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Acute Retinal Necrosis Associated with Herpes Simplex Virus Type II Infection – Case Report

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Abstract: **Introduction:** Acute retinal necrosis is a rare, severe retinitis that may lead to loss of vision. This condition is caused mainly by the Herpesviridae. It can affect both immunocompromised and immunocompetent patients of all ages.
Case report: A 54-year-old female patient, came to the eye emergency department with a history of rapid and progressive loss of vision in the left eye. Due to uveitis, the disease was treated without any improvement. After ophthalmological examination the diagnosis of acute retinal necrosis was taken into consideration. The patient was treated with a combination of systemic and intravitreal antivirals, together with oral corticosteroids. During hospitalization, pars plana vitrectomy was performed. Herpes simplex 2 found in the sample taken from the vitreous body confirmed the diagnosis. Six weeks after hospitalization, the patient was readmitted to the ophthalmology emergency department with a sudden loss of vision in the left eye. As a consequence, retinal detachment was recognized and the patient was qualified for reoperation. At the last follow-up visit, the patient presented with the best corrected visual acuity at the level of 0.6 in distance, without symptoms of disease activity.
Conclusions: Due to the rapidly progressive character of acute retinal necrosis, an immediate diagnosis and intensive treatment are crucial. Nevertheless, despite all our efforts, we cannot completely prevent further complications, including retinal detachment.

Key words: acute retinal necrosis (ARN), herpes simplex virus (HSV), acyclovir, retinal detachment.

Introduction

Acute retinal necrosis (ARN) is a rare but potentially sight-threatening eye disease. It is caused by viruses of the *Herpesviridae* family, including the Varicella Zoster Virus (VZV) and the Herpes Simplex Virus 1 (HSV-1) and Herpes Simplex Virus 2 (HSV-2) [1, 2]. Acute retinal necrosis is characterized by rapidly progressing retinitis, potentially resulting in severe complications such as retinal detachment and vision loss [3]. The primary diagnostic method is the Polymerase Chain Reaction (PCR) test; however, treatment should not be delayed while awaiting test results. Diagnosis is primarily based on the distinctive clinical presentation, while laboratory and diagnostic tests are used to either support or confirm the diagnosis in uncertain cases. Scientific reports highlight the crucial importance of initiating therapy promptly to minimize the risk of complications and achieve satisfying treatment outcomes [4].

Case report

A 56-year-old female patient was referred to the ophthalmology department from the local outpatient clinic, where she had been treated for five days for uveitis in the left eye (OS). At that time, the treatment regimen included tobramycin, dexamethasone, tropicamide (eye drops), and amoxicillin with clavulanic acid (enteric-coated tablets). During a follow-up examination, the attending physician identified inflammatory changes in the peripheral retina and referred the patient to the hospital. On the day of admission, the patient reported deterioration in vision, along with pain and redness in the OS, which had persisted for approximately a week. The patient's medical history included dermatitis herpetiformis persisting for two years, treated with dapsone; surgery for the removal of an AB type thymoma 10 months prior; and myasthenia gravis diagnosed four months previously. She had no previous diagnoses of immune disorders and denied any infections before the onset of her current symptoms. During the ophthalmological examination, the patient's best corrected visual acuity (BCVA) for distance was 1.0 in the right eye (OD) and 0.16 in the left eye (OS). For near vision, the values were 0.5 in OD and 1.5 in OS. Biomicroscopic and ophthalmoscopic examinations of the OD revealed no abnormalities. In contrast, the OS demonstrated mixed conjunctival irritation, corneal edema with multiple endothelial deposits, tyndallization (++), pigment deposition on the anterior lens capsule following synechiae release, and an inflammatory reaction in the vitreous chamber. The optic nerve (CN II) disc appeared pale, with raised and blurred margins. Patchy, cream-colored areas of retinal necrosis with accompanying petechiae were observed in the peripheral retina, particularly in the superior region (Fig. 1). An ultrasound examination of the left eye was also performed (Fig. 2). In light of the above, the patient was urgently admitted to the ophthalmology department for a comprehensive diagnostic workup and treatment.

