CASE REPORT

Herpes simplex keratitis-induced endophthalmitis in a patient with AIDS with disseminated tuberculosis

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SUMMARY

We present the case of a 42-year-old man with AIDS who had lost complete vision of his left eye for the past 15 days. MRI and brightness scan ultrasonography were performed on his eyes that suggested of endophthalmitis with dendritic involvement in the left eye. Viral DNA PCR was performed in aqueous humour sample that confirmed the presence of herpes simplex virus and showed a negative result for cytomegalovirus. The patient was treated with a high dose of oral acyclovir for 10 days and long-term topical acyclovir. Neodymium-doped yttrium aluminum garnet procedure was performed to clear up the cornea, and intraocular pressure was controlled with brimonidine and timolol maleate. The patient was diagnosed to have disseminated tuberculosis (tuberculoma of the brain) and was started with antituberculosis therapy. His condition improved significantly after the treatment, and keratitis in cornea started to clean up.

BACKGROUND

We believe this is a rare case of herpetic dendritic keratitis in a patient with HIV infection. There are only a few data on ocular infection, apart from the skin, brain and the genital infections, caused by herpes viruses in patients with AIDS with other opportunistic infections such as tuberculosis. This case presents the clinical features, investigational procedures and different treatment aspects for all these diagnosed complications.

CASE PRESENTATION

A 42-year-old male patient was admitted, in June 2013, with a chief problem of total vision loss in his left eye. The patient disclosed that he developed the gradual loss of vision in his left eye for the past 1.5 months; it was progressive and was associated with pain and redness but with no lacrimation. For the past 15 days before admission, he had lost the complete vision in his left eye. For further diagnosis, the physician consulted with ophthalmology department of the hospital. The ophthalmologist had seen the diffuse thickening of the entire uveal tract that was showing postcontract enhancement in the left eye through MRI technique; vitreous exudates were also present in the same eye. These findings were suggestive of endophthalmitis. Topical antiseptic and mydriatics with oral corticosteroids were started on the basis of diagnosis. After some time the patient developed ocular discomforts such as moderate pain and lacrimation in his left eye. The ophthalmologist went through the brightness scanning that was showing keratitis with

dendritic involvement. Aqueous humour sample was taken from the anterior chamber for viral DNA PCR detection. Viral DNA PCR confirmed the presence of herpes simplex virus (HSV). Now the patient was started on acyclovir, mydriatics and corticosteroids topically with high dose of oral acyclovir. Intraocular pressure (IOP) was increased to 30 mm Hg so neodymium-doped yttrium aluminum garnet (Nd-YAG) procedure was performed to clear up the cornea with topical brimonidine and timolol maleate. IOP decreased to 20 mm Hg. In Nd-YAG procedure, laser was applied slightly posterior to the lens to avoid pitting of the lens. The patient had a history of weight loss of 7 kg in 3 months. Five days before the admission in another hospital, he was diagnosed to have miliary tuberculosis (TB) and was started on antituberculosis therapy (ATT). In our hospital, multiple small lesions measuring approximately 2.0 mm, which are hyperintense on T2 and fluid-attenuated inversion recovery (FLAIR) (showing homogeneous contrast enhancement), are seen in an MRI of the brain in both cerebral hemispheres, which is suggestive of tuberculoma of the brain.

The patient is a known case of retroviral illness detected 12 years ago, and no antiretroviral therapy (ART) was taken during this period. His CD4⁺ cell counts were 134 cells/mm³ on admission. All biochemical investigations were normal except for sodium. The patient had hyponatraemia, on admission, and was treated with 5% dextrose solution. The patient showed signs of improvement, and was discharged in the last week of August 2013.

INVESTIGATIONS

The patient was well built and conscious on admission. Physical examinations showed redness and round corneal oedema of the left eye. An MRI was performed, which revealed brain deformities and ocular complications that were suggestive of endophthalmitis (figure 1). Brightness scanning (B-scan) ultrasonography was performed which confirmed keratitis with dendritic involvement (figure 2). Viral DNA PCR was performed for HSV, cytomegalovirus and Japanese Encephalitis virus, which was positive only for HSV. Aqueous humour (10 µL) sample was taken for viral DNA PCR that was aspirated from the anterior chamber. Anterior chamber tap was performed 2 days prior to collecting the sample. Aspiration was performed passing a 30-gauge needle through the limbus. Lymphocyte proliferation assay was performed but no significant changes have found. The acid-fast bacilli sputum test was negative for TB but chest X-ray showed

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Figure 1 MRI image showing the left eye endophthalmitis.

disseminated TB (figure 3). Multiple small lesions of miliary TB measuring approximately 2.0 mm in both hemispheres (figures 4 and 5) and TB granulomas in the hypoechoic region of the spleen were shown in an MRI of the brain and USG of the abdomen, respectively. Cerebrospinal fluid analysis raised protein level, but with no neutrophils suggestive of a negative result for TB meningitis and viral markers. Hepatosplenomegaly and TB granulomas in the hypoechoic region of the spleen were found through ultrasonography of the abdomen. HIV serological testing responded to HIV 1 antibodies. Serological testing for hepatitis B virus and hepatitis C virus was negative.

