Prominent papilledema with dense peripapillary hemorrhage in AIDS patients with cryptococcal meningitis

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Case Report

Keywords: Papilledema, AIDS, cryptococcal meningitis

Posted Date: February 21st, 2019

DOI: https://doi.org/10.21203/rs.2.157/v1

Abstract

Background: To describe the clinical characteristics of prominent papilledema with dense peripapillary hemorrhage in AIDS patients with cryptococcal meningitis.

Case presentation: Case1. A 35-year-old male with acquired immune deficiency syndrome (AIDS) complicated with cryptococcal meningitis had a severely visual loss in both eyes after 33 days of highly active anti-retroviral therapy (HAART). Funduscopic examination revealed marked bilateral papilledema with dense peripapillary hemorrhages and macular exudates. The patient was treated with intravenous mannitol and intermittent lumbar punctures. His vision was improved after 4 months of treatment. Case2. A 43-year-old male with AIDS suffered from severe vision deterioration in both eyes. He has not accepted HAART at that time. Dilated fundoscopic examination revealed marked disk edema with dense peripapillary hemorrhages in his right eye and mild papilledema with slight peripapillary hemorrhages in his left eye. The diagnosis of cryptococcal meningitis was made. His BCVA didn't improve after treatment. He died 3 months after the hospitalization.

Conclusion: Prominent papilledema with dense peripapillary hemorrhage is uncommon, which maybe the sign of an opportunistic infectious associated with IRIS or the sign of poor prognosis in AIDS patients with cryptococcal meningitis.

Keywords: Papilledema, AIDS, cryptococcal meningitis

Background

Cryptococcal meningitis is mainly caused by Cryptococcus neoformans, and is the most common fungal infection in central nervous system (CNS) in acquired immune deficiency syndrome (AIDS) patients. AIDS patients with cryptococcal meningitis often manifest as increased intracranial pressure which can cause papilledema, the non-inflammatory, obstructive swelling of optic disc resulting only from increased intracranial pressure. Papilledema commonly occurs bilaterally, and may be asymptomatic in the early stage. Here we report 2 cases of prominent papilledema with dense peripapillary hemorrhage in AIDS patients with cryptococcal meningitis.

Case Presentation

Case1

A 35-year-old male with AIDS was admitted to our hospital with headache, fever and unconsciousness. The HIV viral load was 124122copies/ml and CD4+ T lymphocytes cell count was 61 cells/ul. Lumbar puncture revealed that the opening pressure was over 330mmH2O. Cerebrospinal fluid (CSF) examination showed cryptococcus on India ink preparation and the cryptococcal antigen titer was significant positive. CSF chemistry showed significantly elevated protein level of 111.1mg/dL and slightly decreased glucose of 2.2mmol/L. CT scan of the brain did not show any evidence of obstructive hydrocephalus or mass

lesions. He was diagnosed with cryptococcal meningitis and was treated with intravenous amphotericin B and fluconazole. Mannitol was given intravenously to reduce intracranial pressure. Highly active anti-retroviral therapy (HAART) started 17 days later. His vision was severely decreased after 33 days of HAART therapy and he came to the ophthalmic clinic. His best-corrected visual acuity(BCVA) was 20/100 in both eyes. Slit-lamp examination and intraocular pressure measurements in both eyes were normal. Pupils were round and reactive without a relative afferent papillary defect. Dilated fundoscopic examination showed marked bilateral papilledema with dense peripapillary hemorrhages and macular exudates(Fig1). Visual field examination revealed an enlarged blind spot. In addition to medication, he was given lumbar punctures every three days to relieve the high CSF pressure.

After 4 months of treatment, his vision was improved to 20/30. Funduscopic examination revealed improvement of the optic disk edema without intraretinal hemorrhages (Fig2). The visual field defects were improved.