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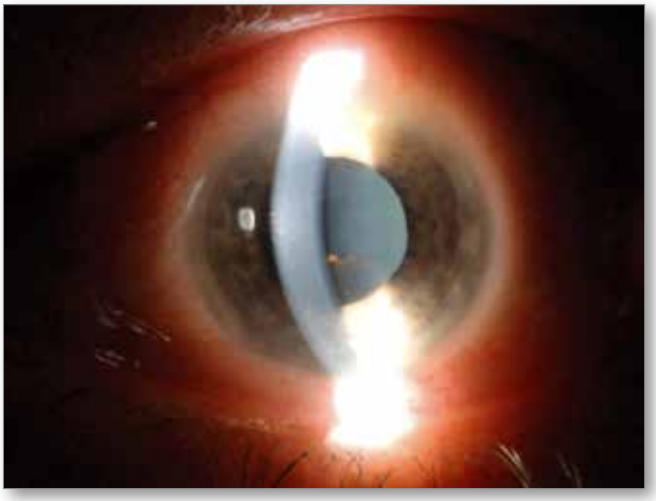

Fig. 1. Slit-lamp photograph of the patient's left eye upon admission to the ward.

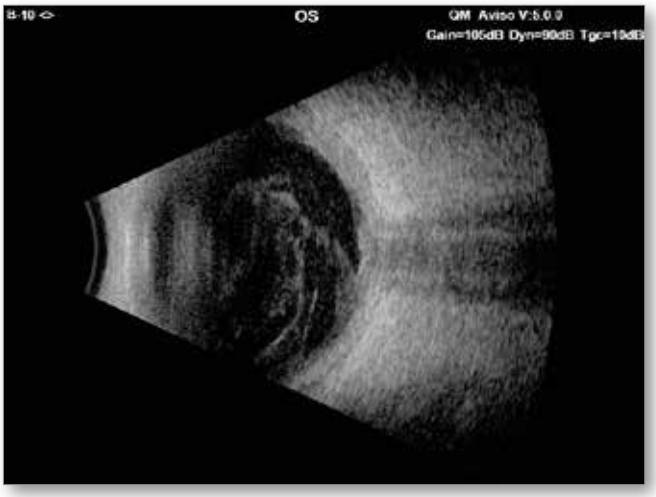

Fig. 2. B-scan ultrasound of the left eyeball on admission – noticeable dense, hyperechoic consolidations in the vitreous chamber and the thickening of the eyeball wall.

Upon admission, oral acyclovir was initiated immediately at a dose of 800 mg five times daily. Basic laboratory tests were performed, including a C-reactive protein (CRP) test, which yielded a result of 9.23. Serum protein electrophoresis revealed decreased levels of gamma globulins. The following day, as the effusion in the vitreous chamber increased, a decision was made to initiate intravenous acyclovir and expand the laboratory diagnostic workup to include infectious diseases that could potentially explain the patient's clinical condition, including the Quantiferon-TB test and antibodies against VZV, HSV, cytomegalovirus (CMV), syphilis, *Borrelia*, and toxoplasmosis. In the following days, the local condition in the patient's eye gradually worsened. The exudate in the vitreous chamber steadily increased, significantly hindering the assessment of the fundus. By the third day of hospitalization, the BCVA had decreased to 0.05. Therefore, it was decided to administer ganciclovir via intravitreal injections, and the patient was referred for microsurgical pars plana vitrectomy (PPV). The following day, acyclovir administration was switched from oral to intravenous at a dose of 500 mg three times daily. Laboratory blood tests revealed positive IgG against HSV types 1/ 2 and positive IgG and IgM against *Borrelia*, following which oral doxycycline was added to the therapy. On the same day, a combined posterior vitrectomy with phacoemulsification was performed, during which a vitreous sample was collected for microbiological PCR testing. Circumferential laser photocoagulation was performed, demarcating the areas of pale, necrotic retina with a barrage. During the surgery, triamcinolone and ganciclovir were administered into the vitreous chamber. Endotamponade with 5000 cSt silicone oil was performed. The fundus of the OS visualized during the procedure revealed a pale pink retina at the posterior pole. In the periphery, except for the area around the temporal vascular arches, the retina appeared white and edematous. Some posterior pole vessels were obliterated. In the periphery, apart from the temporal vascular arches, the retina was necrotic throughout, with mostly obliterated vessels, vascular thrombi, and retinal hemorrhages. On the second day following the procedure, oral prednisone (60 mg) and acetylsalicylic acid (75 mg) were initiated. Microbiological analysis of a vitreous sample detected HSV-2 at a concentration of 10^7 copies/ml. The patient, showing significant improvement in her local condition (Fig. 3) and a BCVA of 0.05, was discharged on the fifth postoperative day. She was instructed to continue oral acyclovir at a dose of 800 mg five times daily, acetylsalicylic acid 75 mg once daily, and steroid therapy with prednisone 60 mg, with a weekly dose reduction of 20 mg.

