Unusual association of diseases/symptoms

An unusual cause for an optic disc haemorrhage

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Summary

A 51-year-old male on chemotherapy for myeloma presented initially with a unilateral optic disc haemorrhage and signs of optic neuropathy. This rapidly progressed to affect both eyes and within a few days he developed retinal features suggestive of progressive outer retinal necrosis. He was treated with intravenous acyclovir that was subsequently changed to ganciclovir when serological tests for cytomegalovirus were found to be positive for immunoglobulin M antibodies. His visual loss continued to deteriorate despite treatment, and he subsequently developed a retinal detachment in one eye. The causes of optic neuropathy in immunocompromised patients and the importance of eliminating an infective cause are discussed.

BACKGROUND

Progressive outer retinal necrosis (PORN) is most frequently seen in patients with AIDS but may also be seen in patients who are immunosuppressed from other causes. In immunosuppressed patients presenting with an optic neuropathy, an infective cause should always be sought. Infectious optic neuritis in these patients is usually secondary to meningitis. However, rarely, optic neuropathy can be the first sign of PORN.

PORN usually presents with diagnostic signs on retinal examination, but it occasionally presents with optic neuropathy without any retinal signs. Optic disc haemorrhage is a previously unreported finding in PORN. In the absence of other clinically evident causes of optic neuropathy and disc haemorrhage, we suggest that a diagnosis of PORN be considered in immunosuppressed patients. Early diagnosis and treatment are crucial in improving visual outcome.

CASE PRESENTATION

A 51-year-old male presented with right-sided blurring of vision. He was on his fifth cycle of chemotherapy (thalidomide/cyclophosphamide/dexamethasone) for myeloma that was responding well to treatment. He had no relevant ophthalmic history but gave a history of recent cutaneous varicella zoster infection that had resolved. His visual acuities were 6/60 right 6/6 left and a right relative afferent pupillary defect was noted. Anterior segment examination and his intraocular pressures were normal. Fundal examination revealed some macula oedema and a large optic disc haemorrhage on the right side. He presented 2 days later with complaints of blurring in his left eye. His visual acuities were 6/60 right and 6/18 left and his colour vision was markedly reduced bilaterally. He now had macula oedema and disc haemorrhages in both eyes with multiple patches of pale oedematous retina without vitritis, see figure 1A and B. The following day, his vision dropped further to counting fingers right and 6/60 left with evidence of worsening retinal oedema, pallor and arteriolar attenuation.

INVESTIGATIONS

Blood tests revealed chronic anaemia, mildly reduced white cell count (lymphopenia), chronic renal impairment and normal electrolytes, erythrocyte sedimentation rate, C reactive protein, glucose and vital observations.

Serological assays for varicella zoster, herpes simplex, *Pneumocystis carinii*, adenovirus and *Toxoplasma gondii* were negative. Cytomegalovirus (CMV) immunoglobulin M (IgM) antibodies were positive.

CT brain was normal and excluded a space-occupying lesion.

DIFFERENTIAL DIAGNOSIS

- ▶ Optic neuritis secondary to meningitis.
- ▶ Optic neuropathy preceding PORN.
- ▶ Thrombotic vein occlusion secondary to chemotherapy with thalidomide.
- ▶ Haemorrhage in bone marrow-suppressed patient (secondary to anaemia, thrombocytopenia).
- ▶ CMV retinitis.

TREATMENT

He was admitted to the hospital and started on intravenous acyclovir for presumed PORN. This was subsequently changed to ganciclovir when the IgM serology results returned positive for CMV.

OUTCOME AND FOLLOW-UP

The patient's vision continued to deteriorate to no perception of light right and perception of light left. He developed a retinal detachment in the left eye, which was treated surgically with silicone oil tamponade.

DISCUSSION

In an immunosuppressed patient presenting with optic neuropathy, an infective cause should always be sought. Most infective causes of optic neuropathy in such patients are secondary to meningitis. However, in the absence of

Figure 1 Fundal photographs of the (A) right eye and (B) left eye. Note the bilateral optic disc haemorrhage, macula oedema and patchy areas of necrotic retina.

other clinical parameters suggestive of meningitis, PORN should also be considered in the differential diagnosis.

PORN is a rare rapidly progressive condition that is most frequently seen in patients with AIDS, but has been reported to occur in patients with lymphoma,¹ nephrotic syndrome,² rheumatoid arthritis³ and other immunodeficient states.⁴

In a large case series, 85% of patients with PORN presented with peripheral lesions and 15% presented with both macula and peripheral lesions.⁵ PORN has been reported to present as an optic neuropathy (retrobulbar neuritis and swollen optic nerve head) but this is rare with only a few published case reports.^{6–8} No cases of PORN presenting with optic disc haemorrhage have been reported to the authors' knowledge. If retinal signs of PORN are present, a vitreous biopsy should be taken for molecular diagnostic tests for viruses.

Although PORN is usually caused by varicella zoster virus (VZV), CMV, herpes simplex virus and Epstein–Barr virus have rarely been implicated as aetiological agents in PORN.^{5 9 10} The majority of patients with PORN demonstrate evidence of current or recent cutaneous or disseminated VZV infection.⁵ This may help make a diagnosis. However, treatment with acyclovir is relatively ineffective and concurrent treatment with intravitreal ganciclovir and foscarnet is recommended.⁵ There has been a single report of gammaglobulin use with a favourable visual result.¹¹

Our patient's positive IgM antibody for CMV suggests recent infection with the virus. However, it is uncertain whether this was a subclinical concurrent infection or whether this was secondary to PORN caused by CMV. Although our patient's treatment regimen was changed to ganciclovir, no clinical improvement was noted. PORN is associated with a poor visual outcome but diagnosis in the early stage of the disease and early treatment with intravitreal ganciclovir and foscarnet appear to stabilise both the disease and the patient's vision.¹² Advanced disease responds poorly to aggressive treatment and has a poor outcome. Having a high index of suspicion of PORN and starting treatment without delay are crucial in the care of these patients.

At initial presentation, a haemorrhage at the disc could have alerted one to the possibility of CMV retinitis. However, the progressive changes in the retina did not match the classic signs of CMV retinitis. Considering

treatment with ganciclovir, at this stage, may have been reasonable.

Some non-infectious causes of haemorrhagic optic neuropathy may be considered in a bone marrow-suppressed individual. Venous thromboembolic disease has been reported in patients started on treatment with thalidomide for myeloma.¹³ In our patient, the rapid progression to PORN eliminated the diagnosis of retinal venous thrombosis. Similarly, haemorrhage due to anaemia or thrombocytopenia does not usually present with signs of rapidly progressive optic neuropathy and can safely be discarded as the cause of optic disc haemorrhage.

Learning points

- ▶ Exclude infectious causes of optic neuropathy in immunocompromised patients.
- ▶ An early sign of PORN may be optic neuropathy with or without disc haemorrhage.
- ▶ PORN is most frequently caused by VZV but other viruses such as CMV should also be considered.
- ▶ Consider ganciclovir as first line antiviral treatment for PORN, if unsure about causative agent.
- ▶ Delay in treatment of PORN results in irreversible visual loss.

Competing interests None.

Patient consent Obtained.

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