DIFFERENTIAL DIAGNOSIS

Redness of the left eye and presence of vitreous exudates with corneal oedema were related to keratitis which supports endophthalmitis as primary diagnosis. The differential diagnosis for endophthalmitis was HSV infection. Also, dendritic keratitis with increased IOP was the differential diagnosis for endophthalmitis. Cytomegalovirus, Japanese encephalitis virus and TB meningitis testing were performed as differential diagnosis but showed negative results.

The chest X-ray suggested disseminated TB as primary diagnosis. As per his history, the patient is a known case of retroviral illness; HIV serology testing and CD4+ count confirmed this. Thus, the final diagnosis was herpetic dendritic keratitis with AIDS and disseminated TB.

Figure 2 MRI showing the left eye keratitis with endophthalmitis.

TREATMENT

On admission, the patient had total vision loss of his left eye; the patient was started on topical moxifloxacin and homatropine as anti-eye infective drugs with oral corticosteroids for pain and inflammation. But redness and moderate pain appeared after some time. After the positive result of HSV, the patient was started on high-dose acyclovir 400 mg five times a day for 10 days with topical acyclovir for 6 months. Topical brimonidine, atropine and timolol maleate were given to reduce the IOP with Nd-YAG procedure. Inflammatory effect was controlled by topical and oral corticosteroids in a tapered dose.

The patient was initially started with ATT tab. containing rifampicin 150 mg, isoniazid 75 mg, ethambutol 275 mg and pyrazinamide 400 mg () since admission and ART containing efavirenz 600 mg, emtricitabine 200 mg and tenofovir disoproxil fumarate 300 mg (0-0-1) was started recently in August 2013. Initially, TB was treated as per guidelines for AIDS treatment.

OUTCOME AND FOLLOW-UP

As the patient was treated for 1.5 months with acyclovir and corticosteroids, he recovered from corneal complications and felt better. Inflammation of internal chamber had subsided. Visual acuity of the left eye increased after treatment but some of the keratitis particles persisted. IOP of the left eye came down to normal after Nd-YAG procedure and continuous use of brimonidine, atropine and timolol maleate.

TB symptoms recovered by continuous administration of ATT. In the last week of August, a sputum test for acid-fast bacilli was negative but ATT was continued until completion of therapy as per guidelines. The patient discharged on 31 August when he was free from symptoms. The patient was suggested to visit the hospital after 1 month for a review and follow-up or if he feels any complications/symptoms related to the disease.

DISCUSSION

The clinical pattern of HIV and its opportunistic infections (OIs) show variation from country to country and even from patient to patient.¹ Tuberculosis is one of the most common coinfection with HIV in India. It is classified into pulmonary and extrapulmonary. In this patient, disseminated TB as part of extra-pulmonary TB resulted in tuberculoma of the brain² in the central nervous system. Tuberculoma of the brain was documented rarely with HIV infection (<1% of extra-pulmonary TB infections with AIDS).^{3,4} Commonly, four drugs rifampicin, isoniazid, pyrazinamide and ethambutol in different combinations

Figure 3 Chest X-ray of the patient showing disseminated tuberculosis.

Figure 4 MRI of the brain showing contrast enhancement of both cerebral hemispheres suggestive of tuberculoma.

are used to treat disseminated TB. Other drugs such as amikacin, ethionamide, moxifloxacin, para-aminosalicylate sodium and streptomycin are given in case of drug resistance.^{4, 5} Our patient was treated with standard ATT containing a combination of rifampicin 150 mg, isoniazid 75 mg, ethambutol 275 mg and pyrazinamide 400 mg (orally four tablets daily) for disseminated TB.

Tuberculoma is a non-neoplastic mass, which usually develops in the brain or lungs as a result of TB infection (a form of disseminated/miliary TB).⁵ CT scan and MRI are the important modalities for evaluation of tuberculomas.⁶ In MRI investigations of this patient, multiple small lesions measuring approximately 2.0 mm which are hyperintense on T2 and FLAIR, showing a homogeneous contrast enhancement, are seen scattered in both cerebral hemispheres. MRI finding of tuberculomas depends on their stage of evolution. There are three stages as a result of active macrophage phagocytic action: (1) inflammatory, (2) fibrosis and (3) free radical formation.⁷ Gupta *et al* described that the signal intensity on T2-weighted images varies with the relative proportion of macrophages, cellular infiltrates and fibrosis. The granulomas showing more macrophages, fibrosis and gliosis appeared hypointense on T2-weighted images but the tuberculoma showing minimal macrophages, marked cellular infiltrates and minimal fibrosis appeared hyperintense on T2-weighted images.⁷⁻⁹

According to the WHO guidelines, ART (or highly active antiretroviral therapy) should be started between 2 weeks and 2 months after the initial TB treatment in patients with CD4+

Figure 5 MRI of the brain showing tuberculoma of the brain in the left hemisphere.

count less than 200 cells/mm³.^{1, 4} As this patient had untreated HIV for 12 years and CD4+ count was 134 cells/mm³, he was started on ART containing the combination of efavirenz 600 mg, emtricitabine 200 mg and tenofovir disoproxil fumarate 300 mg daily.