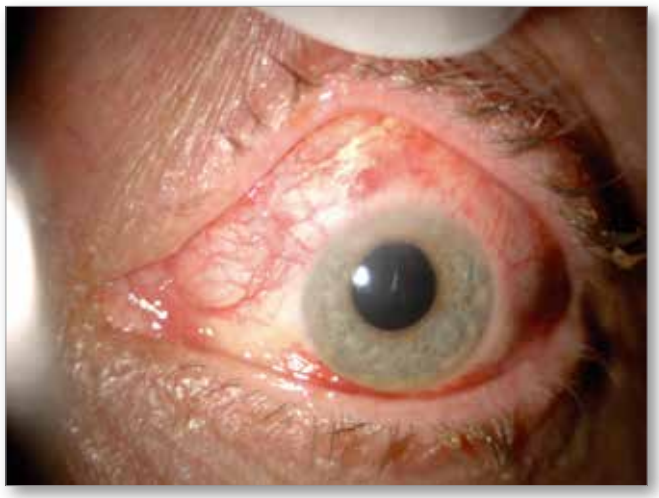

Fig. 3. Slit-lamp photograph of the patient's left eye on the day of hospital discharge – significant improvement in the local condition.

Over the following weeks, the patient remained under close ophthalmological monitoring, reported no complaints, and exhibited no active inflammatory foci on fundus examination (Fig. 4). BCVA values ranged from 0.2 to 0.3 for distance vision and from 2.5 to 3.0 for near vision. The acyclovir dose was continued, along with a maintenance prednisone dose of 10 mg.

Six weeks after the procedure, the patient presented to the emergency department due to a decline in vision in the OS. Ophthalmological examination revealed: BCVA for distance – hand motion, for near – unable to read any print. Fundus examination of the OS showed vitreoretinal proliferations with tractional retinal detachment. A date for the PPV procedure was scheduled. On the day of hospital admission, the patient's local condition was similar to that during the previous examination. A posterior vitrectomy was performed, including the evacuation of silicone oil from the vitreous chamber, partial retinotomy, retinal endolaser coagulation, macular peeling, evacuation of epiretinal membranes, and, finally, the injection of 1300 silicone oil into the vitreous chamber of the OS. The patient was discharged with a recommendation to continue systemic treatment at the current dosage. Over the next two months following the procedure, the patient was regularly monitored by an ophthalmologist. At the final follow-up visit, BCVA was 0.5 for distance and 0.75 for near vision. Ophthalmological examination revealed no signs of disease activity. The patient currently takes acyclovir 400 mg three times daily and prednisone

Fig. 4. Fundus photograph of the left eye at a follow-up visit 1 week after hospitalization – visible reflection of the silicone oil from the posterior pole, foci after endolasercoagulation, areas of pale, necrotic retina and isolated intraretinal hemorrhages in the peripheral retina.

5 mg. Figures 5–8 present optical coherence tomography (OCT) scans of the macula in the OS at various stages of the patient's diagnostic and treatment process, illustrating changes in macular morphology and thickness.

Given the diagnosis of acute retinal necrosis with HSV-2 etiology, reduced blood gammaglobulin levels, and a history of thymoma resection, an expanded diagnostic workup was recommended to assess the patient for potential immune disorders.

