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Acute Retinal Necrosis in Childhood

Yoav Y. Pikkel[a–c] Joseph Pikkel[a–c]

[a]Tzameret Medical Track, Hebrew University, Jerusalem, [b]Department of Ophthalmology, Ziv Medical Center, and [c]Faculty of Medicine, Bar Ilan University, Safed, Israel

Key Words
Retinal necrosis · Children · Methylprednisolone

Abstract
Background: Acute retinal necrosis (ARN) is a viral syndrome consisting of uveitis/vitritis, occlusive vasculitis and peripheral necrosis. Few incidents are reported in children. The etiology is reactivated herpes simplex virus (HSV) or varicella-zoster virus (VZV). Treatment with acyclovir is often used. The administration of oral glucocorticosteroids is of unproven benefit. Prognosis is variable but poor. ***Methods:*** Three weeks after contracting mild chickenpox, a healthy 4-year-old girl developed blurred vision in her right eye. Severely reduced visual acuity was noted, together with anterior uveitis, 'mutton-fat' precipitates and vitral flare. Retinal vasculitis with necrosis was present. Serology for toxoplasma, cytomegalovirus and HIV was negative, while HSV and VZV IgG antibodies were positive. She was treated with 30 mg/kg of intravenous methylprednisolone (3 days), 30 mg of oral prednisone (3 days), and tapering for 8 weeks. Intravenous acyclovir was given for 10 days, followed by oral acyclovir for 4 months. Aspirin (100 mg/day) was given for 4 months. ***Results:*** At 12 months, the girl felt good. Her right eye acuity was 6/9, with an intraocular pressure of 17 mm Hg. The peripheral retina showed scarring but no detachment. ***Conclusions:*** This is the first report of a once-daily high-dose methylprednisolone pulse therapy in one of the youngest known ARN cases. Pulsed steroid therapy was based on its known effectiveness in vasculitis, which is the main pathophysiology in ARN. There was no evidence of steroid-related viral over-replication. Our case achieved an excellent clinical and ophthalmic recovery in spite of the poor prognosis. The positive result of this case report provides a basis for further evaluation of high-dose steroid pulse therapy in ARN.

Yoav Y. Pikkel
Hebrew University
Haarazim 12/34
IL–9618221 Jerusalem (Israel)
E-Mail yoav.pikkel@mail.huji.ac.il

Introduction

Acute retinal necrosis (ARN) is a viral retinal syndrome that is defined by the presence of all three signs – anterior uveitis and vitritis, occlusive vasculitis and peripheral necrosis [1]. Incidence is usually in nonimmunocompromised adults aged 20–60 years. Reports of ARN in children who might be immunocompetent [2] or not [3] were found. Low-grade fever is common [1]. The recovery phase, which lasts on average 65 days after disease onset [4], may include retinal tears, vitreal fibrous traction and retinal detachment (RD). ARN is bilateral in 30–70% of patients, with involvement of the second eye developing 5 days to 20 years after the disease in the first eye [5]. The etiology of ARN is usually reactivated herpes simplex virus (HSV) 1 or 2 or varicella-zoster virus (VZV) after chickenpox [6]. Recent reports suggest that an undiagnosed neonatal HSV2 can also play a role as a pathogen [3]. Primary VZV infection is rarely associated with ARN. Thus, it is important to verify the occurrence of an actual infection of HSV1, HSV2, VZV, Epstein-Barr virus or cytomegalovirus (CMV) either by anamnesis or by laboratory findings.

The prognosis of ARN is usually severe. Permanent damage to vision usually occurs, with best-corrected visual acuity (BCVA) reaching 6/60 to 6/9 [3, 7], and sometimes deteriorating to no light perception [8]. Treatment of ARN aims to prevent further damage and targets the virus, namely HSV or VZV. Most publications suggest either systemic or intravitreal antiviral therapy [9]. Many physicians believe that corticosteroids, especially in high dose, may be harmful and may cause early infection of the healthy eye [10]. Argon laser might be used prophylactically to prevent RD.

We describe a 4-year-old girl who was diagnosed with a severe case of ARN. Treatment was aggressive with an unusual megadose of corticosteroids, which eventually preserved the patient's vision.