Case2

A 43-year-old male with AIDS was admitted with a history of severe headache, confusion and visual loss for 10 days' duration. He hasn't accepted HAART at the time of admission, the HIV viral load was 353029 copies/mL, CD4 cell count was 105 cells/μL. A lumbar puncture showed an opening pressure of more than 330mmH2O, a protein of 76.6mg/dL and glucose of 0.42mmol/L. India ink staining showed Cryptococci. The cryptococcal antigen titer was significant positive. MRI showed multiple mottling lesions in the frontal region. On ophthalmic examination, BCVA was finger count in the right eye and no light perception in the left eye. His left pupil reacted with a relative afferent pupillary defect. Anterior segment was unremarkable. Dilated fundoscopic examination revealed marked disk edema with dense peripapillary hemorrhages in his right eye and mild papilledema with slight peripapillary hemorrhages in his left eye. (Fig3) The diagnosis of cryptococcal meningitis was made. His treatment included frequent lumbar punctures to relieve the high CSF pressure and drug treatments including amphotericin B, fluconazole and mannitol. A month later, he came back to our department. His BCVA didn't improve. Funduscopic examination revealed improvement of the optic disk edema. (Fig4) This patient died 3 months after the hospitalization.

Discussion

Cryptococcus neoformans is a ubiquitous, encapsulated, yeast like fungus that infects patients with AIDS. Hematogenous spread from the lung to the CNS can result in meningitis. Approximately 40% patients with cryptococcal meningitis incur damage to the eye[1]. The most frequent ophthalmic manifestations are papilledema and multifocal chorioretinitis. Papilledema is due to increased intracranial pressure. With the receipt of HAART, the incidence of cryptococcal meningitis has decreased significantly. Complications related to HAART-induced immune reconstitution are called immune reconstitution inflammatory syndrome (IRIS). Several studies showed that Cryptococcus is one of the opportunistic infectious organisms associated with IRIS. Rahul and co-workers[2] described the ocular

findings of 4 HIV-positive patients who were diagnosed with IRIS associated with Cryptococcus neoformans. Three of them presented with severe papilledema and massive peripapillary haemorrhage. In 2017, Astrid et al[3] reported a HIV-positive patient developed progressive optic disc edema despite normal intracranial pressure after undergoing treatment for cryptococcal meningitis. Funduscopic examination revealed bilateral optic nerve edema with massive retinal hemorrhages and macular exudates. Another case showed a patient with AIDS had dense peripapillary retinal hemorrhages with papilledema one month after receiving treatment for cryptococcus meningitis[4]. According to above cases, the duration of HAART upon presentation with IRIS ranged from 17 to 35 days. The subsequent decline in vision coincided with the initiation of HAART therapy, just as our case 1. IRIS is a common complication in patients starting HAART. It is an inflammatory syndrome affecting various organ systems of immunosuppressed patients after initiation of HAART and has been associated with previous cryptococcal infection. It has been reported that 30–35% of HIV patients with cryptococcosis will develop IRIS 4–6 weeks after initiating HAART[5]. In case 1, the patient had worse visual loss 33 days after initiation of HAART. Unfortunately, CD4 cell count lately wasn't checked. Given the temporal relationship between starting HAART therapy, we suspect that this patient represents a manifestation of IRIS. Therefore, the ocular manifestations including papilledema with dense peripapillary retinal hemorrhages after the initiation of HAART should alert the ophthalmologist to the suspicion of IRIS.

In case 2, the papilledema and peripapillary hemorrhages in the right eye was more severe than that in the left eye. However, the visual acuity in the left eye was worse. He hadn't started HAART when he suffered the sudden visual loss. Therefore, it was impossible that the papilledema and peripapillary hemorrhages were due to IRIS. Corti[6] reported an AIDS patient with a diffuse Cryptococcal meningoencephalitis developed a rapid and bilateral blindness. After he died, autopsy report showed that Cryptococcus invaded the optic nerves, the optic tracts, and the periphery of the optic chiasm adjacent the meningeal membranes. Combining with the acute visual loss and clinical findings, the diagnosis of optic neuritis was considered. It was possible that infection of the visual pathway by Cryptococcus was the leading cause of sudden bilateral blindness, as in Case 2.

Conclusion

In conclusion, several studies have showed that prominent papilledema with dense peripapillary hemorrhage maybe the sign of an opportunistic infectious associated with IRIS in AIDS patients with cryptococcal meningitis. However, the patient who has not accepted HAART shows the same sign of prominent papilledema with dense peripapillary hemorrhage. These patients should require highly attention because of the neuritis and the poor prognosis.

Abbreviations

CNS: central nervous system; AIDS: acquired immune deficiency syndrome; CSF: cerebrospinal fluid; HAART: highly active anti-retroviral therapy; BCVA: best-corrected visual acuity; IRIS: immune reconstitution inflammatory syndrome.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent to publish

Written informed consent was obtained from each patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the editor of this journal.