Discussion

Acute retinal necrosis was first described by Urayama *et al.* in 1971 [5]. It is an inflammatory eye syndrome characterized by a triad of symptoms: 1. arteritis and phlebitis of the retinal and choroidal vasculature, 2. necrotizing retinopathy involving the peripheral retina, 3. vitritis [6]. Complications associated with ARN include retinal necrosis, retinal detachment, proliferative vitreoretinopathy (PVR), optic neuritis, macular involvement, and ischemic vasculitis [7].

Electron microscopy studies have shown that viruses play a significant role in the pathogenesis of acute retinal necrosis. The primary pathogens associated with this condition include VZV, HSV-1, HSV-2, CMV, and the Ebstein Barr Virus (EBV) [5].

Acute retinal necrosis is a relatively rare condition, most commonly observed in immunocompromised patients [7]. It is important to note that ARN can also develop in patients with a normally functioning immune system who become immunosuppressed following treatment with corticosteroids or chemotherapeutic agents. The disease occurs with equal frequency in men and women. The incidence of ARN increases in the elderly population due to impaired immunity to VZV, as well as in younger patients with a history of herpes simplex encephalitis [2]. Approximately 20% of ARN cases are binocular. Patients who initially have monocular disease very frequently develop symptoms in the other eye as well [8].

Patients with ARN typically report sudden pain in or around the eye, which worsens with eye movements. Other common symptoms include eye redness and hypersensitivity to light. Patients also experience significant vision deterioration, including blurring, narrowed visual field, and the presence of floaters in the vitreous body, which severely impact daily functioning [2].

The primary diagnostic method is biomicroscopy, which is used to identify characteristic and pathognomonic changes associated with ARN including 1. one or more foci of peripheral retinal necrosis, appearing as sharply defined, deep yellow-white infiltrates, possibly with retinal hemorrhages, 2. peripheral spread of retinal changes, with the posterior pole remaining spared for an extended period, 3. obliterative retinal vasculitis with involvement of the arterial vessels, 4. anterior uveitis and vitritis (*panuveitis*), 5. rapid disease progression in the absence of antiviral treatment [9].

In doubtful or atypical cases, modern diagnostic methods, such as PCR analysis of vitreous and/or aqueous humor samples collected during the procedure, are employed to detect viral DNA [6, 9, 10].

The main risks associated with the disease include the possibility of permanent vision damage or even complete vision loss, due to the aggressive nature of the infection and the challenges in controlling it. Only 30% of individuals affected by the disease achieve a final visual acuity greater than 0.1. The most common and most significant complication of ARN, associated with the highest risk of permanent visual impairment, is retinal detachment. This can occur in 20% to 73% of cases, particularly if the disease is not diagnosed and treated promptly [5, 11–14].

