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CASE REPORT

Fulminant bilateral acute retinal necrosis after chickenpox – a case report

Dascalu Ana Maria*, Stana Daniela, Popa-Cherecheanu Alina*, Popa-Cherecheanu Matei***, Serban Dragos***
***"Carol Davila" University of Medicine and Pharmacy, Bucharest**
****Ophthalmology Department, University Emergency Hospital, Bucharest**
*****"Prof. Agrippa Ionescu" Emergency Hospital, Balotesti**

Correspondence to: Alina Popa-Cherecheanu, MD,
"Carol Davila" University of Medicine and Pharmacy, Bucharest
8 Eroii Sanitari Blvd, code 050474, District 5, Bucharest, Romania,
Mobile phone: +40732 507 047, E-mail: alina_cherecheanu@yahoo.com

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Abstract

We present the case of a 34-year-old male, admitted for progressive bilateral loss of vision after a recent episode of chickenpox. Ophthalmological exam revealed bilateral acute retinal necrosis. As the patient was following a drug detoxification program, he was tested for HIV, HVB, HVC, and results highly positive.

Immediate intravenous therapy with high doses of acyclovir and methylprednisolone was initiated, but the evolution was extremely severe resulting in necrotic retinal detachment. Surgery was performed in right eye, but no improvement of visual acuity was observed.

Conclusions: The fulminant evolution of bilateral acute retinal necrosis and the lack of response to maximal intravenous therapy were clinical elements indicating coexistent immunosuppressive disease. Very severe acute retinal necrosis may occur in immunosuppressed patients, leading to blindness.

Keywords: acute retinal necrosis, varicella, HIV, viral opportunistic infections, intravenous drug addiction

Introduction

Acute retinal necrosis (ARN), also known as Kirisawa-type uveitis, is a rare but devastating disease caused by varicella-zoster virus or herpes simplex viruses, typically described to occur in immunocompetent patients. It is characterized by full-thickness necrotizing retinitis, arteritis, and severe inflammation involving the anterior chamber and vitreous. The visual outcome is generally poor, mostly due to rhegmatogenous retinal detachment or optic atrophy.

Case report

The paper presents the case of a 34-year-old male, admitted in emergency for progressive bilateral vision loss, after a recent episode of chickenpox (3 weeks before). The patient was following a drug detoxification program for intravenous drug addiction and had no other medical history.

The ophthalmological exam at admission revealed a visual acuity of light perception in both eyes. Biomicroscopy showed a normal aspect of the anterior segment.

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Fundus examination evidenced a hyperemic, swollen optic disk in both eyes, with flame-shaped peripapillary hemorrhages, narrow arteries with segmentary occlusions, tortuous dilated veins and multiple large areas of white edematous necrotic retina and hemorrhages located in the macular region and along the blood vessels, with moderate associated vitritis (**Fig. 1 a,b**).

Fig. 1 a,b Fundus photography at admission (right and left eye): Ophthalmoscopic aspect at admission: bilateral acute retinal necrosis (ARN) with large confluent areas of whitish necrotic retina, hemorrhages, narrow arterial vessels with distal occlusions

The differential diagnosis took into account other causes of multifocal retinochoroiditis and vasculitis, such as syphilitic neuroretinitis, cytomegalovirus (CMV), toxoplasmosis, Behcet disease, acute multifocal hemorrhagic retinal vasculitis, sarcoidosis, and intraocular lymphoma.

An extensive array of laboratory work up was performed, including: complete blood cells, acute and convalescent serum titers to herpes simplex virus (HSV1 and HSV2), herpes zoster virus (HZV), CMV, Epstein Barr Virus (EBV), toxoplasmosis titers, chest X-ray, angiotensin-converting enzyme (ACE) level, purified protein derivative PPD skin tests, rapid plasma reagin (RPR) rest, and human leukocyte antigen (HLA) testing. The results showed moderate leukocytosis with lymphocytosis (13000/ mmc), increased anti-HVZ IgM and IgG well correlated to the recent clinical history of chickenpox as well as HLA-DR9 +. Due to the toxicological history, the patient was tested for HIV, HVB, HVC and the results were positive, suggesting an immunocompromised state. The other lab tests were within normal limits.

