



A RARE CASE OF REVERSIBLE BLINDNESS IN CRYPTOCOCCAL MENINGITIS WITH NORMAL INTRA CRANIAL PRESSURE

Vaibhav Mathur	Junior Resident, Department of Medicine, Rajendra Institute of Medical Sciences, Ranchi-834009, India
Prajit Mazumdar*	Junior Resident, Department of Medicine, Rajendra Institute of Medical Sciences, Ranchi-834009, India. *Corresponding Author
Malyaban Das	Junior Resident, Department of Medicine, Rajendra Institute of Medical Sciences, Ranchi-834009, India
Vidyapati	Professor, Department of Medicine, Rajendra Institute of Medical Sciences, Ranchi - 834009, India

ABSTRACT Ocular complications in cryptococcal meningitis (CM) is mainly attributed to elevated intracranial pressure(ICP). Our patient had sudden onset painless loss of vision as a result of concomitant ART (anti retroviral therapy) intake by the patient. We report a case of reversible vision loss complicating AIDS-related Cryptococcal Meningitis(CM) with a normal intracranial pressure(ICP) due to Immune reconstitution inflammatory response(IRIS) as a result of concomitant ART (anti retroviral therapy). The potential significance of this case report is to highlight a possible role of corticosteroids to treat blindness due to Cryptococcal Meningitis.

KEYWORDS : ART(antiretroviral therapy), corticosteroids, Cryptococcal Meningitis(CM), Immune reconstitution inflammatory response(IRIS)

Introduction:

Cryptococcus neoformans is an encapsulated yeast and it has wide spectrum of clinical manifestations ranging from a harmless colonization of the airways and asymptomatic infection to meningitis or disseminated disease. It is commonly found in pigeon excreta and decaying organic material. The most serious infections usually develop in immunocompromised patients in which it disseminates to the central nervous system (CNS). It is the most frequent CNS infection seen in retropositive patients of sub-Saharan Africa¹. Ocular involvement is seen in 30% cases of neurocryptococcosis²

Ocular complications in cryptococcal meningitis (CM) is mainly attributed to elevated intracranial pressure(ICP). We report a case of reversible vision loss complicating AIDS-related Cryptococcal Meningitis(CM) with a normal intracranial pressure(ICP).

The patient had sudden onset painless blindness during the therapy and on detailed evaluation, clinical and radiological findings of optic neuritis were present. While ruling out other causes of blindness in Cryptococcal Meningitis, we concluded the cause of blindness as optic neuritis due to Immune reconstitution inflammatory response (IRIS) as a result of concomitant ART (anti retroviral therapy) intake by the patient. We witnessed dramatic visual improvement in the patient after use of systemic corticosteroids. The potential significance of this case report is to highlight a possible role of corticosteroids to treat blindness due to Cryptococcal Meningitis.

Case Report

A 36 yr old male was admitted with headache, fever and intermittent Vomiting of 1-month duration. He was a diagnosed HIV (Retro positive) from outside 6 months back but started taking ART(anti retroviral therapy) for only last 10 days, His recent CD4 count was 76 cells/mm³.

On examination the patient had altered Sensorium, meningeal signs like neck rigidity, kernig's sign were positive, photophobia was present. Patient was febrile to touch with PR- 98/min. & BP- 104/70mmHg. Rest of the general & systemic examination was normal.

Post-admission his routine blood investigations along with CSF(Cerebro Spinal Fluid) were sent for investigation & patient was started on Antibiotics & Antipyretics.

Cerebrospinal fluid (CSF) examination showed clear fluid with opening pressure 40 mm H₂O, protein 103 mg/dL, glucose 29 mg/dL, and white blood cell count 100/mm³ with 100% lymphocytes.

Cerebrospinal fluid (CSF) also revealed Budding Cryptococcus with capsule on India Ink preparation.