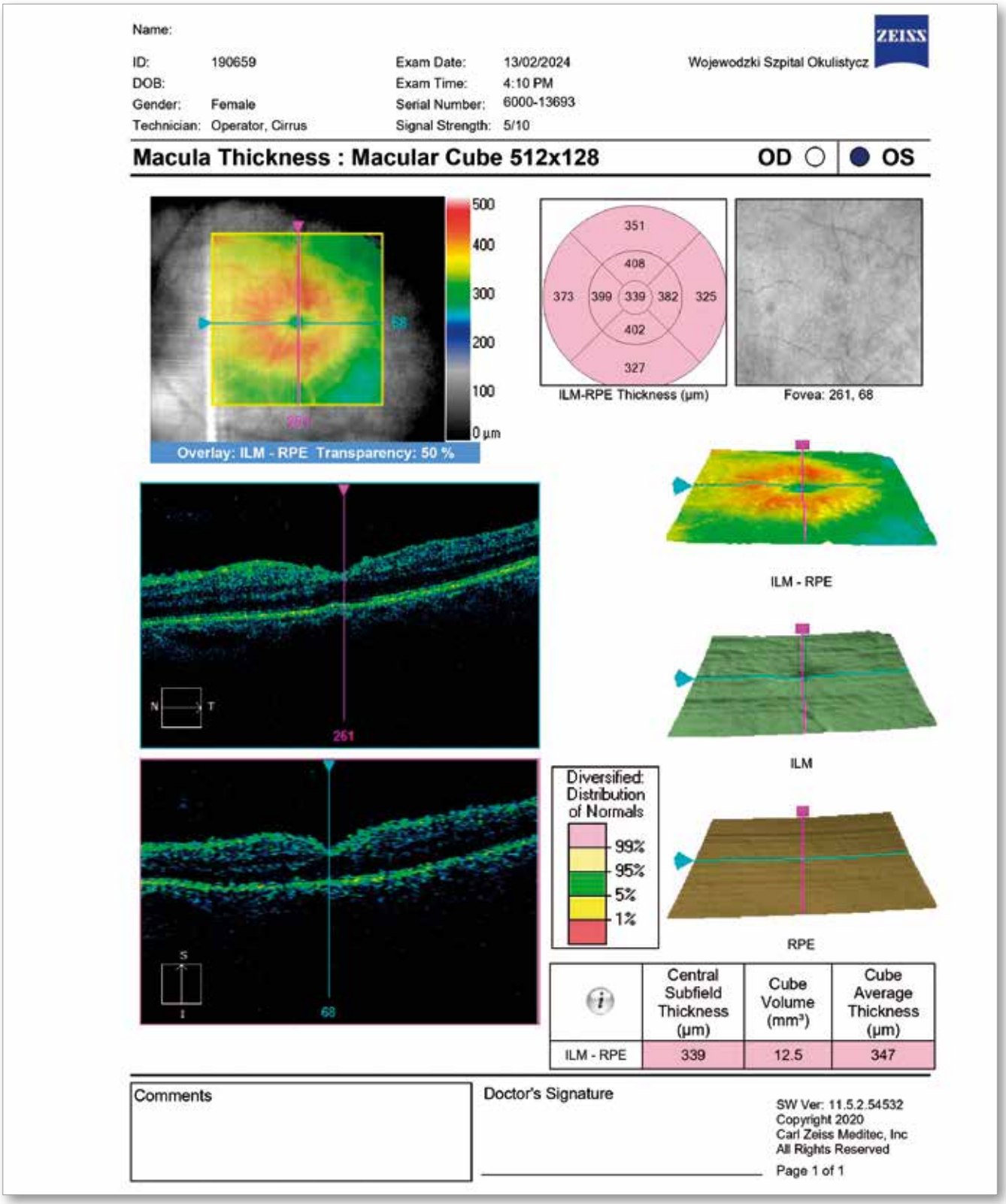

Fig. 5. OCT scan of the macula on admission – thickened area of the central retina.

Treatment for ARN is based on the early administration of antiviral medications to inhibit viral replication and prevent disease progression. Antiviral therapy: according to the American Academy of Ophthalmology (AAO) guidelines, the recommended treatment for ARN begins with intravenous acyclovir, one of the most commonly used antiviral medications. Alternatives include oral preparations, such as valacyclovir or famciclovir, which may be effective in inhibiting viral activity [4]. In cases resistant to acyclovir or those with a severe disease course, combination therapy using foscarnet or ganciclovir delivered through intravitreal injections is used [4, 15]. Adjunctive treatment: in addition to antiviral therapy, topical and systemic glucocorticosteroids are often prescribed to mitigate inflammation, which can otherwise contribute to further damage to the optic nerve and retinal vessels. The medical literature also recommends low-dose acetylsalicylic acid as antithrombotic therapy, particularly in cases complicated

