CASE REPORT

Progressive outer retinal necrosis: manifestation of human immunodeficiency virus infection

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SUMMARY

We present the case of a 54-year-old man who developed progressive outer retinal necrosis (PORN) as an initial manifestation of HIV infection without any significant risk factors for infection with HIV. PORN is usually found as a manifestation of known AIDS late in the disease. Our patient presented with transient visual loss followed by decrease in visual acuity and facial rash. Subsequent investigation revealed anterior chamber tap positive for varicella zoster virus (VZV), as well as HIV positivity, with an initial CD4 count of 48 cells/ μ L. Systemic and intravitreal antivirals against VZV, and highly active antiretroviral therapy against HIV were started, which halted further progression of retinal necrosis. This case highlights the importance of suspecting PORN where there is a rapidly progressive retinitis, and also testing the patient for HIV, so appropriate treatment can be started.

BACKGROUND

Progressive outer retinal necrosis (PORN) is a herpetic viral retinopathy with the following clinical features: multifocal lesions without granular borders in deep retinal layers, lesions in the peripheral retina with or without macular involvement, rapid progression, absence of vascular inflammation and minimal or no intraocular inflammation.^{1 2} This is a condition that typically affects immunocompromised patients, although it has also rarely been reported in immunocompetent patients.¹ PORN may be caused by herpes simplex virus (HSV) and cytomegalovirus (CMV) although varicella zoster virus (VZV) is most commonly seen.^{1 3} Very rarely is PORN an initial manifestation of HIV infection.⁴ In most cases of patients affected with PORN, a diagnosis of AIDS is already known at consultation.⁵ To the best of our knowledge, this is the first case report of such a scenario in the UK. The case underscores the importance of suspecting the diagnosis of PORN where there is a rapidly progressive retinitis, and also of testing the patient for HIV, so that appropriate treatment can be started.

CASE PRESENTATION

A 54-year-old man presented with an episode of sudden loss of vision in the left eye, initially diagnosed as a probable cilioretinal artery occlusion, and was subsequently referred to the transient ischaemic attack clinic.

He then re-presented to the emergency department 1 week later with reduction in vision in the

right eye, headache and a widespread maculopapular rash on his face. He also reported a weight loss of 6.35 kg over the past month. Preceding this, he had a history of herpes zoster ophthalmicus (with a painful skin rash over V1 dermatomal distribution) 4 weeks before the initial presentation. He did not have a significant medical history, however, his ocular history includes being myopic, previous multiple vitrectomies for retinal detachment on the left eye and right amblyopia. He is a heterosexual and there was no history of any intravenous drug use.

On examination with the slit lamp, visual acuity was hand movement in the right eye and perception of light in the left eye. He had iritis in both eyes as well as vitritis in the left eye. The intraocular pressures measured 12 and 15 mm Hg in the right and left eye, respectively.

Fundus examination, as shown in figure 1 A, B, revealed yellow-white patchy irregular areas of retinitis with pigmented scars in the periphery in both eyes, without retinal vasculitis.

Figure 1 (A) Right eye at presentation and (B) left eye at presentation.

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Figure 2 Right eye fluorescein angiogram. (A) superotemporal periphery; (B) posterior pole and (C) inferior periphery. These show the typical irregular-sized retinitis lesions on the posterior pole and peripheries, without associated retinal vasculitis, typical of progressive outer retinal necrosis. (D) Left eye fluorescein angiogram, posterior pole. Extensive involvement of the posterior pole with retinitis lesions, worse than on the right eye. This eye rapidly developed total retinal detachment despite aggressive treatment.

INVESTIGATIONS

The patient had a fluorescein angiogram (figure 2 A–D), which confirmed widespread retinitis in both eyes, involving the posterior pole and peripheries.

An anterior chamber paracentesis was performed and the fluid was sent for PCR analysis for *Toxoplasma gondii*, HSV, VZV and CMV. The results were positive for VZV and negative for the other organisms.

The patient also had serology testing for HIV, syphilis, Lyme disease, toxoplasmosis, CMV, *Bartonella*, T-spot, Mantoux test, antinuclear antibody (ANA) receptors and antineutrophil cytoplasmic antibody (ANCA). He was found to be HIV positive with a CD4 count of 48 cells/ μ L. The other serology tests were negative.

DIFFERENTIAL DIAGNOSIS

The clinical presentation and investigation results were strongly suggestive of PORN secondary to VZV. The main differential diagnoses include CMV retinitis, syphilis and tuberculosis, which were ruled out with serological and PCR testing as described above.

