CASE REPORT

Atypical cytomegalovirus retinitis in non-Hodgkin's lymphoma

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SUMMARY

A 54-year-old woman, a known case of non-Hodgkin's lymphoma (NHL) in complete remission, presented with floaters and diminution of vision in her left eye. The eye had vitritis with non-haemorrhagic retinitis mimicking intraocular lymphoma and acute retinal necrosis. A vitreous sample was positive for cytomegalovirus (CMV) and herpes simplex virus 1 (HSV-1) DNA by PCR. The possibility of intraocular lymphoma was not confirmed by the immunohistochemistry of the vitreous sample. The patient had a relapse of NHL along with rapid deterioration of vision in her left eye to no perception of light, due to optic nerve involvement. The right eye developed a new patch of focal haemorrhagic retinitis threatening the fovea. Based on the laboratory results and the clinical findings, she was successfully managed as a case of bilateral CMV retinitis and the vision in her right eye was salvaged.

BACKGROUND

This case represents the atypical ocular manifestations that cytomegalovirus (CMV) infection can present with, in cases of lymphomas that are HIV negative and that have higher CD4 counts than expected in usual cases of CMV retinitis. The analysis of intraocular fluids in conjunction with a close follow-up of the clinical picture is the key to correct diagnosis and management of such cases. We present one such case, which presented as CMV retinitis in a patient of non-Hodgkin's lymphoma (NHL). The timely diagnosis and the appropriate treatment salvaged vision in one of the two eyes.

CASE PRESENTATION

A 54-year-old woman presented with floaters and diminution of vision in her left eye for the past 2 weeks. She was a known case of B-cell NHL with bone marrow involvement, and had completed six cycles of chemotherapy 6 months ago in the form of rituximab plus cyclophosphamide, doxorubicin, vincristine and prednisolone (R-CHOP). On presentation, she had visual acuity of 20/20 in the right eye and 20/60(P) in the left eye. The intraocular pressure was 16 and 18 mm Hg in the right and the left eye, respectively, by Goldmann applanation tonometry. The anterior segment was normal in both eyes except for early nuclear sclerosis in the crystalline lens. The fundus of the right eye had a focal retinitis lesion temporal to the fovea (figure 1A). The fundus of the left eye had hazy media due to vitritis, non-haemorrhagic retinitic lesions in the macula, and nasal and superior quadrants, and a few superficial

retinal haemorrhages (figure 1B). There was retinal arteritis in the inferonasal quadrant.

INVESTIGATIONS

The complete haemogram revealed pancytopenia with haemoglobin of 9.4 g/dL and a total leucocyte count of 1800 cells/ μ L. The CD4 count was 193 cells/ μ L. The patient was started on oral valacyclovir at a dosage of 1000 mg eight hourly and vitreous biopsy of the left eye was performed on the same day.

On histopathology, the vitreous sample showed monomorphic population of round cells with deep basophilic nuclei and a scant rim of cytoplasm. The T-cell reactivity on immunohistochemistry confirmed that the sample showed reactive inflammatory infiltrate and no lymphomatous infiltration. The vitreous sample was subjected to a PCR test, which detected both CMV and herpes simplex virus 1 (HSV-1) DNA.

DIFFERENTIAL DIAGNOSIS

In view of the patient's medical history and clinical presentation, differential diagnoses of acute retinal necrosis (ARN), atypical CMV retinitis and intraocular lymphomatous infiltration in the left eye were considered. However, the immunohistochemistry of the vitreous sample did not confirm an intraocular lymphoma.

TREATMENT

Oral prednisolone at a dosage of 1 mg/kg body weight was started and systemic valacyclovir was continued. In the meanwhile, the patient had a relapse of lymphoma, for which she was started on a salvage chemotherapy regimen of rituximab plus cisplatin, cytosine arabinoside and dexamethasone (R-DHAP). The systemic deterioration led to non-compliance with the ocular therapy subsequent to which the visual acuity in the left eye rapidly deteriorated over the next 2 weeks to no perception of light, while it was sustained at 20/25 in the right eye. On examination, the right eye had a quiet anterior segment with a new patch of focal haemorrhagic retinitis temporal to the fovea (figure 2A). The left eye showed diffuse keratic precipitates on the corneal endothelium, cells in the anterior chamber and dense vitritis allowing a hazy visualisation of the optic disc (figure 2B). Seeing the haemorrhagic nature of the lesion in the posterior pole of the right eye threatening the fovea, a clinical diagnosis of bilateral CMV retinitis was concluded. Since the left eye had no visual prognosis, only the right eye was treated with an induction

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Figure 1 Colour fundus photos of the right and the left eye on the first day of presentation. (A) Right eye (best corrected visual acuity (BCVA) 20/20) showing focal areas of retinal whitening close to fovea. (B) Left eye (BCVA 20/40) showing vitritis, retinitis in inferior macula and arteritis in inferonasal quadrant.

dosage of intravitreal ganciclovir (2500 µg in 0.05 mL) twice weekly for 3 weeks, followed by a maintenance dose of the same injection weekly for the next 3 weeks. The oral prednisolone was rapidly tapered and oral valganciclovir in a daily dosage of 900 mg 12 hourly was started after stopping intravitreal ganciclovir.