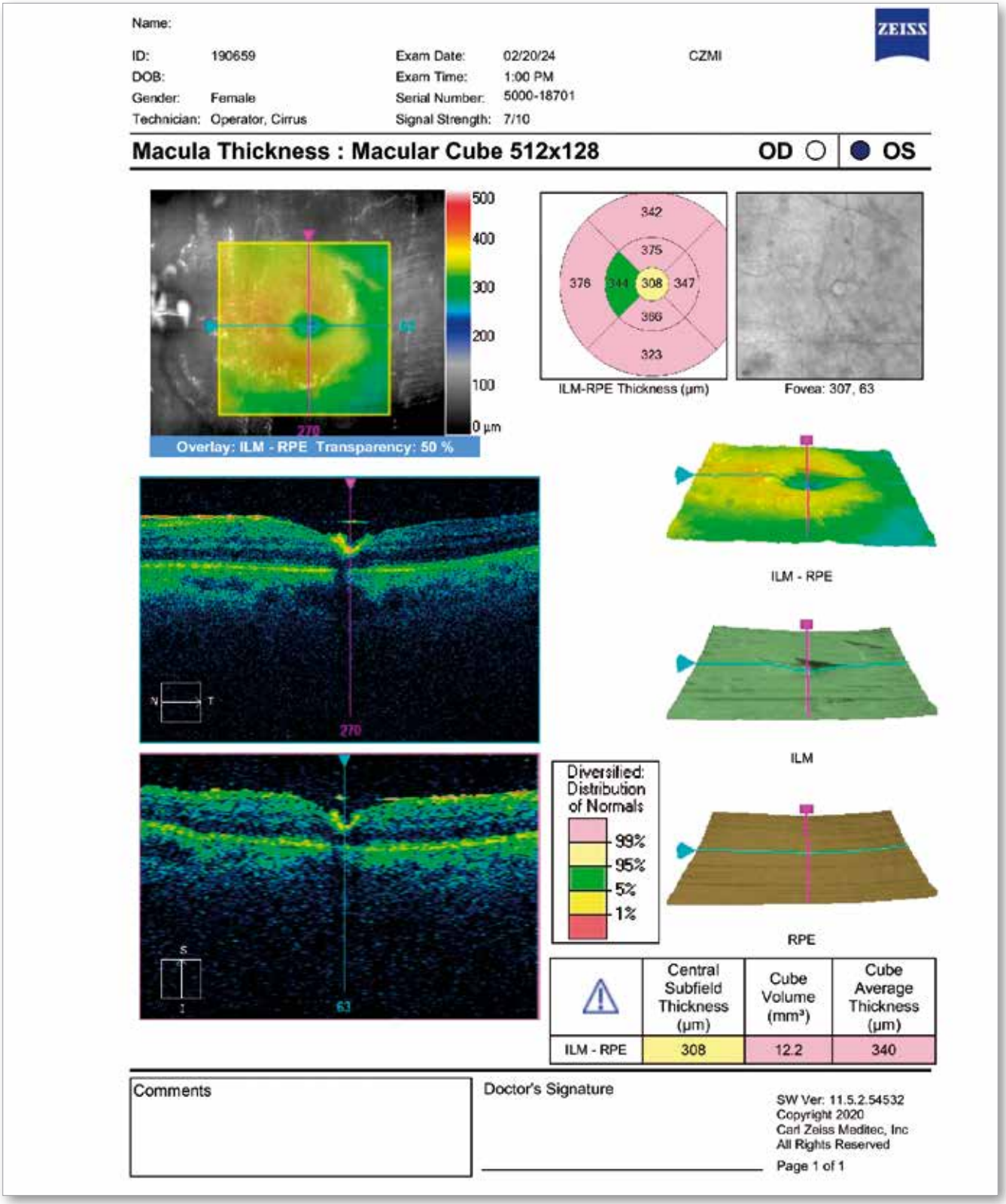

Fig. 6. OCT scan of the macula of the left eye after the first diagnostic and therapeutic PPV procedure – reduction in the thickness of the central retinal layers, in the fovea residue from triamcinolone administration.

by retinal thrombophlebitis [16]. Surgical treatment: in advanced cases, when retinal detachment occurs, PPV may be required to optimize the prognosis in terms of preserving the best possible visual acuity. In recent years, reports have suggested potential benefits of prophylactic vitrectomy or laser retinopexy before retinal detachment occurs; however, this approach remains controversial and requires further research [4, 17, 18].

Conclusions

Acute retinal necrosis is a severe ocular condition with a multifactorial etiology, in which viruses from the *Herpesviridae* family play a key role.

