A rare presentation of ocular histoplasmosis in a patient with systemic nocardiosis

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Histoplasmosis is a granulomatous infection caused by a dimorphic fungus *Histoplasma capsulatum,* found in old buildings, bird habitats, and bat caves. It most commonly affects the lungs by inhalation of spores present in nitrogen-rich soil and droppings of bats and birds.[1] Histoplasmosis involves the retina and choroid most commonly in the eye, as presumed ocular histoplasmosis syndrome, characterized by chorioretinal scars and peripapillary atrophy in the absence of vitreous cells.[2] Conjunctival and scleral involvement, however, is exceedingly rare, and has been seen in both immunocompromised and immunocompetent individuals.[3-5] This report describes the first case of superadded conjunctival histoplasmosis in a patient with disseminated nocardiosis.

A 48-year-old male presented to cornea and lens services of our tertiary care institute in India with a 2-month history of gradually increasing painless mass, associated with yellowish discharge, in the right eye. Unaided visual acuity was 20/30 and 20/20 in the right and left eye, respectively, with normal intraocular pressure in both the eyes. Anterior segment examination revealed an irregular, pink, firm mass in the medial part of the bulbar conjunctiva in the right eye, with chemosis and diffuse conjunctival congestion [Fig. 1]. The mass, measuring 18 mm × 12 mm, had purulent discharge around it and was straddling the entire

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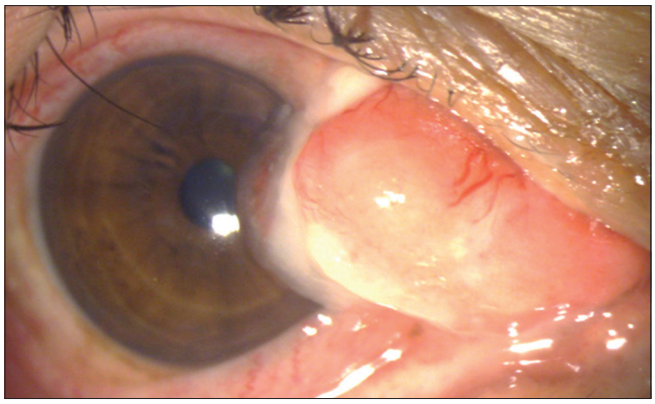

Figure 1: Anterior segment photograph showing a firm, pink mass in the medial bulbar conjunctiva, straddling the medial canthus and encroaching up to one-third of the cornea

medial bulbar conjunctival area and encroaching upon the medial one-third of the cornea. The lesion was freely mobile with no attachments to the underlying scleral bed. Ocular examination of the left eye was unremarkable, and fundus of the right eye had no evidence of chorioretinal histoplasmosis syndrome. The patient was on systemic immunosuppression, oral tacrolimus, and systemic steroids for the past 2 years, after undergoing renal transplantation for mesangioproliferative glomerulonephritis. Few days before the patient was affected with the complaint of eye mass, he developed persistent fever, cough, and multiple thigh abscesses with discharging sinuses, with the computed tomography (CT) scan revealing bilateral lung nodules. Similar focus was also found in the form of cerebellar abscess. There was clinically no evidence of any skin lesion. Serology for human immunodeficiency virus (HIV), hepatitis B and C was negative. Fine needle aspiration cytology of the lung nodules and thigh abscess revealed *Nocardia farcinica*, suggestive of systemic nocardiosis. There was no evidence of any gram-positive or gram-negative bacterium, and culture revealed the growth of commensal organisms. CD4 count of the patient was 96/µl. Due to resistance of the organism to septran, patient was stared on ceftriaxone and imipenem. A few days later, the patient developed ocular mass and presented to us after 2 months, once he was systemically stable. Since the patient was a diagnosed case of disseminated nocardiosis, the ocular lesion that occurred was also clinically suspected to reveal nocardia infection.

Anterior segment optical coherence tomography revealed superficial lesion with no scleral involvement. Swabs of the discharge did not reveal any mycobacteria, fungus, or bacteria. After the orbital involvement was ruled out in CT scan, excision biopsy of the lesion was done. The excised tissue was sent for microbiological and histopathologic examination. After treatment with 10% KOH, the lesion showed round yeast bodies, with positive calcofluor staining [Fig. 2a and b]. Giemsa stain showed encapsulated bodies inside a bloated macrophage, diagnostic of *Histoplasma capsulatum* [Fig. 2c]. A positive polymerase chain reaction was also indicative of fungal etiology [Fig. 2d]. Classical organisms were also seen on histopathology, confirming the diagnosis of histoplasmosis. Histoplasma serology and antigen were negative, suggesting isolated ocular involvement. The patient was doing well few weeks after the biopsy, and topical drugs were stopped. No recurrence or keratinization of the cornea has been noted 9 months after the biopsy.

