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Acute retinal necrosis – a case report

Ostra martwica siatkówki – opis przypadku

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Summary: We present a case of acute retinal necrosis (ARN) which is a rare but devastating and rapidly progressive viral retinitis. It is caused mainly by *Herpes simplex virus* (HSV) or *Varicella zoster virus* (VZV) (2), but also Cytomegalovirus (CMV) and Epstein-Barr virus infections may be aethiological factors of ARN.

A 17 years old male patient was referred with history of painful sudden worsening of visual acuity in the left eye and the presence of floaters in the visual field of the right eye. Based on the ophthalmological examination the diagnosis of bilateral ARN was established. Aqueous humor aspirates were analyzed using polymerase chain reaction (PCR) for *Herpes simplex virus* (HSV), *Varicella zoster virus* (VZV), Cytomegalovirus (CMV) and Epstein-Baar virus (EBV). PCR confirmed the presence of *Varicella zoster virus* in aqueous humor samples. Prompt systemic antiviral therapy combined with steroids was initiated.

Since a rapid and accurate diagnosis is crucial for prompt administration of antiviral therapy, PCR-based analysis of intraocular fluids provides a valuable tool in the establishing an etiologic factor in patients with retinitis caused by herpesvirus.

Key words: acute retinal necrosis, polymerase chain reaction, Varicella zoster virus.

Streszczenie: Wstęp: ostra martwica siatkówkowa (ARN) jest rzadkim, ale bardzo ciężkim zapaleniem siatkówki. Dotyka osób w każdym wieku, ogólnie zdrowych, lecz niekiedy może wystąpić u chorych o obniżonej odporności. ARN jest chorobą wywołaną przez wirusy *Herpes simplex* (HSV), *Varicella-zoster* (VZV) i – rzadko – przez wirus cytomegali (CMV) i Epstein-Barr wirus.

Opis przypadku: siedemnastoletni pacjent został skierowany do Kliniki Okulistyki i Onkologii Okulistycznej w Krakowie z powodu bólu, pogorszenia widzenia i obecności licznych mętów w ciele szklistym oka prawego. Na podstawie badania okulistycznego postawiono rozpoznanie obustronnej ostrej martwicy siatkówki. Metodą reakcji łańcuchowej polimerazy (PCR) wykonano badanie aspiratu płynu z przedniej komory w kierunku obecności wirusa *Herpes simplex* (HSV), *Varicella-zoster* (VZV), Cytomegalowirusa (CNV) i wirusa Epstein-Baar (EBV). Po potwierdzeniu obecności wirusa *Varicella-zoster* w próbkach natychmiast włączono ogólne leczenie przeciwwirusowe wraz ze steroidoterapią.

Wnioski: w przypadku ostrej martwicy siatkówki natychmiastowa diagnoza decyduje o włączeniu skutecznej celowanej terapii przeciwwirusowej. Badanie PCR płynu wewnątrzgałkowego stanowi cenne narzędzie służące ustaleniu czynnika etiologicznego u pacjentów z zapaleniem siatkówki wywołanym przez wirusy z grupy *Herpes*.

Słowa kluczowe: ostra martwica siatkówki, reakcja łańcuchowa polimerazy, wirus *Varicella-zoster*.

Introduction

Acute retinal necrosis (ARN) was firstly described in 1971 (1). It is a rare disease that is caused mainly by *Herpes simplex virus* (HSV) or *Varicella zoster virus* (VZV) (2,3), but also Cytomegalovirus and Epstein-Barr virus infections may be etiologic factors of ARN (3,4). It usually affects otherwise healthy individuals of all ages. Males are more frequently affected than females by a 2: 1 ratio. Very few cases of necrotizing retinopathy have been described in children and young adults and even fewer are those indisputably related to a primary herpetic infection (3,5). The most common clinical signs of ARN are: arteritis and periphlebitis of the retinal and choroidal vasculature, confluent necrotizing retinitis affecting the peripheral retina and moderate to severe vitritis (6,7). Anterior granulomatous uveitis is universal and unless the fundus is examined the diagnosis may be missed. The intraocular inflammation resolves within 4-12 weeks, leaving necrotic retina with retinal pigment epithelium atrophy. The fellow eye becomes involved in 30-50% of patients, usually within 2 months (8,9). The posterior pole is usually spared until late stage of the disease so visual acuity may remain good despite severe necrosis of the peripheral retina. The most common causes of visual loss are: rhegmatogenous retinal detachment, tractional retinal detachment and ischaemic optic neuropathy.

