Bilateral acute retinal necrosis associated with neuroinfection in patient after renal transplantation

Joanna Brydak-Godowska1, Szymon Szczepanik1,2, Michał Ciszek3, Dominika Białas1, Miroslaw Grzeszczyk4, Dariusz Strzelecki5, Dariusz Kęcik1

1 Department of Ophthalmology, Medical University of Warsaw, Warsaw, Poland
2 Chair and Department of General and Experimental Pathology, Medical University of Warsaw, Warsaw, Poland
3 Department of Immunology, Transplantology and Internal Medicine, Medical University of Warsaw, Warsaw, Poland
4 Department of Transplant Medicine and Nephrology, Medical University of Warsaw, Warsaw, Poland
5 Department of Infectious Diseases, Warsaw Hospital for Infectious Diseases, Warsaw, Poland

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Summary

Background: Acute retinal necrosis (ARN) is characterized by the triad of acute vitritis, peripheral necrotizing retinitis and vasculitis.

Case Report: We report a case of 54-year-old woman with bilateral acute retinal necrosis associated with neuroinfection. Her past medical history included renal transplantation, hypertension and aortic stenosis. Observational case report: Diagnostic investigations included biochemical tests, lumbar puncture, eye ultrasonography and MRI of the brain.

Anti-HSV IgG antibody titers were elevated in the blood and cerebrospinal fluid. In MRI T2-mode, inflammatory changes were found in the white matter of the right hemisphere. The patient was treated with systemic acyclovir, itraconazole, metronidazole and ciprofloxacin for 3 weeks. Retinal detachment was observed in both eyes.

Conclusions: Acute retinal necrosis can be the single manifestation of herpes virus reactivation in patients after organ transplantation.

key words: acute retinal necrosis • renal transplantation • immunosupression • neuroinfection

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Author’s address: Joanna Brydak-Godowska, Department of Ophthalmology, Medical University of Warsaw, Lindley 4 Str., 02-005 Warsaw, Poland, e-mail: joannabg@tlen.pl
Background

Acute retinal necrosis (ARN) is a viral inflammation of the retina, characterized by the triad of vitritis, severe occlusive vasculitis and progressive retinal necrosis, which usually occurs in healthy individuals with normal immune system function [1]. ARN was first described in 1971 by Urayama, and in Poland the first reports by Dróbecka-Brydak and Kmera-Muszyńska date from 1998 [1,2]. Usually 1 eye is involved, while bilateral acute retinal necrosis (BARN) is observed in approximately 30% of patients. ARN is caused by an acute infection with a member of the herpes virus family, primarily VZV (Varicella Zoster Virus), HSV (Herpes Simplex Virus) type 1 and 2, and very rarely by EBV (Epstein-Barr Virus) [1]. ARN has also been observed in immunocompromised patients (eg, those who are HIV-infected, drug addicts, with immunodeficiency syndromes, on long-term immunosuppression) [1,3]. The diagnostic criteria were published by the American Uveitis Society in 1994 and were based on the characteristic clinical picture. Examination of the blood or the vitreous fluid and vitreous body for anti-virus antibodies is not required [1].

ARN causes progressive inflammation in the posterior segment of the choroid and retina and in the anterior segment of the eyeball. Obliterative inflammation (primarily of arteries) develops, manifested by formation of sheaths along the vessel wall, vascular stenosis and occlusion of the lumen accompanied by ecchymosed and intraretinal hemorrhages. When the inflammatory lesions resolve, the retina becomes thin and atrophic, with multiple breaks which may result in retinal detachment.

Prompt diagnosis and institution of topical and systemic treatment (acyclovir, prednisone, and aspirin) is vitally important to prevent development of ARN in the other eye. The patient requires frequent ophthalmologic examination due to the risk of development of a hole in the affected retina. When the retinal holes develop, laser photocoagulation is used to prevent retinal detachment. When systemic and topical treatment is not effective, vitrectomy (surgical extraction of the vitreous body) and silicone oil placement are treatments of choice [1].

Case Report

We present the case of a 54-year-old woman after renal transplantation with bilateral acute retinal necrosis associated with neuroinfection.

A 54-year-old woman, after renal transplantation 6 years previously, on long-term immunosuppressants (Encorton [prednisone] 5 mg once daily, CellCept [mycophenolate mofetil] 750 mg bid and Neoral [cyclosporine A] 100 mg bid), with aortic stenosis, arterial hypertension and secondary anemia treated with erythropoietin, presented at the Department of Ophthalmology, Medical University of Warsaw in June 2007 with the complaint of sudden deterioration of vision in the right eye with normal visual acuity on near vision testing, and in the left eye normal visual acuity in near and far vision testing. Best Corrected Visual Acuity (BCVA) for distance of the right eye was 0.2, BCVA of the left eye was 1.0, and BCVA for reading for right and left eye was 0.5. Examination of the anterior segment of the right eye revealed the following: the cornea was without pathological changes, the anterior chamber was clear, and there were pigment accumulations on the lens and massive inflammatory reaction in the vitreous body. Changes in the anterior segment made a thorough evaluation of the fundus difficult. White, flat foci of inflammation with scattered pigment and associated obliterated arteries were seen. In the left eye no changes were found apart from discrete opacification of the lens. Acute retinal necrosis was diagnosed by ophthalmoscopic examination according to the American Uveitis Society criteria published in 1994 [1,4].