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

Funding

This study was supported by BeiJing Talents Fund(2015000021469G202)

Authors' contributions

Study concept and design (FFM); data collection (DL, SNW); analysis and interpretation of data (FFM, DL); writing the manuscript (FFM); critical revision of the manuscript (HYS); supervision (HYS). All authors have read and approved the manuscript.

Acknowledgements

None.

Figures

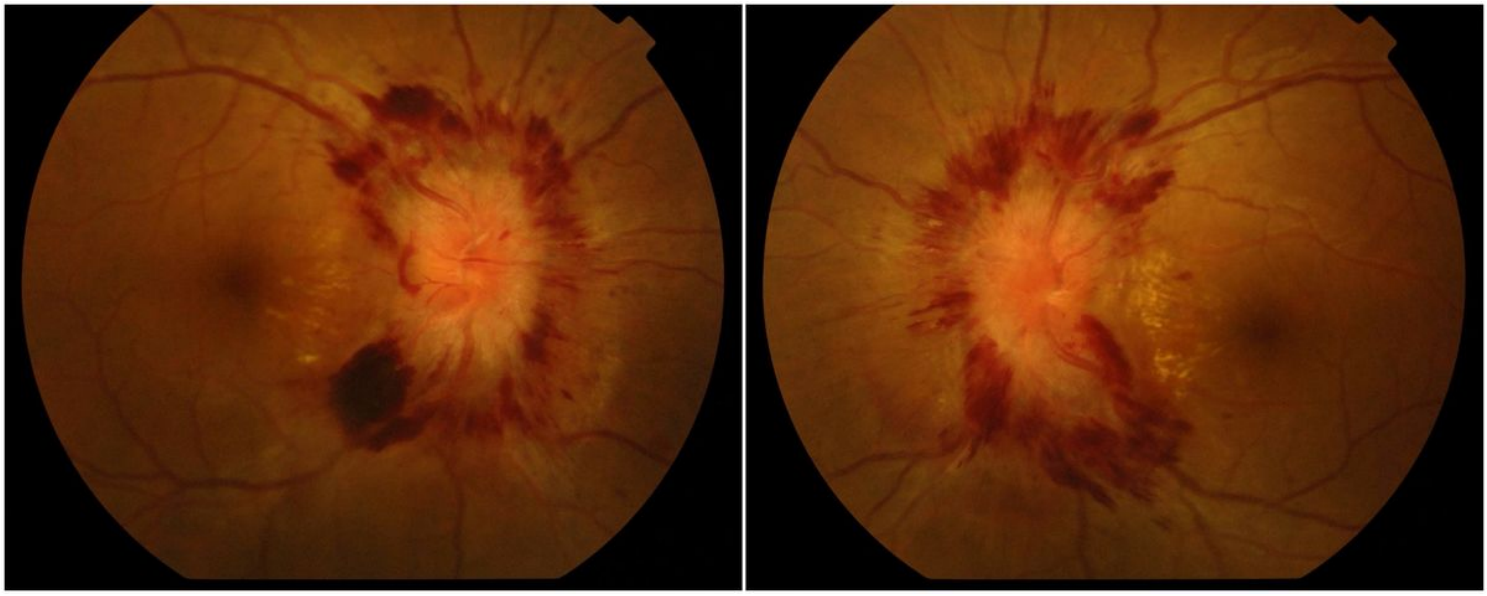

Figure 1

Dilated fundoscopic examination revealed marked bilateral disk edema with dense peripapillary hemorrhages.

