Isolated Unilateral Acute Retinal Necrosis Syndrome as the Initial Manifestation of HIV Infection

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The lifetime cumulative risk of at least 1 abnormal ocular lesion for an HIV-positive person ranges from 52% to 100%. Ophthalmic involvement can occur during the early phase of HIV infection, and ocular lesions are mainly noted in the posterior segment.1,2

The posterior segment manifestations are HIV vasculopathy, infectious retinopathy, choroidopathy, and rare neoplasms. HIV vasculopathy has included HIV microangiopathy and large-vessel disease. HIV microangiopathy is the most common manifestation (40% to 60% of cases) of AIDS in developed countries. Usually, HIV microangiopathy develops when the CD4+ cell count is low (less than 100/µL), but most affected patients usually have no ocular symptoms. Manifestations of HIV microangiopathy include cotton-wool spots, retinal hemorrhages, microaneurysm, telangiectatic vessels, and ischemic maculopathy.1,2

Cytomegalovirus (CMV) retinitis is the most common (15% to 40%) cause of infectious retinopathy in AIDS. CMV retinitis and its complications (eg, immune recovery uveitis, retinal detachment) are the most common causes of visual morbidity.1,2 Other infectious retinopathies include toxoplasmic retinitis, necrotizing herpetic retinitis (eg, acute retinal necrosis syndrome, progressive outer retinal necrosis), and syphilitic retinitis. Infectious choroidopathy includes Pneumocystis jiroveci choroidopathy, cryptococcal choroidoretinopathy, and mycobacterial choroiditis.1,2

Acute retinal necrosis syndrome occurs most commonly in otherwise healthy patients. In general, patients are not immunocompromised or systemically ill.3 However, this syndrome may demonstrate subclinical immune dysfunction.4

Ocular manifestations may be the presenting sign of a systemic infection in an otherwise asymptomatic HIV-positive person.3 Ocular involvement in these cases is varied and can affect almost all structures of the eye. Most of the visually disabling ocular manifestations, particularly those caused by an opportunistic infection, occur in late-stage HIV disease or AIDS, whereas presumed HIV-related asymptomatic ocular lesions occur in the earlier stages.4,5

Although HIV-infected patients may present with an isolated ophthalmic complication as the initial manifestation of their HIV infection without any other sign of opportunistic infection or condition attributed to HIV infection or indicative of a defect in cell-mediated immunity, HIV infection is relatively less commonly diagnosed by ophthalmologists in its initial presentation. We describe a case of isolated unilateral acute retinal necrosis in a patient as the initial manifestation of his HIV infection, and to the best of our knowledge, this phenomenon has not been previously reported.

CASE SUMMARY

A 30-year-old man presented to our outpatient department with a history of gradual decrease in vision with floaters in the right eye for 1 month. He also had a history of mild pain in his right eye for 2 weeks. There was no history suggestive of adnexal or corneal involvement or of significant dermatological, neurological, or other systemic illness.

On ocular examination, the visual acuity in the right eye was limited to perception of light and the projection of rays was inaccurate; the left eye was 6/6 using the Snellen visual acuity chart. Findings from an examination of ocular adnexa and ocular movement of both eyes were normal. The anterior chamber cell of the right eye was 3+ with fresh keratic precipitates in the cornea, and there was also pigment deposition over the anterior capsule. The anterior chamber of the left eye was normal. Right eye direct and left eye consensual pupillary reflex was absent. Left eye direct and right eye consensual pupillary reflex was present. Intraocular pressures in both eyes were normal (12 mm Hg) by Goldman applanation tonometry.
Figure 1. Fundus photograph of the right eye of a 30-year-old HIV-positive man showing multiple foci of confluent retinal necrosis with discrete borders in the peripheral retina suggestive of acute retinal necrosis syndrome.