Case Presentation

A 4-year-old girl of Israeli-Arab descent presented with complaints of blurred vision for 7 days prior to her admission. Anamnesis revealed mild chickenpox 3 weeks prior to her admission, which resolved without complications. The girl's medical history was unremarkable, with no previous admissions or visual problems. At physical examination on admission, she was afebrile, without rash, and looked well. BCVA was 6/60 in her right eye and 6/12 in her left eye. In the right eye, there were anterior uveitis, 'mutton-fat' keratitic precipitates, vitral flare +3–4 cells, vasculitis in the superior temporal arcade and white patches of retinal necrosis in the far temporal periphery (fig. 1). The left eye was normal. Laboratory studies were in the normal range, including blood count and differential, sedimentation rate, liver and renal function, antinuclear antibody, rheumatoid factor, corticotropin-releasing factor and c3-c4. Serology for toxoplasma, Epstein-Barr virus, CMV, HIV and syphilis were negative. Serology (IgG) for HSV and VZV was positive.

Differential Diagnosis

Following the laboratory results, differential diagnosis included a number of options: (1) Behçet's disease, an autoimmune inflammatory disease, mainly found in individuals of Turkish or 'silk road' descendants. Behçet's disease usually manifests in episodic bilateral uveitis [11]. (2) Endophthalmitis, which is usually due to bacteria or fungus infection. Endophthalmitis generally occurs postoperatively or traumatically, with endogenous endophthalmitis being a rare entity [12]. (3) CMV retinitis, which usually occurs in

immunocompromised hosts, though there is some evidence for CMV retinitis in immunocompetent hosts [13]. CMV retinitis is usually described in pediatric patients with a link to lymphoma [14] or immunocompromised children. (4) Sarcoidosis, which manifests with ocular lesions of anterior or posterior uveitis, keratoconjunctivitis, retinal vasculitis and conjunctival follicles [15]. To diagnose sarcoidosis, other conditions with similar symptoms should be excluded. (5) Syphilis and toxoplasmosis, which present with extraocular symptoms and require laboratory findings to establish diagnosis. With all factors taken into account, including the history of chickenpox, the most probable diagnosis was ARN.

Treatment

The patient was started with an initial treatment of 30 mg/kg of intravenous methylprednisolone (600 mg in total for a total body weight of 18 kg), once daily for 3 days. This was followed by oral administration of a prednisone dose of 30 mg/day for 3 days, which was slowly tapered for 8 weeks. Aspirin was given orally (100 mg/day) for 3 months. To treat the HSV/VZV infection, an intravenous acyclovir dose of 275 mg, 3 times a day, was given for 10 days. The treatment was later changed to oral acyclovir 350 mg, 5 times a day for 3 months, which was tapered slowly for another 3 months.

Follow-Up

After 1 year, BCVA was 6/9 in the patient's right eye, the same as in her left eye. No signs of anterior uveitis were seen in the right eye. An attached retina with peripheral depigmentation was noted (fig. 2). The left eye was normal.

Discussion

Most reported cases of ARN secondary to varicella-zoster infection have poor prognosis. BCVA after an episode of ARN usually ranges from 6/60 to 6/24, though it can be deteriorated to no light perception [8]. Peripheral RD is a known complication of ARN [7]. Treatment of ARN is mainly aimed to prevent further damage and targets the virus, namely HSV or VZV. Most publications suggest treatment with antiviral therapy, either systemic or intravitreal [9]. Many physicians believe that the use of corticosteroids, especially in high dose, might be harmful, and may actually cause early infection of the healthy eye [10]. Argon laser is sometimes used prophylactically to prevent RD. Another approach advocates the use of corticosteroids, though not in high-dose, followed by antiviral therapy [7]. Lau et al. [7] reviewed a series of patients who were given a dose of corticosteroids before a diagnosis was established and switched to antiviral therapy when ARN was confirmed. We did not find documentation in the current literature of megadose corticosteroids as initial treatment following a known ARN diagnosis. Moreover, we did not find any records of treatment with megadose corticosteroids of pediatric cases of ARN. In our perspective, this is the main finding of our case presentation, which raises the possibility of the use of megadose corticosteroids instead of high-dose corticosteroids.

The use of corticosteroids, especially at high doses or megadoses, should not be taken lightly. Corticosteroids could worsen the status of a damaged eye or cause an infection in the second eye, given that it is not already infected. Thus, it is important to use corticosteroids wisely and under close supervision. The use of corticosteroids in cases of ARN is controversial. While some think that it can actually worsen the patient's well-being, others believe that a high dose of corticosteroids is beneficial for the patient. The use of corticosteroids is not

suggested for the common practice, and even though this case had shown a good outcome, much is to be investigated yet.

In our case, we showed an excellent response to megadose corticosteroids as treatment of ARN in a 4-year-old girl. This treatment was chosen because of the expected poor outcome, in an attempt to prevent immune-mediated damage to the retina. Since there was no evidence of RD, and due to the young age of the patient, prophylactic treatment with argon laser was not administered in order to avoid further damage to the peripheral vision of the patient.