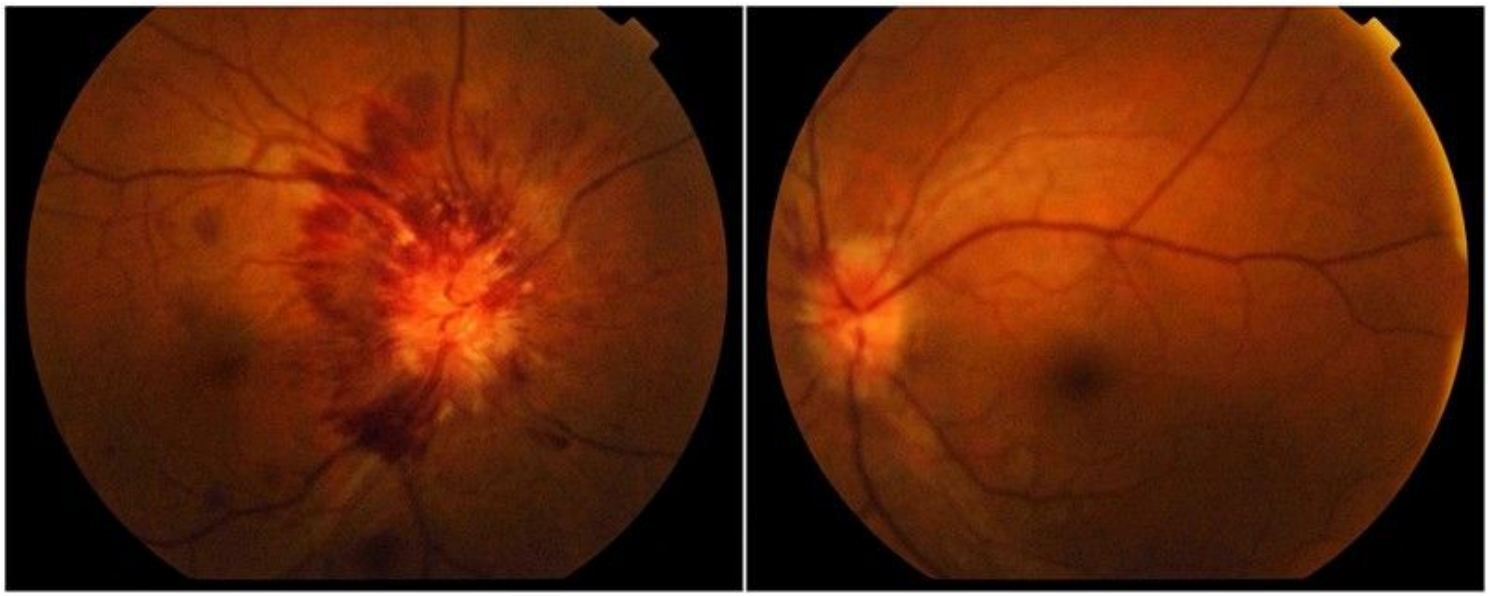

Figure 2

Lesion of optic disk swelling without intraretinal hemorrhages at four months after treatment