The positive diagnosis of bilateral fulminant ARN was established based on recent history of varicella, immunology positive for HZV and clinical appearance of the ocular fundus, according to the American Uveitis Society diagnostic criteria: (1) one or more discrete foci of peripheral retinal necrosis (located outside the major temporal vascular arcades), (2) circumferential spread (if antiviral therapy has not been administered), (3) occlusive retinal vasculopathy, (4) prominent vitreous or anterior chamber inflammation, and (5) rapid disease progression in the absence of therapy [**1**].

Immediate intravenous therapy, with high doses of acyclovir (10 mg/ kg at every 8 h, 10 days), followed after 24 hours by corticosteroids (methylprednisolone 500ml/ day, for 5 days, followed by oral prednisone 2mg/kg) was initiated. Antiplatelet treatment with low dose aspirin (75mg/ day) was started in order to limit the extensive retinal arterial and venous occlusions. Foscarnet 2.4 mg/ 0.1 mL was administrated intravitreally in both eyes, taking into account the severity of the clinical aspect at presentation, with bilateral extensive macular and optic nerve involvement. The evolution was extremely severe, with a total necrotic retinal detachment and no improvement of visual acuity. Ultrasonography was performed and total retinal detachment was evidenced in both eyes (**Fig. 2 a,b**).

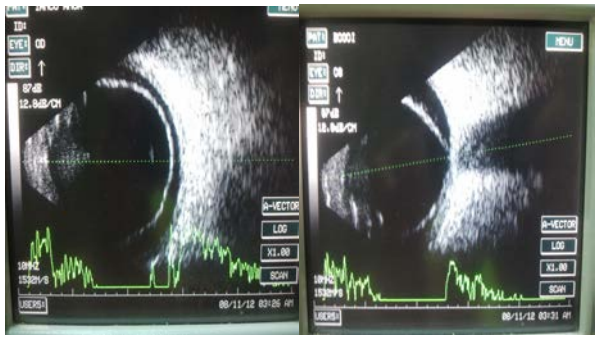

Fig. 2 Ultrasound aspects in right eye (a) and left eye (b): total retinal detachment

Ten days after the initiation of antiviral therapy, the patient was referred to the Vitreoretinal Department for surgical treatment. Vitrectomy, excision of the preretinal

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membranes, endophotocoagulation and tamponade with silicone oil were performed in the right eye, but without improvement of visual function, the patient remaining legally blind (**Fig. 3 a,b**). Aqueous humor and vitreous fluid samples were taken during surgery for PCR testing. Surgery was not performed in left eye because of lack of success in first eye.

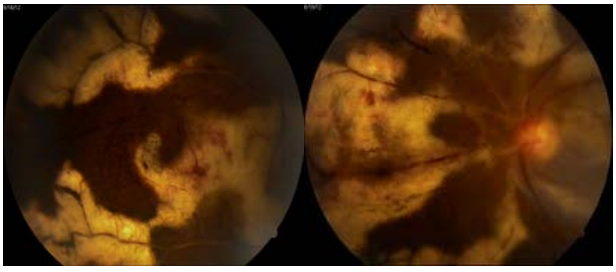

Fig. 3 a,b Fundus photography after surgery: retina is attached, but with large, confluent, multiple areas of necrosis, sheathing and obstructions of retinal vessels

Discussions

Described as a clinical syndrome 40 years ago, ARN is still a challenging pathological entity. New evidence suggests that, along with herpes virus family, CMV and EBV as well as toxoplasmosis, it may be considered as an infectious agent causing the disease [**2-4**].

