). His ocular condition worsened to panophthalmitis despite anti-tubercular therapy (ATT) and adequate HAART. Diagnosis by histopathology and molecular diagnostics and clinical course is presented.

Case Report

A 35-year-old HIV positive male reported with history of pain, redness, and diminution of vision (DV) in right eye (OD) for 3 months. He was on regular HAART (Efavirenz, Emtricitabine, and Tenofovir) for 1 year and his last known CD4 counts 2 months back was 324 cells/cu.mm. He had undergone YAG peripheral iridotomy (PI) for angle closure glaucoma elsewhere and was on topical steroids, cycloplegics, and antiglaucoma medications (AGMs) when he presented to us. He was not on any systemic steroids. On examination, his best-corrected visual acuity (BCVA) was no perception of light (PL) in OD and 20/20, N6 in left eye (OS). Anterior segment examination-OD showed mutton fat keratic precipitates, rubeosis iridis, ectropion uvea, shallow anterior chamber (AC) with 0.5 mm hypopyon, and complicated cataract. Intraocular pressure (IOP) was 56 mm of Hg in OD and 16 mm in OS by applanation tonometry (AT). Four-mirror indirect gonioscopy showed closed angles with 360-degree peripheral anterior synechiae (PAS). Fundus examination showed grade 4 vitritis. Ultrasound (USG) B-scan of OD showed moderate vitreous echoes and diffuse choroidal thickening. Aqueous humor (AH) analysis was positive for *Mycobacterium tuberculosis* (MTB) genome and negative for eubacterial and panfungal genome. High resolution computed tomography of chest was normal and systemic TB was ruled out by infectious disease specialist. The patient was started on ATT along with topical steroids, cycloplegics, and antiglaucoma medication.

He was lost to follow up after that and reported one and half months later with an increase in pain and redness in OD. BCVA was no PL in OD and 20/20, N6 in OS. His CD4 counts were 410 cells/cu.mm and was on ATT and regular HAART. He did not have any systemic complaints. An inferior scleral abscess [Fig. 1] with limitation of ocular motility and yellow reflex on ophthalmoscopy was noted. USG showed [Fig. 2] significant vitreous echoes with retinal detachment. Conjunctival scraping was negative. A diagnosis of panophthalmitis in a painful blind eye with restricted ocular movements was made. Patient underwent enucleation with ball implant. Gross examination showed a whitish mass filling the vitreous cavity with posterior thickened sclera [Fig. 3a]. Pathological examination of enucleated specimen showed caseating granulomatous inflammation involving intraocular contents and sclera with numerous acid-fast bacilli (AFB) on Ziehl–Neelsen staining [Fig. 3 b-d]. Real-time polymerase chain reaction (RT-PCR) from paraffin section was positive for MTB with 4714 copies/ml [Fig. 4].

Patient completed the full course of ATT and at final follow-up, right socket was healthy with acceptable cosmesis. His systemic condition was stable.

Discussion

Ocular TB has been reported in 3.8% of HIV patients in a large study from India.[2] It can present with varied manifestations although choroidal granuloma is the commonest feature. Panophthalmitis is uncommonly reported, especially in HIV patients.[1-3]

Our patient had hypopyon granulomatous uveitis as a presenting feature of ocular tuberculosis. Hypopyon which is uncommonly seen in HIV patients with OTB,[4] can be noted in patients with endophthalmitis. He did not have other signs and symptoms of underlying active systemic TB. He was on regular HAART with moderate CD4 counts. Cell mediated immunity has been suggested as a cause of such fulminant inflammation in previous studies.[2]

With an uncommon presentation like this, AH PCR was done which was positive for MTB genome.