In the right eye, dilated fundus examination showed vitreitis (retrolental cell 3+) and concentric confluent areas of retinal necrosis. The areas had discrete borders in the peripheral retina encroaching the posterior pole and accompanied with vascular occlusion and papillitis (pale disc). These features were characteristic of acute retinal necrosis syndrome (Figures 1 and 2). Findings from the dilated fundus examination of the left eye were normal. Detailed systemic evaluation was carried out in consultation with the physician.

The findings from the patient’s physical and dermatological examinations were normal. A Mantoux test showed no induration (anergy). A chest radiograph was normal. Toxoplasma, hepatitis B virus, hepatitis C virus, CMV, herpes simplex virus (HSV), and varicella-zoster virus (VZV) antibody titers were negative. All laboratory test results were negative or within reference (normal) ranges, except he was found to be HIV-positive, and his CD4⁺ cell count was 129/µL.

Figure 2. Fundus photograph of the right eye of a 30-year-old HIV-positive man showing concentric
confluent areas of retinal necrosis encroaching the posterior pole accompanied with occlusive vasculitis and papillitis (pale disc) suggestive of acute retinal necrosis syndrome.

On the basis of the above clinical findings and investigations, right eye acute retinal necrosis syndrome with concurrent HIV infection was diagnosed. A standard twice-daily antiretroviral regimen of lamivudine 150 mg, stavudine 30 mg, and nevirapine 200 mg was begun. Intravenous acyclovir (1500 mg/m² per day in 3 divided doses) was given for 10 days followed by oral acyclovir maintenance (800 mg 5 times daily). On follow-up at 1 year, there was no improvement of vision in his right eye; the retinal lesions were showing resolution, although the disc was still pale (optic atrophy) with retinal arterial narrowing. There was no deterioration of renal function. In addition, there was no retinal detachment in the affected eye, no significant changes in the fellow eye, and no significant systemic or dermatological involvement.

DISCUSSION

Acute retinal necrosis syndrome is a rare disease, and the exact pathological mechanism is not completely understood. It has been postulated to be caused by one of the neurotropic human herpesviruses: HSV (type 1 or 2), VZV, or Epstein-Barr virus. The American Uveitis Society criteria for a diagnosis of acute retinal necrosis include focal, well-demarcated, peripheral areas of retinal necrosis; rapid circumferential progression; occlusive vasculopathy with arteriolar involvement; and a prominent inflammatory reaction in the vitreous and anterior chamber. The diagnosis of acute retinal necrosis syndrome is clinical, and the presence of optic neuropathy, scleritis, and pain supports the diagnosis. The immunological status of the patient does not influence the clinical diagnosis of acute retinal necrosis syndrome. The fellow eye becomes involved in about 36% of patients with acute retinal necrosis, usually within 6 weeks of involvement of the first eye.

Our patient had classic clinical features of unilateral acute retinal necrosis syndrome in the form of panuveitis, vitreitis, and peripheral concentric confluent areas of retinal necrosis encroaching the posterior pole and accompanied with vascular occlusion and optic neuropathy. In patients with HIV infection, acute retinal necrosis tends to be severe and bilateral with a poorer visual prognosis. In these patients, acute retinal necrosis usually involves the posterior pole and optic nerve early, and their CD4+ cell count is typically above 60/µL. Large retinal holes with retinal detachment occur within 2 months in 25% to 75% of patients with acute retinal necrosis syndrome. Acute retinal necrosis in HIV-positive patients occurs when they are not totally immunosuppressed as opposed to CMV retinitis, which is seen in severely immunosuppressed patients, often with systemic infection.

CMV retinitis, the most common necrotizing retinitis in patients with AIDS, generally occurs in immunocompromised persons with CD4+ cell counts below 50/µL. Unlike that of acute retinal necrosis syndrome, the clinical course of CMV retinitis is chronic and indolent with minimal or absent vitreous inflammation. CMV retinitis manifests initially with 1 or 2 patches of white granular retinal lesions. These lesions are usually distributed near retinal vessels, suggesting a hematogenous spread. Active retinitis occurs adjacent to atrophic areas demonstrating a brush-fire appearance. Hemorrhage is more common with CMV retinitis than with acute retinal necrosis syndrome. Progressive outer retinal necrosis (PORN) is another variant of herpetic retinitis in patients with AIDS. With PORN, the CD4+ cell count is usually below 50/µL. It is an extremely progressive necrotizing retinitis characterized by an early patchy multifocal, deep outer retinal lesion, often initially in the parafoveal region, with late diffuse thickening of the retina, absence of vascular inflammation, and minimal or no vitreous inflammation. PORN progresses from the posterior pole to involve the peripheral retina, resulting in widespread retinal necrosis and atrophy.