TREATMENT

The patient was started on intravenous foscarnet and acyclovir and was given intravitreal injections of ganciclovir two times per week. This treatment regiment was continued for 3 weeks, and subsequently he continued on oral acyclovir. He was also given topical cyclopentolate and prednisolone. For treatment of his HIV/AIDS he was started on *Mycobacterium avium*-intracellulare and *Pneumocystis carinii* pneumonia prophylaxis and highly active antiretroviral therapy (HAART).

OUTCOME AND FOLLOW-UP

The patient's left eye, which had a visual acuity of perception of light at presentation, had a rapidly progressive retinal necrosis and he developed a total rhegmatogenous retinal detachment. The visual acuity, unfortunately, deteriorated to no perception of light. This was reviewed in conjunction with our vitreoretinal surgeons and a decision to not surgically treat the eye was made because of multiple retinal breaks and a poor prognosis.

In the patient's right eye (figure 3), the extent of the necrosis halted with treatment. Over time, he developed pigmentation and scarring of the affected retina. His vision, however, was preserved at 6/36 at 12 weeks of follow-up. With HAART, his CD4 count gradually improved and was 102 cells/ μ L 3 months after his initial diagnosis.

DISCUSSION

Ocular manifestations of HIV are common, affecting about 70–80% of patients.⁶ A CD4 count of less than 100 cells/ μ L in HIV-positive patients is known to be associated with microvasculopathy, which tends to be retinal or conjunctival. Patients are also more susceptible to infectious agents leading to diseases such as PORN, CMV retinitis and cryptococcosis.⁶ CD4 count levels are useful in predicting the infectious agents patients are likely to be susceptible to.

Timely recognition and prompt treatment of PORN is crucial, as visual acuity deteriorates rapidly. Most patients who present have an initial loss of vision, and in a descriptive series published by Engstrom and colleagues in 1994, two-thirds of eyes progress to no light perception within 4 weeks of onset.⁷

There is no current consensus on the optimal treatment regime for PORN, as it is such a rare disease entity. Generally,

Figure 3 Right eye after successful treatment with intravitreal and systemic antivirals. The retinitis lesions show pigmentation and inactivity.

one or more systemic antivirals, as well as an intravitreal injection of ganciclovir or foscarnet, have been used in the treatment of PORN.¹ Oral acyclovir has a low bioavailability, hence, in the past, patients would need to be admitted for intravenous induction of acyclovir to boost initial levels of the drug for treatment. However, with the development of newer agents such as valganciclovir and valganciclovir, the oral bioavailability has increased to that comparable to intravenous acyclovir.⁸ Nevertheless, in acute cases or first presentation of PORN, the intravitreal route is preferred as an initial treatment as a bolus of antiviral can be administered directly to the affected eye. As in our patient, an intravitreal bolus was first administered followed by intravenous antivirals before tapering off with oral antivirals.

In HIV-positive patients, HAART therapy has also been suggested to modify prognosis by reducing viral load and increasing CD4 count.⁹ A study reported by Woo *et al*⁹ suggested that CD4 counts improved and retinal lesions regressed after the commencement of HAART. It has also been postulated that if patients were receiving HAART therapy at the onset prior to the necrosis, the retina was less likely to detach, as it regresses progression.¹ Hence it was concluded that HAART regresses progression of PORN and potentiates effects of antiviral treatment by increasing host immunity in HIV-positive patients.⁹

Notably, PORN is usually seen in patients who already have a diagnosis of AIDS. This case is unusual as PORN is an initial manifestation of AIDS. Thus, when confronted with a rapidly progressive retinal necrosis with mild intraocular inflammation, PORN should always be part of the differential diagnosis, even when the patient has no history to suggest a compromised

immune system. A high index of suspicion in the right clinical context will allow early diagnosis and treatment of this condition. Where patients are not known to be immunocompromised, they should also be offered an HIV test since PORN can be the first manifestation of AIDS, as illustrated by our case.

Learning points

- ▶ Uveitis can be a manifestation of life-threatening disease.
- ▶ Very rarely, progressive outer retinal necrosis (PORN) may be an initial manifestation of HIV infection.
- ▶ Timely referral and intensive intervention on PORN might preserve some vision.

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Contributors PFL was involved in overall design of article and most of the writing. RL reviewed the article and involved in general care of the patient. SNA was responsible for collection of images, involved in the general care of the patient and consented the patient. GCA supervised and reviewed the article.

Competing interests None declared.

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