Serological studies were performed for active CMV infection, and no early pp-65 CMV antigen was detected. Systemic treatment with oral Heviran (acyclovir sodium) 400 mg bid, Encorton (prednisone) 40 mg once daily, itraconazole 100 mg once daily and Aspirin 500 mg once daily and topical treatment of the right eye with dexamethasone 1%, tropicamide 1% and Naclof (diclofenac sodium) were prescribed. After the treatment the reaction in the vitreous body was reduced, foci of retinal inflammation in the periphery healed and visual acuity in the right eye improved (BCVA for distance was 0.7 and 0.5 for reading; Figure 1).

In September 2007 systemic acyclovir and itraconazole were discontinued due to deteriorating renal function. Visual acuity dramatically deteriorated in the right eye (the patient was just able to count fingers directly in front of the eye) and inflammation in the vitreous body increased to a degree precluding evaluation of the eye fundus. Ultrasound examination found retinal detachment in the right eye and the patient was referred for vitrectomy (Figure 2).

In early December 2007 the patient was admitted to the Department of Ophthalmology for vitrectomy in the right eye. On admission she was found to suffer from thought disorder and memory impairment. The patient gave a history of deteriorating vision in the left eye for 3 weeks but could not explain why she had not consulted an ophthalmologist. On examination, BCVA for distance of the right eye was 0.02 and 0.06 of the left eye. The patient was not able to read with her right eye and best corrected visual acuity for reading in the left eye was only 3.0. The eyeballs were pale, scattered pigment deposits were seen on opacities of the lenses, and the left iris was dilated without mydriatics.
In the vitreous bodies of both eyes massive exudate was seen with numerous floaters. Vitrectomy was adjourned because of the general condition of the patient. Systemic treatment was used: acyclovir IV 500 mg once daily, metronidazole IV 500 mg bid, Proxacin (ciprofloxacin) IV 250 mg once daily, oral itraconazole 100 mg once daily and topical dexamethasone 1% and NaCl ofl instilled into both eyes tid. MRI of the brain was performed and in scans in a T2 mode a hyperintense area was identified in the white matter of the right hemisphere above the lateral ventricle extending along its entire length, with discrete patchy contrast enhancement of the lesion corresponding to encephalitis. In T2 mode scans, small hyperintense foci were seen in the white matter of both hemispheres (vascular changes; Figure 3).

The patient was transferred with suspected neuroinfection to the Warsaw Hospital for Infectious Diseases. Lumbar puncture was performed and IgG antibodies for HSV (weakly positive) were found in the CSF but not IgM antibodies for HSV. In the blood, IgG antibodies for HSV were measured, but not class IgM antibodies. Encephalitis was diagnosed. During treatment, left-sided pneumonia developed and insufficiency of the grafted kidney requiring dialysis. The patient was treated with acyclovir IV 500 mg once daily, oral itraconazole 100 mg once daily, metronidazole IV 500 mg bid and ciprofloxacin IV 250 mg once daily for 3 weeks.

On ophthalmologic examination in March 2008, visual acuity in both eyes deteriorated in the degree of light perception, and persistent inflammatory exudate was observed. As the eye fundi were difficult to visualize, ultrasound examination was performed which revealed retinal detachment involving the entire retina in the right eye and retinal detachment in the inferior and superior temporal quadrants of the left eye. Ophthalmologic procedures were not performed due to deterioration in the general condition resulting from aggravation of circulatory failure associated with artery valve stenosis.

In retrospect it was discovered that the recurrence of inflammation in the right eye was associated with the fact that the patient stopped taking medication without consulting her doctor. Deterioration of vision in the left eye started 3 weeks before her planned admission to hospital for vitrectomy in the right eye. She underestimated the seriousness of her condition, which may have been due to CNS inflammation. Probably CNS inflammation onset occurred after discontinuing systemic acyclovir in September 2007, which allowed a viral infection of the right eye to transfer through the right optic nerve to the CNS and then spread to the retina of the left eye, either via the cerebrospinal fluid or through the left optic nerve.

**DISCUSSION**

Acute retinal necrosis results from reactivation of latent neurotrophic members of the herpes virus family, especially HZV and HSV, dormant in the retina. In a review by Dróbecka-Brydak of 500 patients after renal transplantation evaluated in the Department of Ophthalmology, not a single case of acute retinal necrosis was observed [5].

According to Ng and McCluskey, who retrospectively evaluated 860 patients after transplantation of organs other than the kidney (heart, heart-lungs, lungs, liver), different ocular lesions were observed in 19 patients (2%). The patients were treated with immunosuppressive drugs: prednisone, cyclosporine A and azathioprine, given in combination. In over half of patients, ocular lesions were associated with opportunistic infections, especially herpetic retinitis with onset in the second year post-transplantation; it was not seen in any patient after liver transplantation [6]. In a review by Chung et al. of 1198 patients who underwent organ transplantation (kidneys, heart, heart-lungs, lungs, liver, bone marrow) in the years 1995–2005, opportunistic complications involving the retina (CMV, ARN, fungal infection, toxoplasmosis) were found in 21 organ recipients (most received a kidney). Acute retinal necrosis was found in 3 patients without features of graft rejection or systemic infection [7].

**CONCLUSIONS**

Acute retinal necrosis may be a risk factor for inflammatory conditions of the central nervous system, due not only to the anatomical proximity of the eyes to the brain, but mainly because herpes viruses are prone to activation in the central nervous system. Cases of herpetic retinitis developing in otherwise healthy individuals with subsequent involvement of the central nervous system were reported by Garty and Spalton, Cardine, and Diaz [8–10].

Patients with transplanted organs, who are on long-term immunosuppressive treatment, should be regularly monitored.
by ophthalmologists due to the risk of infection that may be first manifested in the eye.

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