Conclusions

ARN may occur in childhood. Though ARN is not highly prevalent, it must be excluded in any child presenting with uveitis, retinal vasculitis and fever. Early diagnosis is the cornerstone of a good treatment. The administration of intravenous megadoses of steroids should be considered, in addition to antiviral therapy. Prophylactic treatment with argon laser should be considered in older patients. We suggest that laser treatment should not be performed in younger patients in order to prevent damage to the peripheral vision.

Since debate exists in the current literature regarding the role of corticosteroids, especially of high and megadoses, further investigation is needed to establish the optimal corticosteroid treatment.

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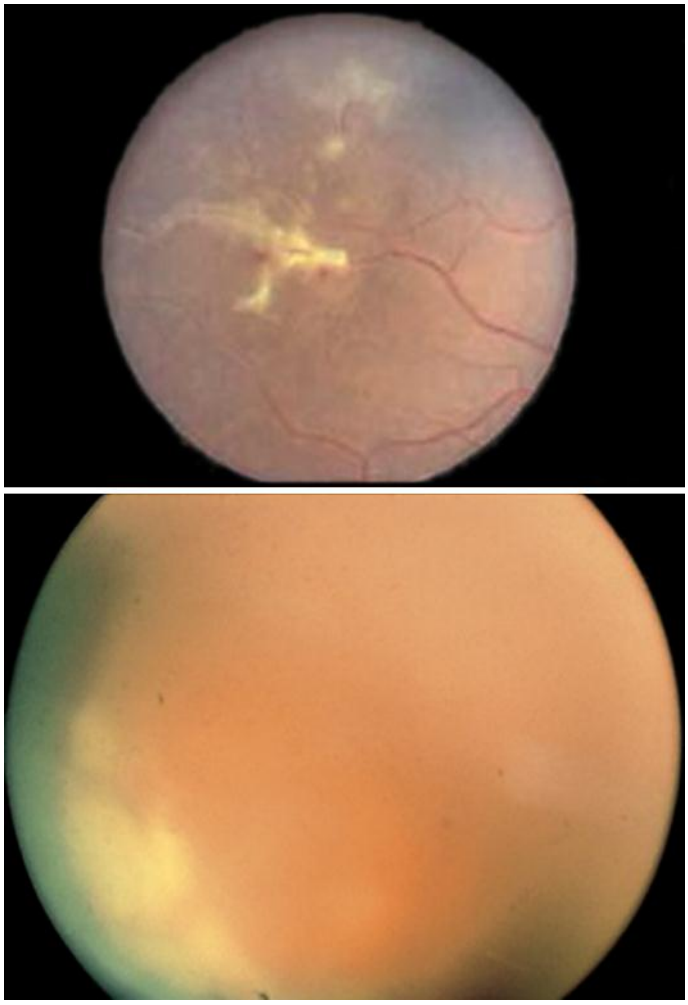

Fig. 1. Acute phase of the disease. Upper image: vasculitis and peripheral white patches; lower image: white patches of retinal necrosis in the far temporal periphery.

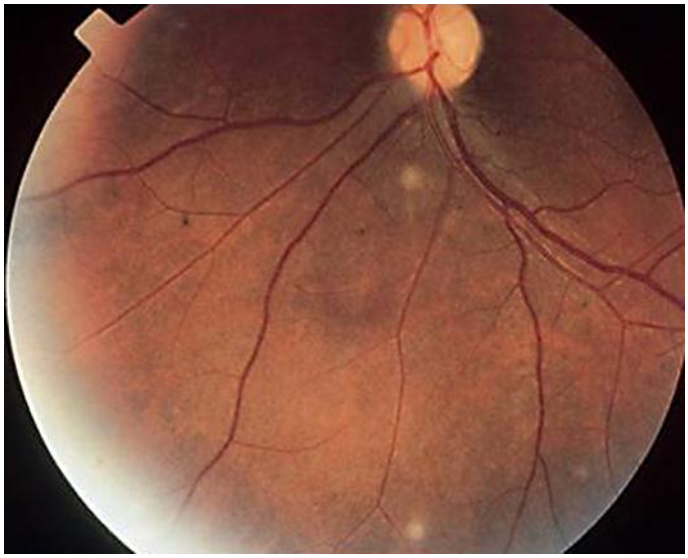

Fig. 2. One year after the acute episode, an attached retina with peripheral depigmentation can be observed.