A case report

A 17 years old male patient was referred with the diagnosis of retinitis of unknown aetiology. He presented progressive visual acuity (VA) worsening and pain of the left eye during eye movements. Best corrected visual acuity (BCVA), in right eye (RE) was 1.0 and hand movements at the distance of 1 meter in the left eye. The pupillary reactions were normal. Intraocular pressure was 16 mmHg in RE and 17 mmHg in LE. Slit-lamp examination revealed mild inflammatory reaction in the anterior chamber of RE and severe inflammatory response in the anterior chamber of LE. Indirect ophthalmoscopy of RE showed pap-

illoedema and small, whitish inflammatory lesion with retinal haemorrhages in the temporal periphery of the fundus (Fig. 1).

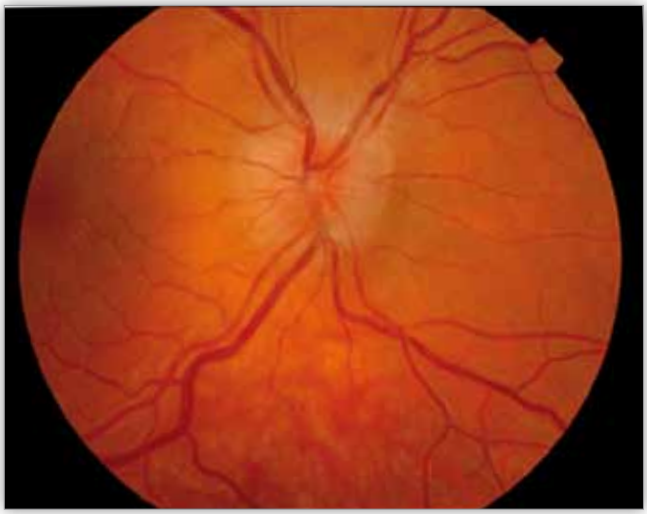

Fig. 1. The fundus of the right eye – papilloedema is present.
Ryc. 1. Dno oka prawego – obrzęk tarczy nerwu wzrokowego.

The fundoscopy LE revealed papilloedema, multiple confluent necrotic lesions in the periphery of the retina with arteritis associated with intraretinal haemorrhages and severe vitritis (Fig. 2).

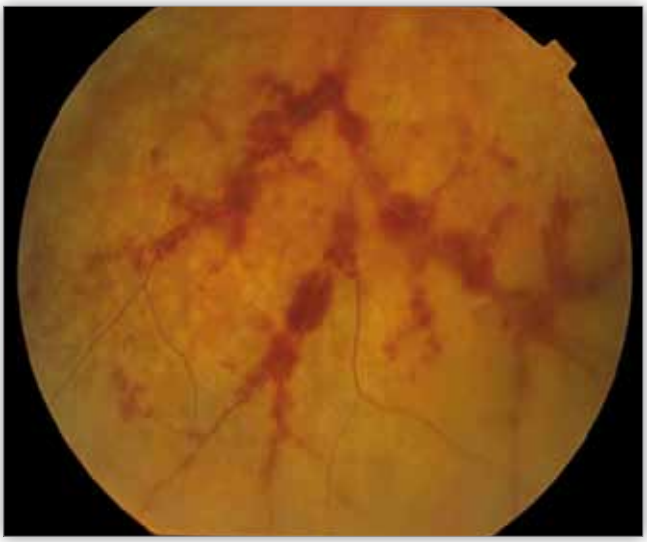

Fig. 2. The left eye showing confluent necrotic lesions in the periphery of the fundus with arteritis and intraretinal haemorrhages along the vessels.
Ryc. 2. Dno oka lewego – zlewne obszary martwiczo zmienionej siatkówki na obwodzie z zapaleniem tętnic i wewnątrzsiatkówkowymi wybroczynami wzdłuż naczyń.

The patient underwent the additionally laboratory tests including serum screening for the presence of antibodies against: *Herpes simplex virus* (HSV), Epstein-Barr virus (EBV), Cytomegalovirus (CMV) which were negative and also *Varicella zoster virus* (VZV) which gave positive results. Aqueous humor aspirates were analyzed using polymerase chain reaction (PCR) for *Herpes simplex virus* (HSV), *Varicella zoster virus* (VZV), Cytomegalovirus (CMV) and Epstein-Baar virus (EBV). PCR confirmed the presence of *Varicella zoster virus* DNA in aqueous humor samples. Magnetic resonance imaging (MRI) of the central nervous system and lumbar puncture were unremarkable.

Treatment with intravenous acyclovir 3 x 750 mg daily for 10 days with additional systemic steroids (prednisolon 1mg/ kg/ day), and aspirin (500 mg/ day), was initiated. Steroids were started a few days after the initiation of antiviral therapy. During a follow-up period intraocular inflammation and retinitis decreased and patient was converted to oral acyclovir 5 x 800 mg/ day for 10 weeks. The total regression of the retinal inflammatory lesion and papilloedema in the right eye was observed and the vision remained unchanged. However in the left eye, despite the inflammation resolution, the tractional retinal detachment developed and the vision declined to light perception. The patient was qualified for vitreoretinal surgery but he refused to be operated on.