Toxoplasmic chorioretinitis is characterized by diffuse multifocal retinitis and vitreitis. In immunocompromised hosts, it can mimic acute retinal necrosis syndrome. These persons generally present with a primary infection and lack the typical chorioretinal scar seen in immunocompetent patients, which further complicates the diagnosis. Such patients have a more fulminant presentation, which includes dense yellow-white lesions with better-defined granular borders, occasionally with small satellite lesions. Inflammation is usually more intense; retinal hemorrhage occurs less frequently; and vasculitis is more prominent adjacent to areas of necrosis. The peripheral retina is usually less involved in toxoplasmic chorioretinitis than in acute retinal necrosis syndrome. Treatment of acute retinal necrosis syndrome is complex. Controlled, randomized, prospective treatment studies on acute retinal necrosis syndrome have not been conducted, so current recommendations are solely based on anecdotal data. It has been suggested that early use of antiviral therapy (eg, intravenous acyclovir) before the appearance of confluent lesions greatly speeds regression and delays or prevents hole formation; however, the main advantage of this approach is to prevent involvement of the fellow eye. A systemic corticosteroid can be given 24 to
48 hours after starting intravenous acyclovir therapy to reduce inflammation, but HIV infection should be ruled out before administering a systemic corticosteroid. Ando and colleagues discovered hyperaggregation of platelets in 6 of 7 patients with bilateral acute retinal necrosis, as determined by adenosine diphosphate aggregation testing and measuring the active partial thrombin time. Aspirin combined with systemic corticosteroids was found to normalize this hypercoagulation state.

Acute retinal necrosis syndrome typically occurs in healthy patients and is probably related to an immune dysfunction. It was first described in an immunocompromised patient in 1985 and has been increasingly observed among persons with HIV infection. Several cases have been reported in HIV-infected patients presenting with acute retinal necrosis syndrome in association with skin manifestations of VZV infection. Chess and Marcus reported a case of bilateral acute retinal necrosis syndrome associated with unilateral herpetic ophthalmicus as the presenting sign of HIV infection.

In our case, a young man presented with right eye acute retinal necrosis syndrome without any history of associated herpes zoster or other conditions associated with HIV infection or indicative of a defect in cell-mediated immunity. In addition, we were not able to find any infectious etiology for acute retinal necrosis syndrome in this patient except for his HIV infection. HIV infection is a hypercoagulable state, and the immune system is continually activated owing to the chronicity of infection and persistence of virus replication. This activated state causes hyperactivation of B cells leading to hypergammaglobulinemia. A hypercoagulable state may be related to lupus anticoagulant, clotting abnormalities, elevated levels of tumor necrosis factor-α, and development of immune complexes in the HIV-infected patient. Another possible mechanism for the acute retinal necrosis is a severe hypercoagulable state.

After extensive search in the published literature (using PubMed), we did not find any report of isolated acute retinal necrosis syndrome as the initial manifestation of HIV infection. This report may be the first report of such a case. HIV-infected patients may present with an isolated atypical ophthalmic complication as the initial manifestation of HIV infection without any other sign of opportunistic infection or other conditions attributed to HIV infection or indicative of a defect in cell-mediated immunity. This case highlights the need for an increased index of suspicion for HIV infection because isolated acute retinal necrosis syndrome may be the presenting sign of HIV infection. In such settings, ophthalmologists may have an important and unique role in the initial screening for and diagnosis of HIV infection.

References:
26 cases. AIDS. 1996;10:55-60.

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