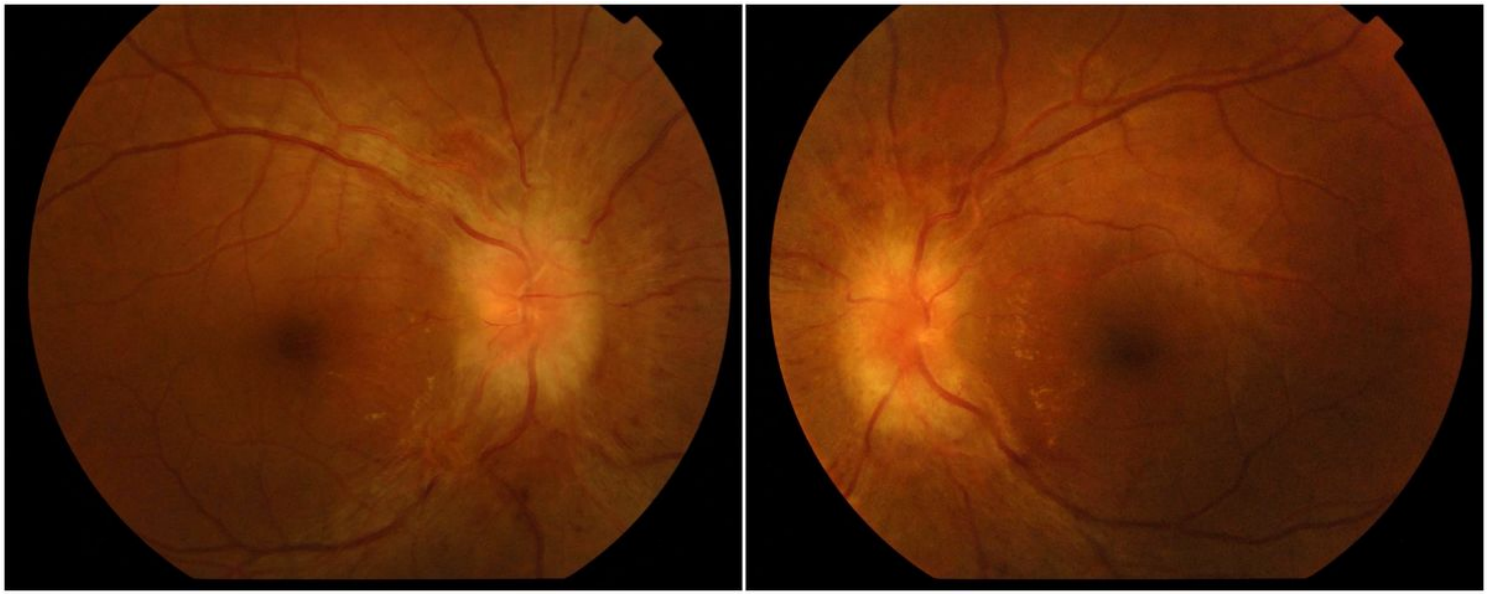

Figure 3

Marked disk edema with dense peripapillary hemorrhages in his right eye and mild papilledema with slight peripapillary hemorrhages in his left eye

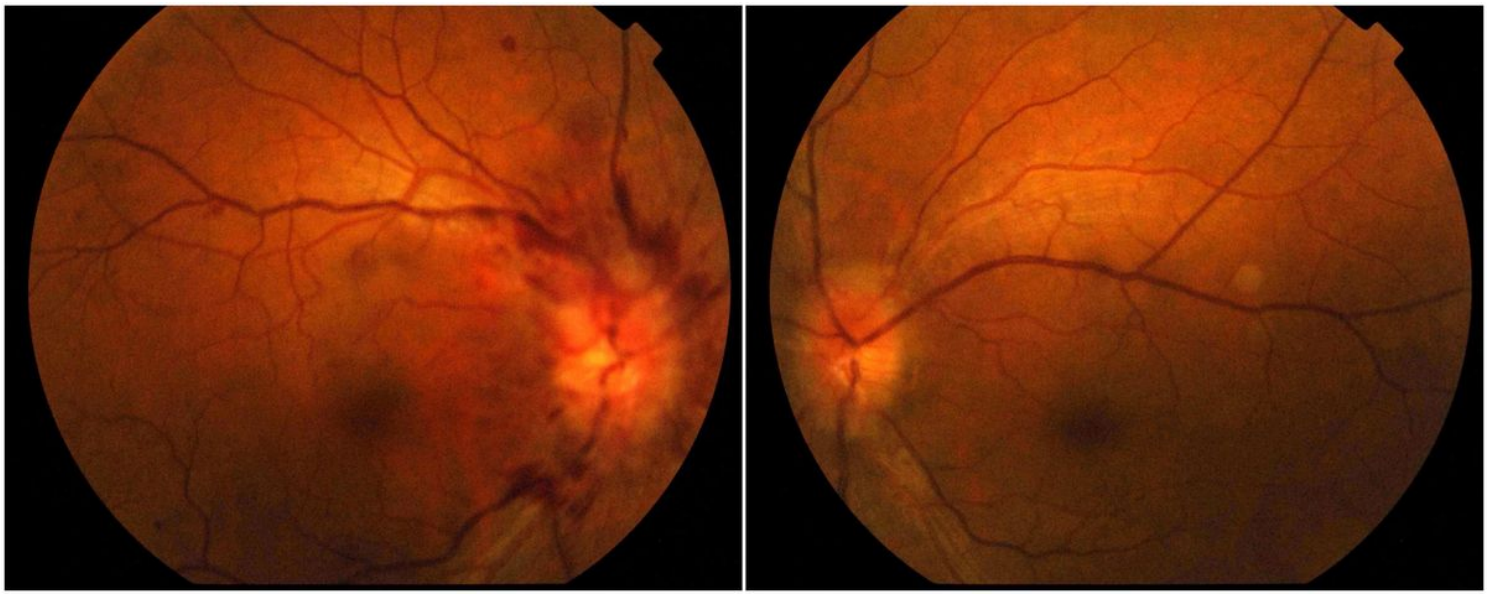

Figure 4

Lesion of optic disk swelling with intraretinal hemorrhages at one month after treatment

Supplementary Files

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- supplement1.pdf