Discussion

ARN is a multiform syndrome with different levels of severity and inflammatory reaction. Clinical features of the disease were found to be significantly influenced by the immunologic condition of the host (9). In spite of characteristic clinical signs, the diagnosis of ARN may be difficult in some cases because the clinical presentation may range from focal to extensive involvement and the clinical course may be mild or fulminating (10,11). The following conditions should be considered in differential diagnosis of ARN: CMV retinitis, progressive outer retinal necrosis (PORN), *Syphilitic neuroretinitis*, *Candida albicans* endophthalmitis, acute multifocal haemorrhaghic retinal vasculitis, sarcoidosis, atypical peripheral toxoplasmatic retinochoroiditis and Behçet syndrome (2,8,10). The clinical syndromes most commonly misdiagnosed as ARN in healthy patients are syphylitic neuroretinitis and acute multifocal hemorrhagic retinal vasculitis (9,10). Presence of retinal hemorrhages and initial venous involvement are more frequent in these cases. Very poor response to antiviral therapies, absence of vitritis and anterior chamber inflammation with extremely rapid progression to complete retinal necrosis is observed in patients with PORN (11). Differential diagnosis for *Candida albicans* endophthalmitis, sarcoidosis and Behçet's disease can be established on the basis of the clinical history and systemic signs (2,8,10).

The use of PCR in intraocular fluids samples makes the diagnosis of ARN much more accurate and helps to identify the etiology of the disease. Confirmation of the diagnosis through PCR is recommended to improve the medical management and prevent fellow eye involvement and disease progression with an increased risk of complications (12).

The use of steroid often poses challenge in treating infections. Timing of initiation of steroids is important as one wants to be sure that the battle against infection has been started before the fight for inflammation begins. Therefore, one can start anti-infectious therapy first and then begin steroids (13). In our patient systemic steroids were induced three days after the antiviral therapy was initiated. Steroids are indicated in severe cases with optic nerve involvement and marked vitritis (2,13). Because active viral particles have been identified in eyes with ARN subsequent to intravenous acyclovir therapy and the risk of involvement of the fellow eye, oral acyclovir should be ad-

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ministrated at a dosage of 2-4 g daily for 4-12 weeks after completion of intravenous acyclovir (8,13).

Periarteritis and intraluminal narrowing are believed to be associated with humoral and cell-mediated mechanisms and contributing stasis and vascular thrombosis in patients with ARN. This may result in vision loss from both optic nerve dysfunction and retinal infarction. Thus in addition to treatment with antiviral and anti-inflammatory agents, antiplatelet therapy with aspirin 500-650 mg daily has been recommended (8,13).

Systemic acyclovir may hasten the resolution of acute retinal lesions and reduce the risk of second eye involvement but it does not prevent retinal detachment (6). In our case in spite of regression of intraocular inflammation traction in retinal detachment, it caused severe visual impairment. Retinal detachment is the most serious complication of ARN even with prompt administration of acyclovir and steroid therapy. It ranges from 75-85% of cases and the majority of retinal detachments occur within 3 months of the onset of the symptoms (2). Peripheral argon laser coagulation to demarcate zones of retinitis during the active phase of the disease has been recommended as a potent effective prophylactic procedure if the media permits treatment (14). In our patient pronounced vitritis enabled the laser coagulation of the peripheral retina. The alternative strategy for retinal detachment prophylaxis in ARN patients is early pars plana vitrectomy combined with endophotocoagulation and scleral buckling (8,15). However eyes with associated severe intraocular inflammation may develop ocular hypertension, PVR and choroidal detachment after surgery. Some authors suggest that vitrectomy associated with intravitreal acyclovir lavage may lower incidence of secondary retinal detachment (15).

Eyes with retinal detachment complicating ARN have a more unfavorable visual and anatomic prognosis as a result of retinal detachment associated with large, multiple posteriorly located retinal tears and severe proliferative vitreoretinopathy (PVR). Reports suggest that vitrectomy with silicone oil endotamponade as compared to conventional scleral buckling procedures appeared to be more favourable (15).

The prognosis in ARN is relatively poor, with 60% of patients having a final visual acuity of less than 6/60 as a result of complications such as traction or rhegmatogenous retinal detachment and optic nerve involvement (2,8).

Conclusion

Acute retinal necrosis still has poor visual prognosis. Thus early diagnosis and initiation of treatment are crucial. However in spite of aggressive antiviral and anti-inflammatory treatment the vision threatening complications may develop.

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