Bilateral disease may appear in up to one-third of patients. The contralateral involvement occurs within weeks, but rarely recurrence can also occur decades later [**5**]. In presented case, the disease was bilateral from the admission and the patient reported loss of vision in both eyes simultaneously and rapid progression to retinal detachment was also bilateral despite antiviral treatment, for many years, ARN has been considered to appear in normal, apparently healthy adults; some authors have proposed an immunogenetic predisposition for ARN. HLA-DQw7, Bw62, DR4 phenotype antigens were found more frequently in patients who developed ARN compared to the general population. However, HLA-Aw33, -B44 and -DRw6 antigens were more commonly expressed among Japanese patients, and fulminant ARN was associated with HLA-DR9 [**6**]. Interestingly, the presented case was also positive for HLA-DR9. There is increased evidence that ARN is associated either with a peculiar immune response or with an immunocompromised state. Cases were for instance reported after varicella vaccination in elderly patients with a recent organ transplant [**7**].

Two forms of ARN have been described: fulminant ARN, which is characterized by a rapidly progressing inflammation leading to retinal detachment; and mild ARN, which is usually a stable, non-progressive disease of the peripheral retina. The term "necrotizing herpetic retinopathies" (NHR) has been recently proposed due to a variety of clinical manifestations of viral retinal infections that range in intensity from mild to severe, depending on the patient's immune status, as this term can convey the whole spectrum of ophthalmoscopic findings in viral retinitis [**6**]. Various factors, such as the extent of retinal lesions at the initial presentation, worse visual acuity at first visit, involvement of macula and optic nerve, retinal detachment, occlusive central retinal vasculopathy and associated immunosuppression conditions were associated with the progression and poor prognosis of ARN [**9**]. The present case has presented with all these conditions in both eyes. The current treatment regimen varies widely, including either single medication or combinations of oral, intravenous, and intravitreal agents. Intravenous acyclovir is the current medical treatment of choice for the active ARN syndrome. The initial treatment with a 10 days course of high dose intravenous acyclovir (10 mg/ kg at every 8 h) is followed by oral acyclovir (800 mg taken 5 times a day) for up to 14 weeks, especially in the immunosuppressed patients who are at risk for recurrent lesions. The other alternatives are ganciclovir and foscarnet [**12,13**].

The intravitreal injections of ganciclovir or foscarnet may be considered to treat individuals limited by systemic drug toxicity. Although intravitreal treatment did not prevent visual acuity loss in patients with severe disease, patients with a moderate disease (25-50% retina involved) did well with intravitreal therapy with stable or improved visual acuity in most cases [**10,12,13**]. VZV resistance to acyclovir is rare and reported only in a small case series. In these situations, Foscarnet, which does not require

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activation with viral thymidine kinase, is an option to treat acyclovir-resistant HSV and VZV strains [**13-16**]. In the present case, none of the two antiviral agents resulted in improved visual outcome.

Under antiviral protection, systemic corticosteroids are recommended to limit the severe inflammation associated with ARN syndrome. The antiaggregant and anticoagulation therapy may improve the retinal perfusion affected by multiple peripheral vascular obstructions.

Vitrectomy with silicone oil tamponade is mandatory to achieve retinal re-attachment for rhegmatogenous and traction retinal detachment with multiple retinal tears after the fulminant type of ARN syndrome, but the rate of success of the intervention is low. The earlier previous reports indicated that only 23% of the detached retinas are successfully reattached, and only 28% of the eyes affected by ARN syndrome eventually achieved visual acuities of 20/ 200 or better [**8**].

Prophylactic laser barrier treatment is recommended by some authors at the earliest opportunity preferably within the first 2 weeks to reduce the incidence of retinal detachment. Other studies, however, showed that prophylactic laser photocoagulation did not reduce the risk of retinal detachment [**2,3,11,17-19**].

Conclusion

In an HIV-infected patient, with viral opportunistic infections and varicella infection, an extremely severe form of ARN was seen, with a fulminant and bilateral evolution to blindness, despite early and intensive medical and surgical treatment. The immune status of the patient might be an important factor in predicting the visual outcome and responsiveness to treatment.

Disclosure

None.

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