OUTCOME AND FOLLOW-UP

The patient responded well to the therapy. The visual acuity of the right eye was maintained at 20/25, with the focal haemorrhagic retinitis showing gradual resolution over the next 2 months (figures 3 and 4). The vision in the left eye could not be salvaged, but the retinitis responded to systemic valganciclovir with complete resolution of vitritis (figures 3 and 4). The left fundus showed disc pallor, sclerosed arteries in all quadrants and resolving haemorrhagic retinitis in the macula and in all quadrants. The patient was kept on regular follow-up with continuation of oral valganciclovir.

DISCUSSION

CMV retinitis is known to occur in patients receiving immunosuppressive treatments for malignancy, following organ

transplantation and in those with autoimmune diseases. Pathanapitoon *et al*¹ retrospectively reviewed the records of 18 HIV-negative patients (22 affected eyes) diagnosed as having posterior uveitis or panuveitis who had aqueous positive for CMV by PCR techniques. The commonest ocular features included focal haemorrhagic retinitis, peripheral retinal necrosis, inflammatory reaction in anterior segment and retinal vasculitis mostly affecting arteries, with all patients exhibiting vitritis. Five of the cases had NHL. Our case also presented with similar atypical clinical features, namely focal haemorrhagic retinitis in the right macula, and anterior chamber (AC) reaction with vitritis, retinal arteritis and an ARN-like picture in the left eye.

Svozílková *et al*² reported a case of bilateral CMV retinitis in an HIV-negative patient with NHL, with a normal lymphocyte count, who had white retinal lesions in both eyes. Vitreous fluid analysis showed atypical lymphoid elements, highly suspicious of malignancy, but PCR testing confirmed the presence of CMV in the vitreous. Derzko-Dzulynsky *et al*³ also reported a case of a patient with NHL who developed a chorioretinal infiltrate that was initially difficult to differentiate between intraocular lymphoma and CMV infection, but the analysis of intraocular fluid helped in reaching a conclusive diagnosis. Nasir *et al*⁴

Figure 2 Colour fundus photos of the right and the left eye 2 weeks after presentation. (A) Right eye (BCVA 20/25) showing focal haemorrhagic retinitis temporal to fovea. (B) Left eye showing dense vitritis. Retinal details not visualised. Vision deteriorated to no perception of light.

Figure 3 Colour fundus photos of the right and the left eye after 1 month of treatment. Right eye maintained visual acuity of 20/25. (A) Right eye showing resolving retinitis temporal to fovea. (B) Left eye showing resolving haemorrhagic retinitis.

Figure 4 Colour fundus photos of the right and the left eye after 2 months of treatment. Right eye maintained visual acuity of 20/25. (A) Right eye showing resolving retinitis temporal to fovea. (B) Left eye showing resolving haemorrhagic retinitis.

Patient's perspective

I am glad that my mother can see with one eye at least. She can maintain her daily activities with this one eye. While I feel sad that she has lost the sight in her left eye, I hope that her right eye remains good (Patient's daughter).

Learning points

- ▶ Cytomegalovirus (CMV)-associated infections in HIV-negative patients can present with a wide spectrum of atypical presentations as compared to the classic picture of CMV retinitis in an immunocompromised HIV-positive patient.
- ▶ Patients with non-Hodgkin's lymphoma (NHL) may develop CMV retinitis that may be difficult to differentiate from or may coexist with intraocular lymphomatous infiltration.
- ▶ The immunosuppressive therapy given to these patients is known to cause pancytopenia and increase the susceptibility to such opportunistic infections.
- ▶ It is also important to consider the fact that these patients can present with CMV retinitis even with high CD4 cell counts.
- ▶ The differentiation of lymphomatous infiltration from CMV infection is critical for deciding the treatment regimen, and analysis of intraocular fluid has a major role to play in obtaining the correct diagnosis.

reported a similar case of Hodgkin's disease presenting with an atypical retinitis, vasculitis and a serous macular detachment. The diagnosis of an atypical CMV retinitis simulating possible intraocular involvement by Hodgkin's disease was confirmed by PCR testing of undiluted vitreous. Chawla *et al*⁵ reported a similar diagnostic dilemma in a rare case of bilateral CMV retinitis in a patient with NHL, with high CD4 counts, as in our case.

Contributors MT saw the patient and made the diagnosis. MT, AM and RN managed and treated the patient. The manuscript writing and review of literature were carried out by MT and VA.

Competing interests None declared.

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