Subsequently, he was started on Injection liposomal Amphotericin B (1mg/kg/day) along with Tablet Flucytosine for 2weeks each. With good improvement in next 3 days, the same treatment was continued further for 2 weeks along with anti retroviral therapy (ART).

However, on Day 4 post- admission, the patient started to complain of diminished vision. He denied diplopia, vomiting, headache or any surge in fever. He had decreased vision in both eyes without peripheral sparing. On examination there was no light perception in the left eye and visual acuity was restricted to counting fingers in the right eye. Direct light reflex was absent in left eye but both direct and consensual light reflex was preserved in right eye. Rapid afferent papillary defect was also noted in the left eye.

There was no evidence of retinal artery occlusion, no papilledema and no chorioretinal lesion on fundoscopic examination along with intact extraocular movement bilaterally. There was no other neurologic abnormality. The remaining physical examination was within normal limits.

Urine and blood cultures for bacteria, mycobacteria, and fungi were negative. Serum toxoplasma immunoglobulin G and rapid plasma reagin were negative along with negative cytomegalovirus antigen testing. Lumbar puncture done during his hospitalization revealed normal intracranial pressure.

Magnetic resonance imaging(MRI) findings revealed leptomeningeal enhancement and dilated perivascular Virchow-Robin spaces with gelatinous pseudocysts-all classic findings in neurocryptococcosis.

On presentation to our institution, the patient was taking tenofovir/lamivudine/efavirenz as ART for 10 days after being diagnosed retropositive.

Intravenous methylprednisolone 1 g/day was begun on post blindness and continued for 3 days followed by oral taper of prednisone from 50 mg daily to 5 mg daily over next 1 month, then discontinued.

After receiving the first dose of steroids, the patient's vision dramatically improved. On day 4 of glucocorticoid therapy, pupillary response bilaterally also improved.

Amphotericin B and 5-flucytosine were continued for 2 weeks and transitioned to fluconazole. The patient continues to do well clinically

on follow up and has preserved vision to date.

Discussion:

There are three main causes of vision loss in Cryptococcal Meningitis: a) optic neuritis which is characterized by rapid visual loss. It is due to Optic nerve infiltration/inflammation as a manifestation of the meningoencephalitis that extends to the optic nerve by continuous spread from the diencephalon or a result of direct infiltration of fungi from the perioptic CSF space b) effects of increased intracranial pressure or increased intra ocular pressure in which the visual loss has a slower course.^{3,4} c) The optic nerve sheath compartment mechanism (ONSCS) which occurs due to fungal loading and obstruction of the perioptic CSF space.

Lipson et al.⁵ first described two cases of AIDS associated cryptococcal arachnoiditis resulting in bilateral visual loss secondary to an optic neuropathy. Cohen et al. in 1993⁶ and Corti et al. in 2010⁷ gave histological evidence of cryptococcal infiltration of the intracanalicular segment of the optic nerve. Corti's case also showed a perineuritis, but in addition showed optic nerve infiltration by the fungus. Hoepelman⁸ and Seaton⁹ suggested that corticosteroids could only play a beneficial role in Cryptococcus induced visual loss by reducing the optic nerve inflammation.

Rapid progression of visual loss with normal opening CSF pressure and no papilledema or funduscopic abnormalities on examination suggested optic neuritis as the probable cause of vision loss in our patient. So, the presence of leptomeningeal enhancement with enhancing nerve sheath on MRI further supported optic neuritis due to inflammation as the likely etiology of vision loss.

Further support for an optic neuritis as a cause of blindness in our case has come from De Schacht's report¹⁰ of a 26-year-old Cryptococcal Meningitis patient who developed an immune reconstitution illness with bilateral blindness after starting antiretroviral therapy as was seen in our case.