Although relatively rare, ARN presents a significant risk of vision loss due to its high likelihood of causing retinal detachment. Timely diagnosis and prompt initiation of appropriate treatment

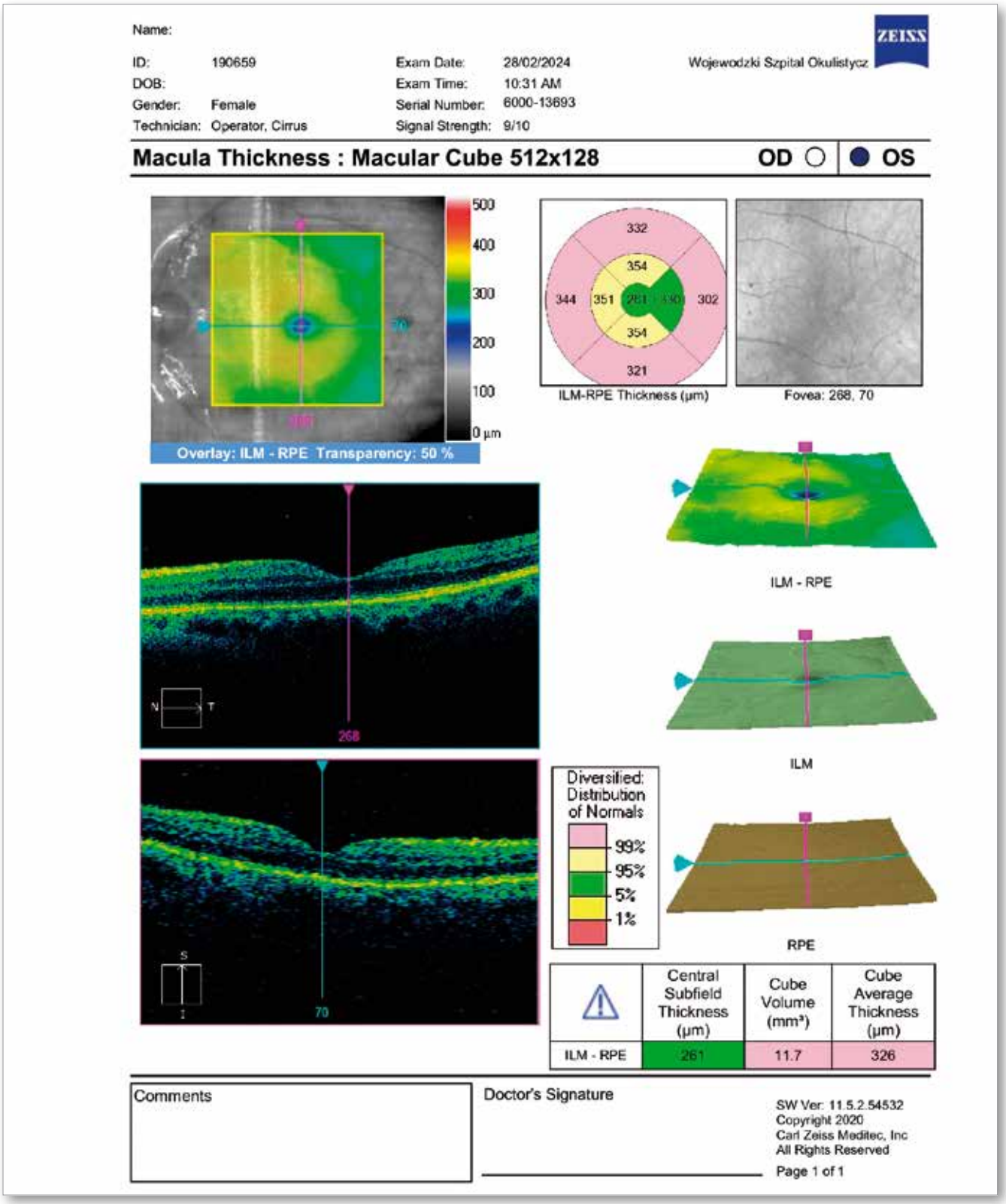

Fig. 7. OCT scan of the macula of the left eye 1 week after hospitalization.

are crucial to halting disease progression and minimizing complications. The cornerstone of therapy is antiviral treatment, supported by glucocorticosteroids and, when necessary, surgical interventions. Despite advances in the diagnosis and management of ARN, it remains a clinical challenge, which highlights the need for further research to optimize treatment strategies and prevent complications.

