Choroidal lesions in patients with AIDS

Marc A Rosenblatt, Carol Cunningham, Steven Teich, Alan H Friedman

Abstract
Seven cases of bilateral, scattered, yellow-white choroidal lesions have been seen in AIDS patients since January 1988. One resulted from presumed extension of cryptococcal meningitis into the optic nerve and choroid. All the remaining six patients had pneumocystis pneumonia at some time during the course of the disease and were receiving aerosolised pentamidine therapy. None died quickly of disseminated *Pneumocystis carinii* infection, unlike previously reported patients. Mycobacterial infection was also present in five of these six patients. The differential diagnosis of this entity in AIDS patients is discussed.

Scattered choroidal yellow-white lesions in AIDS patients have recently been described as a marker for disseminated and rapidly fatal *Pneumocystis carinii* infection. We present a series of seven cases with similar appearances but varied outcomes. Possible alternative aetiologies are discussed.

Case reports

**CASE 1**
A 31-year-old homosexual male with AIDS had four previous episodes of *Pneumocystis carinii* pneumonia and one of cytomegalovirus (CMV) pneumonia. *Mycobacterium avium intracellulare* infection had been noted on endobronchial biopsy. Medications included isoniazid, rifampicin, ganciclovir, and aerosolised pentamidine. During recurrence of pneumonia, which was without visual symptoms and with normal acuity, examination with dilated pupils revealed bilateral, flat, yellow-white choroidal lesions through all quadrants, varying in size from 0.25 to 2 disc diameters. Rapid plasma reagin, toxoplasmosis immunofluorescence antibody test, and serological tests for histoplasmosis, coccidioidomycosis, and cryptococcus were negative. After three weeks of intravenous pentamidine and a reinduction course of ganciclovir the pneumonia cleared. After two months the choroidal lesions became more discrete and orange, with overlying pigment proliferation. He died of staphylococcal septicaemia 11 months later without necropsy.

**CASE 2**
A 32-year-old homosexual male with AIDS was found to have normal acuity and approximately 20 choroidal lesions in each eye while in hospital in June 1988 for cryptococcal meningitis with bone marrow involvement and increased intracranial pressure. Despite treatment with intravenous amphotericin, palsies of cranial nerves III, V, VI, and VII developed. The optic disc was swollen, with dilated retinal venules and peripapillary haemorrhages.

Computerised tomography revealed enlarged optic nerves. Despite treatment with flucytosine and intravenous dexamethasone, vision deteriorated to finger counting in both eyes after one month. An electroretinogram (ERG) was normal, but visually evoked potential (VEP) was unrecordable. Fluorescein angiography revealed diffuse disc leakage and hypofluorescence corresponding to the choroidal lesions. Visual loss was thought to be due to cryptococcal invasion of the optic nerves.

**CASE 3**
A 28-year-old homosexual male with AIDS had multiple episodes of *P. carinii* pneumonia, after which he received aerosolised pentamidine. CMV retinitis of the right eye treated with ganciclovir progressed to a retinal detachment. Isoniazid, rifampicin, and ethambutol were prescribed for bone marrow granulomas. Sub-retinal creamy yellow-white lesions appeared about the macula in the left eye. Over two weeks similar lesions appeared under the bullous detachment in the right eye, and new lesions appeared in the left eye. Vision remained 20/20 in the left eye. Fever developed. Serological testing for rapid plasma reagin, toxoplasmosis, cryptococcus, coccidioidomycosis titres, adenovirus titres, and Epstein-Barr virus titres were negative. A gallium scan showed increased uptake in the mediastinum and retroperitoneal lymph nodes. Intravenous pentamidine was begun for presumed disseminated *P. carinii* infection. The choroidal lesions become more discrete and orange, with pigment proliferation at their edges. The patient returned home on oral dapsone prophylaxis for *P. carinii* pneumonia (PCP), and one month later his local ophthalmologist noted no evidence of choroidal lesions in either eye. His visual acuity was light perception OD and 20/20 OS.

**CASE 4**
A 37-year-old intravenous drug user with AIDS, maintained on aerosolised pentamidine after five bouts of *P. carinii* pneumonia, had 20/40 vision OD while in the hospital for bronchoscopy-proven pneumocystis pneumonia. Amsler grid testing revealed a large paracentral scotoma OD. Examination under dilated pupils showed a five-disc diameter, flat, grey-yellow choroidal lesion subfoveally with a brighter area as its nasal edge, suggesting more acute inflammation. Ten to 15 smaller choroidal lesions were scattered outside the posterior pole. In the left eye there were at least 20 similar choroidal lesions. The pneumonia improved on trimetrexate and the lesions became
Figure 1A
Figure 1  Case 6. A: Right eye: Scattered lesions with one under the fovea and flame haemorrhages at the disc margin with several cotton-wool spots and haemorrhages. Visual acuity 20/80. B: Left eye: similar retinal lesions on presentation. C: Fluorescein angiogram right eye, early arteriolar phase showing hypofluorescence of lesions. D: Fluorescein angiogram right eye, hyperfluorescence later in sequence.

more distinct. Serological testing for syphilis (VDRL), cryptococcal antigen, and toxoplasmosis gave negative results. A diagnosis of presumed disseminated P carinii infection was made and the patient put on prophylactic therapy with oral dapsone. A splenectomy three months later for idiopathic thrombocytic purpura revealed both P carinii and acid-fast bacteria. Isoniazid and ethambutol were added to the treatment. A year later, during the seventh admission to hospital for P carinii pneumonia, acuity and Amsler grid results had returned to normal and the choroidal lesions had become deep orange.