According to an Indian review article, clinical manifestations of tuberculomas show 29.5% ophthalmological symptoms.⁷ In our case, the patient had the chief symptoms of visual loss, eye pain and irritation similar to endophthalmitis. The main symptoms of endophthalmitis are visual loss, eye pain and irritation, ocular discharge; intense ocular periocular inflammation¹⁰⁻¹² includes corneal oedema and infection. Endophthalmitis is an inflammatory condition of the intraocular cavities usually caused by infection. Two types of endophthalmitis were described in previous studies,^{10, 11} which are exogenous or endogenous based on site of infection. Exogenous is one type where the organism directly inoculates from outside after an ocular surgery and causes infection. The other type, endogenous endophthalmitis, showed spread of organism by circulatory system from a distant site of infection (eg, endocarditis).^{12, 13} As the patient was diagnosed to have endophthalmitis with herpes simplex keratitis (HSK), the source of virus infection was not defined properly. Chen *et al*¹³ found keratitis-induced endophthalmitis in a study.

A variety of ocular manifestations, such as extensive blepharitis and spontaneous lid ulcer,¹³ molluscum contagiosum¹⁴ and CMV retinitis, associated with AIDS in India have been reported.¹⁵

As we went through the literature, there are only a few data on ocular infection by HSV, so we believe that ours' is a rare case of herpetic keratitis in a patient with HIV infection.

Varicella zoster virus (VZV) and HSV are the most common aetiological agents of infectious keratitis.¹⁶ HSK results from an infection with the HSV type 1 (HSV 1).¹⁷ HSV keratitis is usually followed by symptoms such as corneal scarring, iritis and raised IOP. Corneal involvement has been reported infrequently in individuals with AIDS or other immunosuppressed status.^{16, 18} Holland *et al* classified HSV keratitis into four categories: (1) infectious epithelial keratitis which is made up of cornea vesicles, dendritic ulcer, geographic ulcer and marginal ulcer, (2) neurotrophic keratopathy, (3) stromal keratitis and (4) endotheliitis. This classification was based on anatomy, pathophysiology and the level of corneal involvement.¹⁹

MRI of this patient showed a diffuse thickening of the entire uveal tract of the left eye with postcontrast enhancement. Brightness ultrasonography showed the presence of epithelial dendrites on the surface of the cornea of the left eye.²⁰ Previous studies recommended some standard methods and techniques, such as PCR for viral detection, for diagnosis of herpetic keratitis.¹⁶ MRI for endophthalmitis signs and brightness scan for dendritic involvement identification.^{21, 22} Intraocular pressure of the left eye of the patient raised to 30 mm Hg, as shown in the B-scan ultrasonography. On the basis of evidence, the patient was diagnosed to have herpetic dendritic keratitis.²³ According to a systemic review by Guess and Stone on evidence-based treatment of HSV keratitis, trifluridine and topical or oral acyclovir had the best evidence for treatment of HSV epithelial keratitis.^{12, 24} Topical corticosteroids and prophylactic antiviral therapy for a short duration had strong supportive evidence for the treatment of different types of keratitis. Ganciclovir is also a potent inhibitor of members of herpes virus family.^{25, 26} The US Centers for Disease Control and Prevention (CDC) recommends the acyclovir intermittent therapy as 400 mg orally three times a day or 200 mg orally five times a day for 7–10 days.

This patient was initially started on anti eye infection drugs for total vision loss, but when the patient was confirmed to have herpes simplex infection in his left eye, he started on high-dose acyclovir as 400 mg five times a day for 10 days with topical acyclovir and corticosteroids. Oral and topical corticosteroids were given for intraocular inflammation. Topical brimonidine and timolol maleate were given to reduce IOP.^{27 28}

Learning points

- ▶ Herpes simplex keratitis is an unusual and rare combination with tuberculoma of the brain in a patient with AIDS.
- ▶ Vision loss, eye pain and irritation and ocular discharges are the main symptoms to diagnose endophthalmitis.
- ▶ Viral DNA PCR is the gold diagnostic method to confirm the viral infections such as herpes simplex virus, varicella zoster virus and cytomegalovirus.
- ▶ Standard therapy or best evidence-supported therapy should be started immediately after a confirmed diagnosis to prevent deleterious results.
- ▶ Topical acyclovir and corticosteroids with short duration of oral acyclovir therapy have strong supportive evidence for the treatment of herpes simplex keratitis.
- ▶ Highly active antiretroviral therapy should be started between 2 weeks and 2 months after the initial tuberculosis treatment in patients with CD4+ count less than 200 cells/mm².

Competing interests None.

Patient consent Obtained.

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