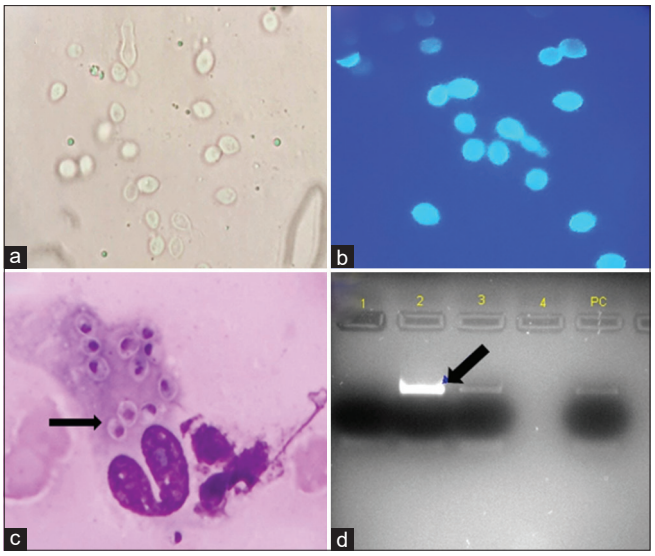

Figure 2: (a) Round yeast bodies seen in smear, after treatment with 10% KOH. (b) Positive calcofluor staining. (c) Giemsa-stained smear showing capsulated bodies inside a bloated macrophage, characteristic of histoplasmosis. (d) Positive polymerase chain reaction for panfungal organism, suggestive of fungal etiology

Discussion

Histoplasmosis is the most common mycosis in the world, typically involving the lungs.[6] It can also present as a disseminated disease. Conjunctival involvement due to *H. capsulatum* is very unusual in clinical practice and was even more surprising in our case as ocular involvement was suspected due to nocardiosis. Moreover, because of high prevalence of histoplasmosis in eastern USA and western Africa compared to Asia, the conjunctival involvement seen in our setting was quite a unique presentation.[4]

Although histoplasmosis has been reported in immunocompetent individuals, it is more common in immunocompromised states like HIV, organ transplantations, and long-term steroid use, as the immune system is unable to fend off the organism, hence causing disseminated disease.[6-8] In our case, long-term immunosuppression after renal transplantation and disseminated nocardiosis made the patient susceptible to histoplasmosis. However, the source of infection for histoplasmosis in our patient is unclear, in the absence of any exposure to bats or birds. Though there have been three case reports of conjunctival histoplasmosis in literature till now, superadded histoplasmosis has never been reported in a patient of disseminated nocardiosis.[4,5,9]

Treatment of such lesions has been reported to be with oral itraconazole and amphotericin B, but since our patient had deranged liver function tests, we could not give oral antifungals. Only topical amphotericin B 0.15% was given post-biopsy. Moreover, Knox *et al*.[3] had also suggested excision biopsy as the cure for such lesions. So, we believe that excision biopsy in such patients is sufficient to prevent recurrence. It is important to note that isolated conjunctival histoplasmosis may be the presenting feature of an immunocompromised disease, hence warranting the need for systemic evaluation in conjunctival histoplasmosis.[4]

The two variants of Histoplasma, *H. capsulatum* var *capsulatum* and *H. capsulatum* var *duboisii*, can be differentiated

histopathologically from the size of the oval yeasts seen.[10] Clustered yeasts may be ingested by macrophages, with features like pericellular/perinuclear halo confirming the diagnosis of histoplasmosis, like in our case. Our case highlights the importance of microbiology and histopathology in such rare cases and the need of detailed workup.

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Conflicts of interest

There are no conflicts of interest.

References

1. Diaz RI, Sigler EJ, Rafieetary MR, Calzada JI. Ocular histoplasmosis syndrome. Surv Ophthalmol 2015;60:279-95.
2. Gass J. Presumed ocular histoplasmosis syndrome. In: Klein E, editor. Stereoscopic Atlas of Macular Diseases: Diagnosis and Treatment. Volume 1. 3rd ed. St. Louis, MO: Mosby; 1987. p. 112-28.
3. Knox DL, O'Brien TP, Green WR. Histoplasma granuloma of the conjunctiva. Ophthalmology 2003;110:2051-3.
4. Pujari A, Rakheja V, Bajaj MS, Sen S, Yadav B. Isolated conjunctival histoplasmosis in an elderly patient: A rare but important scenario. Can J Ophthalmol 2019;54:15-6.
5. Dalvin LA, Thom SB, García JJ, Fadel HJ, Baratz KH. Scleritis due to histoplasmosis. Cornea 2016;35:402-4.
6. Edwards JA, Rappleye CA. Histoplasma mechanisms of pathogenesis—one portfolio doesn't fit all. FEMS Microbiol Lett 2011;324:1-9.
7. Ravindran S, Sobhanakumari K, Celine M, Palakkai S. African histoplasmosis: The first report of an indigeneous case in India. Int J Dermatol 2015;54:451-5.
8. Couppié P, Sobesky M, Aznar C, Bichat S, Clyti E, Bissuel F, *et al*. Histoplasmosis and acquired immunodeficiency syndrome: A study of prognostic factors. Clin Infect Dis 2004;38:134-8.
9. Shirali A, Kini J, Vupputuri A, Kuruvila M, Venkatraya Prabhu M. Disseminated histoplasmosis with conjunctival involvement in an immunocompromised patient. Indian J Sex Transm Dis 2010;31:35-8.
10. Guarner J, Brandt ME. Histopathologic diagnosis of fungal infections in the 21st century. Clin Microbiol Rev 2011;24:247-80.