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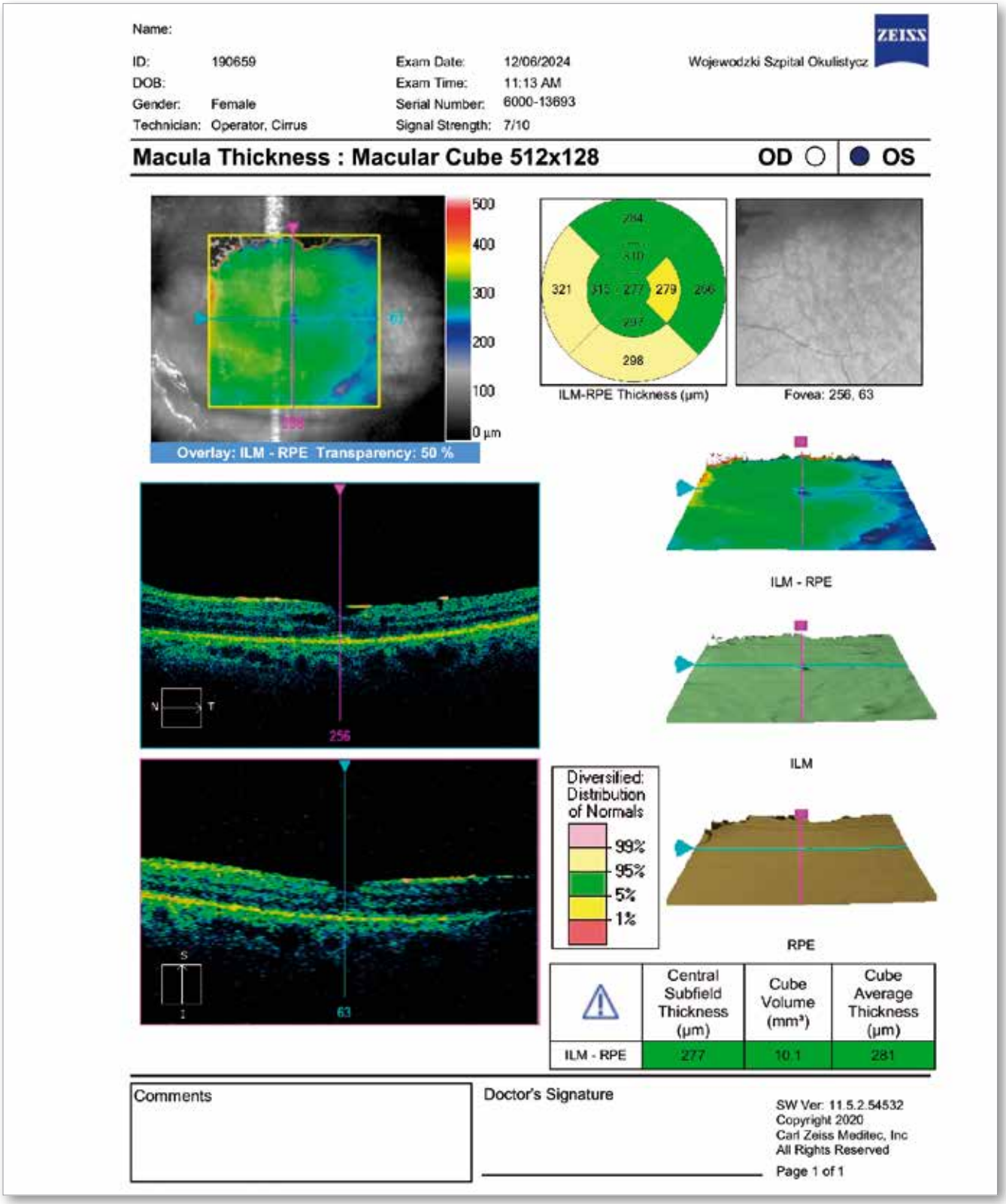

Fig. 8. OCT scan of the macula 3 months after PPV due to retinal detachment.

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