Paradoxical reactions with ATT and HAART have been attributed to the increase in the CD4+ lymphocyte counts with corresponding decrease in the viral load leading to intense inflammation at sites of tubercular disease.[5,6] Tuberculosis-associated immune reconstitution inflammatory syndrome (TB-IRIS) and IRU has been reported with both MTB and with other atypical mycobacteria.[7,8] In HIV-TB co-infection to balance the risks related to worsening of inflammation and systemic mortality, guidelines have been formulated based on CD4 counts regarding initiation of ART.[9] Significantly, in our patient, the increase in CD4 counts was not marked when he presented with panophthalmitis and fulminant spread of infection to the whole of the eye. A possibility of drug resistance was also considered but there was no other supportive clinical evidence for the same. The other eye was normal and he has been systemically stable till the last follow up. Most reports of TB panophthalmitis in HIV/AIDS have been reported in association with extensive systemic TB.[10]

Our case reinforces the fact that significant inflammation with worsening of clinical condition can occur in HIV patients with OTB on HAART even with a marginal increase in CD4 counts. CD4 count values alone may not indicate the immune recovery state. Paradoxical worsening in TB can lead to even loss of eye despite adequate and appropriate ATT.

Conclusion

Medline search revealed limited literature on TB panophthalmitis in HIV patients without systemic involvement especially presenting as hypopyon granulomatous uveitis worsening despite HAART and adequate ATT. The diagnosis of TB was established initially by aqueous PCR and later by histopathology and RT-PCR from ocular specimen. Additional appropriate anti-inflammatory therapy with close monitoring could help reduce inflammation and possibly can save the eye.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other

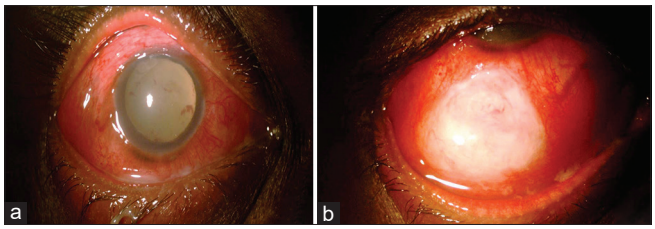

Figure 1: Slit-lamp photograph of right eye (OD); (a) Diffuse illumination of anterior segment showing circum-corneal and diffuse conjunctival congestion and yellow reflex from posterior segment, (b) Diffuse illumination image showing a scleral abscess 2 mm away from the 6'0 clock limbus in the inferior palpebral area with scleral thinning

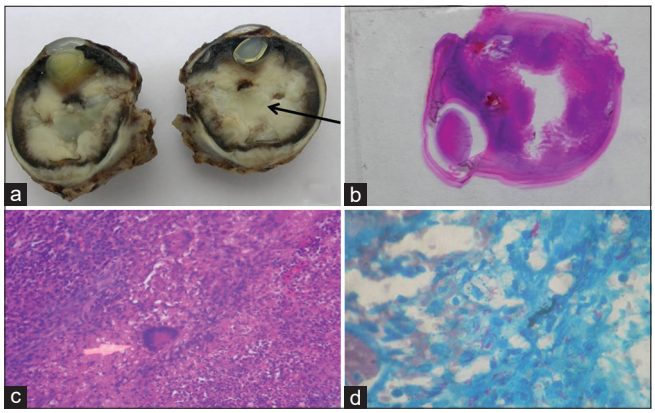

Figure 3: (a) Gross specimen of enucleated right eye showing clear cornea. Anterior chamber is normal; lens is in place. Vitreous cavity is filled with whitish mass (thick black arrow); retina cannot be identified. Posteriorly sclera is thickened. (b) A bread-loaf section of specimen showing extensive inflammation involving vitreous, sclera, and choroid; posteriorly retina is detached. (c) Hematoxylin and eosin (H&E) stained at 100× magnification showing caseating granulomatous inflammation with numerous histiocytes and multinucleated giant cells. (d) Ziehl–Neelsen staining of the specimen showing numerous acid-fast bacilli (AFB)

clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

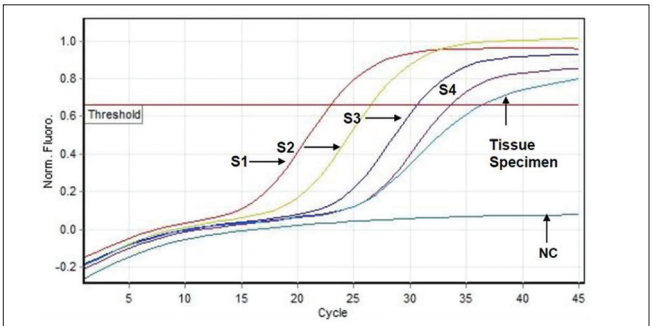
Conflicts of interest

There are no conflicts of interest.

References

1. Gupta V, Gupta A, Rao N. A. Intraocular tuberculosis-an update. Surv Ophthalmol 2007;52:561-87.
2. Babu RB, Sudharshan S, Kumarasamy N, Therese L, Biswas J. Ocular tuberculosis in acquired immunodeficiency syndrome. Am J Ophthalmol 2006;142:413-8.
3. Sudharshan S, Kaleemunnisha S, Banu AA, Shrikrishna S, George AE, Babu BR, *et al*. Ocular lesions in 1,000 consecutive HIV-positive patients in India: A long-term study. J Ophthalmic Inflamm Infect 2013;3:2.
4. Velu J, Agarwal S, Gupta V, Sharma K, Sharma A, Gupta A. Hypopyon uveitis-a rare presentation of intraocular tuberculosis. Ocul Immunol Inflamm 2013;21:251-3.
5. Rathinam S, Lalitha P. Paradoxical worsening of ocular tuberculosis in HIV patients after antiretroviral therapy. Eye 2007;21:667-8.
6. Ganesh SK, Abraham S, Sudharshan S. Paradoxical reactions in ocular tuberculosis. J Ophthalmic Inflamm Infect 2019;9:19.
7. Walker NF, Stek C, Wasserman S, Wilkinson RJ, Meintjes G. The tuberculosis-associated immune reconstitution inflammatory syndrome: Recent advances in clinical and pathogenesis research. Curr Opin HIV AIDS 2018;13:512-21.
8. Rosenbaum PS, Mbekeani JN, Kress Y. Atypical mycobacterial panophthalmitis seen with iris nodules. Arch Ophthalmol 1998;116:1524-7.
9. NACO. 2013. Antiretroviral Therapy Guidelines for HIV-Infected Adults and Adolescents. MoHFW, Government of India. Available from: http://naco.gov.in/sites/default/files/Antiretroviral%20Therapy%20Guidelines%20for%20HIV–Infected%20Adults%20and%20Adolescents.pdf. [Last accessed on May 2013].
10. Srichatrapimuk S, Wattanatranon D, Sungkanuparph S. Tuberculous panophthalmitis with lymphadenitis and central nervous system tuberculoma. Case Rep Infect Dis 2016;2016:6785382.

Figure 2: Ultrasound B scan of right eye showing a high reflective membrane echo extending from optic nerve head (a) to mid periphery in superior and temporal quadrants (b) up to far periphery in inferior quadrant with no widening of tenon's space. Vitreous shows low-to-moderate reflective dot and clump echoes. Incomplete posterior vitreous detachment noted (IPVD) with attachment to a moderately reflective clump echo over Optic nerve head (ONH)



S.No.	Colour	Name	Type	Calc Concentartion
1		S1	Standard	26,020,994
2		S2	Standard	2,684,285
3		S3	Standard	192,314
4		S4	Standard	29,080
5		Tissue Specimen	Sample	4714
6		NC	Negative Control	0

Figure 4: Real- time PCR Quantitation data of the tissue specimen from paraffin block (black arrow) showing a positive result for *Mycobacterium tuberculosis* with 4714 copies/ml. This is above the threshold limit