Our patient had improvement in vision after receiving steroids (intravenous methylprednisolone) as most likely he was suffering from the effects of Immune reconstitution inflammatory response (IRIS). Immune reconstitution inflammatory syndrome (IRIS) consists of a paradoxical worsening of the clinical manifestations or the course of the Cryptococcal disease in spite of an appropriate antifungal therapy when patients regain the ability to mount a suitable immune response. Immune reconstitution inflammatory syndrome (IRIS) is interpreted as an exuberant inflammatory reaction of the host at the sites of Cryptococcal infection, subsequent to a rapid improvement in the cellular immunity "Paradoxical Immune reconstitution inflammatory response" (IRIS), presenting as worsening or recurrence of treated cryptococcal disease after ART (antiretroviral therapy) initiation is a reasonable explanation of sudden blindness in our patient. Early ART (antiretroviral therapy) initiation probably contributed to this. In order to reduce the risk of developing Immune reconstitution inflammatory response (IRIS), according to the principal current guidelines, introduction of ART (antiretroviral therapy) should be delayed for two to 10 weeks after the starting of antifungal therapy.

Conclusion:

Here we report a case of vision loss in a patient with Cryptococcal Meningitis (CM) and normal intracranial pressure. Dramatic improvement of vision in our patient on treatment with corticosteroids suggests that there was an inflammatory component to the vision loss, possibly due to Immune reconstitution inflammatory response (IRIS) caused by early intervention with anti retroviral therapy (ART).

REFERENCES

1. Powderly WG. Cryptococcal meningitis and AIDS. *Clin Infect Dis* 1993; 17:837-42.
2. Kestelyn P, Taelman H, Bogaerts J, et al. Ophthalmic manifestations of infections with Cryptococcus neoformans in patients with the acquired immunodeficiency syndrome. *Am J Ophthalmol* 1993; 116:721-7.
3. Rex JH, Larsen RA, Dismukes WE, Cloud GA, Bennett JE. Catastrophic visual loss due to Cryptococcus neoformans meningitis. *Medicine (Baltimore)* 1993; 72:207-24.
4. Nabeta H, Fosslund N, Bahr N, et al. Accuracy of non-invasive intraocular pressure measurement for prediction of elevated intracranial pressure in meningitis and cryptococcosis [abstract 925]. In: Infectious Disease Society of America Annual Conference, San Diego, 19 October 2012.
5. Lipson BK, Freeman WR, Benitez J, et al. Optic neuropathy associated with cryptococcal arachnoiditis in AIDS patients. *Am J Ophthalmol.* 1989;107:523-527. PMID: 2540660.
6. Cohen DB, Glasgow BJ. Bilateral optic nerve cryptococcosis in sudden blindness in patients with acquired immune deficiency syndrome.

7. Ophthalmology. 19Y4NSIG8kkzwWjMD17euEaQ5PErpxWkP
Corti M, Solari R, Cangelosi D, et al. Sudden blindness due to bilateral optic neuropathy associated with cryptococcal meningitis in an AIDS patient. *Rev Iberoam Micol.* 2010;27:207-209. PMID: 20965271.
8. Hoepelman AL, Van der Flier M, Coenjaerts FE. Dexamethasone downregulates Cryptococcus neoformans-induced vascular endothelial growth factor production: A role for corticosteroids in cryptococcal meningitis? *J Acquir Immune Defic Syndr.* 2004;37:1431-1432. PMID: 15483473
9. Seaton RA, Verma N, Naraqi S, Wembri JP, Warrell DA. The effect of corticosteroids on visual loss in Cryptococcus neoformans var. gattii meningitis. *Trans R Soc Trop Med Hyg.* 1997;91:50-52. PMID: 9093628, [http://dx.doi.org/10.1016/S0035-9203\(97\)90393-X](http://dx.doi.org/10.1016/S0035-9203(97)90393-X)
10. De Schacht C, Smets RM, Callens S, Colebunders R. Bilateral blindness after starting highly active antiretroviral treatment in a patient with HIV infection and cryptococcal meningitis. *Acta Clin Belg.* 2005;60:10-12. PMID: 15981698