CASE 5
A 42-year-old AIDS patient had three recur-

rences of PCP in two years; he was taking rifampicin and isoniazid for Mycobacterium avium intracellulare infection, acyclovir for herpes simplex, aerosolised pentamidine for PCP, and azathioprine. CMV retinitis was found in the left eye, reducing vision to 20/400. After treatment with ganciclovir for three months his acuity was unchanged, but he developed grey-yellow lesions throughout the right fundus at the level of the retinal pigment epithelium. Similar lesions were seen in the non-atrophic areas of the left fundus. Fluorescein angiography revealed early blockage and late staining of the lesions.

CASE 6
A 37-year-old male with AIDS was admitted to hospital in September 1988 for bilateral pleural effusions after eight months of aerosolised pentamidine. His visual acuity was 20/20 OU. Examination under dilated pupils revealed round and oval yellow-white choroidal lesions 0.5 to 2 disc diameters scattered in the posterior pole with one underlying the fovea OD. There were flame haemorrhages on and near the disc OD (Figs 1A, B). Fluorescein angiography revealed blockage early and late staining of the lesions (Figs 1C, D).

A pleural tap revealed acid-fast bacilli; the patient’s vision declined to 20/80 in the right eye. Isoniazid and rifampicin were begun as well as intravenous pentamidine. Two months later the visual acuity returned to 20/20 OD. Cultures grew Mycobacterium avium intracellulare from the pleural fluid, but cerebrospinal fluid (CSF) cultures were negative. By January 1989, four months after the initial examination, the lesions had totally resolved.
CASE 7
A 40-year-old AIDS patient had pneumocystis pneumonia three times treated with co-trimoxazole, intravenous pentamidine, and maintenance aerosolised pentamidine. On routine screening we found 20/20 vision OU and numerous grouped, yellow, deep round lesions in both eyes scattered about the posterior pole, some coalescing into larger oval lesions (Figs 2A, B). One lesion was directly subfoveal in the left eye. Fluorescein angiography revealed early blockage and late leakage (Fig 2C). Rapid plasma reagin, haemagglutination assay test for syphilis, and CMV titres were negative. The CSF was normal, with negative results to cryptococcal antigen and VDRL tests. The patient was anergic to skin testing. Vision remained stable, but the patient developed unexplained fevers.

Discussion
Choroidal lesions have occasionally been reported in AIDS patients. Machet et al described the histopathology of a case of yellow choroidal lesions secondary to P carinii infection.

More recently Rao et al reported three cases of yellow-white choroidal plaques which, on necropsy, revealed trophozoites of P carinii. Visual acuity was decreased in one eye from accompanying CMV retinitis and reported as 20/30 and 20/60 in two other eyes. All the patients had received aerosolised pentamidine prophylaxis for P carinii pneumonia and all died within three weeks of discovery of the retinal lesions. The authors concluded that such fundus findings allow a presumptive diagnosis of disseminated P carinii disease and warrant aggressive chemotherapy. Freeman et al described an AIDS patient, also on aerosolised pentamidine, with similar bilateral choroidal lesions which enlarged over a four-month period, found on transscleral choroidal biopsy to be due to P carinii.

We examined seven patients with AIDS who also had bilateral yellow-white choroidal lesions. All were first noted after January 1988. As Rao et al noted, the increasing discovery of these lesions may relate to increased survival, new therapies, or a change in microbial virulence. Only two patients were symptomatic at diagnosis (cases 4 and 6). Six of the seven patients (all but case 2) had multiple pneumocystis infections and had been treated with aerosolised pentamidine. Such treatment produces low blood drug levels which may allow dissemination of P carinii. Six patients also had Mycobacterium avium complex infections diagnosed from specimens of liver, blood, bone marrow, or pleural fluid. One patient (case 2) had cryptococcal meningitis with optic nerve involvement and died, blind, in four months. Another patient...
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Koyanagi-Harada syndrome, or sympathetic ophthalmitis.

We have been impressed by two aspects of the choroiditis in our patients. Many lesions caused little or no visual problem even with the fovea directly involved and were reversible to some degree with therapy. Our only patient with severe visual loss had cryptococcal choroiditis with optic neuritis.

Secondly, the finding of presumed P. carinii choroiditis in an AIDS patient does not necessarily imply death within a few weeks as previously reported. None of our patients died precipitously; most survived several months after rapid systemic treatment for P. carinii. Increased awareness of this marker for disseminated pneumocystis infection may allow for its earlier detection and therefore treatment. Disseminated P. carinii infection requires systemic treatment, probably on a long-term basis. Future investigation of ocular involvement in the beige mouse model of M. avium infection may be helpful.