CASE REPORT / ПРИКАЗ БОЛЕСНИКА

Dorzolamide in management of cystoid macular edema in a patient with retinitis pigmentosa sine pigmento

Jelena Karadžić1,2, Igor Kovačević1,2, Aleksandra Radosavljević1,2, Ivan Stefanović1,2
1Clinical Centre of Serbia, Clinic for Eye Diseases, Belgrade, Serbia; 2University of Belgrade, School of Medicine, Belgrade, Serbia

SUMMARY

Introduction Retinitis pigmentosa (RP) is a group of inherited retinal dystrophies caused by mutations in various genes. The disease leads to progressive photoreceptors loss (rods predominantly) and retinal pigment epithelium alteration. RP can lead to blindness in the advanced stages of the disease, when the central retina is involved, mostly due to the presence of cystoid macular edema (CME). Several therapeutic approaches for CME in RP patients have been attempted but responses have been variable.

Case outline A 51-year-old man was referred due to progressive six-month-long blurring of vision in both eyes. The patient underwent complete ophthalmological examination at baseline. Based on the clinical presentation of mottled mid periphery of the retina and characteristic tubular visual field loss, hence typical fluorescein angiography and optical coherence tomography (OCT) findings, the patient was diagnosed as bilateral retinitis pigmentosa sine pigmento with CME. In an attempt to control the edema, treatment was started with dorzolamide, instilled three times daily in each eye, which resulted in reduction of macular edema in a one-month-period, as documented by OCT. This effect was further monitored for five months and was stable.

Conclusion In the presented case, we investigate the six-month therapeutic efficacy of dorzolamide for dealing with the CME secondary to RP. Topical carbonic anhydrase inhibitors are considered as the first option for treatment of CME in RP patients, due to their high efficacy and safety.

Keywords: retinitis pigmentosa sine pigmento; cystoid macular edema; topical carbonic anhydrase inhibitors; dorzolamide

INTRODUCTION

Retinitis pigmentosa (RP) is a group of inherited retinal dystrophies caused by mutations in various genes [1]. This disease leads to gradual and progressive loss of photoreceptors (predominantly rods) and alteration of retinal pigment epithelium [2]. RP can occur in sporadic form without any familial history, or it can be inherited as a dominant and recessive autosomal or X-linked disease [3]. The symptomatology consists of night blindness and gradual loss of visual fields [4]. This condition can lead to blindness in the advanced stages of the disease, when the central retina is involved, mostly because of the presence of cystoid macular edema (CME) [5]. The exact CME etiology is not well understood, but it is proposed that the retinal pigment epithelium pump dysfunction and/or compromise of the blood-retinal barrier bring the fluid to accumulate in cystoid spaces within the retina [6, 7]. Cystoid macular edema may cause blurred vision or reduced visual acuity and finally atrophic foveal changes with permanent loss of visual function. Thus, it is necessary to find an optimal and effective treatment for it [7]. Several therapeutic protocols have been considered, such as systemic or topical carbonic anhydrase inhibitors (CAI) (acetazolamide and dorzolamide, respectively), systemic or intravitreal corticosteroids (triamcinolone, dexamethasone), laser photocoagulation and pars plana vitrectomy but responses have been variable [6, 8–12].

We have the opportunity to report a case of cystoid macular edema in a patient with RP sine pigmento treated with topical CAI (dorzolamide). The therapeutic response was monitored by visual acuity assessment, central visual field analysis, and by measuring central macular thickness on optical coherence tomography (OCT).

CASE REPORT

A 51-year-old man was referred to our clinic due to six-month-long progressive blurring of vision in both eyes. He had a history of hypertension, with no family history of diabetes, glaucoma and RP. He reported he was an ex-smoker. The patient underwent complete ophthalmological examination at baseline including visual acuity assessment (measured by Snellen chart), applanation tonometry, and slit lamp examination, indirect ophthalmoscopy with 90D lens and immunological and biochemical investigation.
Upon examination, best corrected visual acuity (BCVA) was 0.9 in the right eye and 0.7 in the left eye. He had normal color vision and no relative afferent pupillary defect. Fundoscopy of both eyes revealed very discrete mid- and far-peripheral mottled retina, arteriolar narrowing, and sheathing. There were no typical pigmentary changes or clumps, nor significant pallor of the optic nerve heads (Figure 1). The intraocular pressure by applanation tonometry was within the normal range (10 mmHg). All investigations at presentation which included complete blood count, erythrocyte sedimentation rate, C-reactive protein, prothrombin and partial thromboplastin time, blood sugar level, renal and liver function tests, rheumatoid factor, and autoantibody profile were within normal range. The visual field tests, fluorescein angiography (FA), OCT, and dark adaptation testing were performed. Fluorescein angiography showed an unusual degree of choroidal hyperfluorescence which surrounded darker central macular zone (Figure 2), and diffuse mid and far periphery mottled hyperfluorescence extended to the equatorial region (Figure 3). Fluorescein angiography did not show any macular edema.

Thinned/disappeared retinal layers including the photoreceptor layer/junction between inner and outer segment of photoreceptors were shown by OCT in the parafoveal region. OCT also detected the subclinical CME (Figure 5a). Automated white-on-white threshold perimetry showed constricted peripheral visual field in both eyes (Figure 4). Dark adaptation testing showed prolonged rod dark adaptation in both eyes. We also performed magnetic resonance imaging of the brain with contrast which was unremarkable. Based on the clinical presentation of discrete mottled mid periphery of the retina and characteristic tubar visual field loss, hence typical FA and OCT findings, the patient was diagnosed with bilateral retinitis pigmentosa sine pigmento and cystoid macular edema. The patient was consulted about therapeutic options for CME. In an attempt to decrease the edema, treatment was started with instillation of dorzolamide three times daily in each eye. As a result of a one-month treatment, the reduction of macular edema was documented by OCT (Figure 5b), while BCVA improved to 1.0 in the right eye and 0.9 in the left eye. The patient was also seen five months later, and the improvement was
maintained with BCVA unchanged (1.0 for the right eye, 0.9 for the left one). The patient did not receive any other kind of therapy for his condition.

**DISCUSSION**

In the current paper, we showed the therapeutic effects of a topical CAI for the management of CME in patients with RP over a six-month period. Retinitis pigmentosa is retinal dystrophy characterized by night blindness, constricted visual fields, pigmented clumps of the retina, and photoreceptor cell dysfunction and loss [13]. The long-term prognosis is unfavorable, as there is a final loss in central vision because of direct involvement of the macula from the photoreceptors loss and/or maculopathy [14]. The diagnosis of retinitis pigmentosa sine pigmento purely from retinal findings is more challenging than in the typical cases. The retinal pigment epithelial defects could be very subtle and discrete and therefore could easily be overlooked. The vascular attenuation is also not always obvious, and sometimes retinal vascular occlusion could
be considered and initially suspected. On the other hand, optic disc pallor may be discreet, partial, or even absent, as in our case [15]. Although the subjective symptomatology is typical for RP, such as night blindness and reduced visual field in its early stages, it could be completely obscured as it affects only the peripheral fundus [16]. Without this typical clinical finding, advances in imaging and testing could help in setting the diagnosis of RP sine pigmento, such as visual field and dark adaptation testing, FA, OCT, and conventional or full-field electroretinography.

CME is an uncommon complication of RP, occurring in 10–20% of patients [9]. Currently, there are no uniform guidelines how to treat this condition. The responses to the treatment seem to be individually variable. There are several therapeutic approaches for CME in RP, such as systemic or intravitreal corticosteroids, grid laser photocoagulation, systemic or topical carbonic anhydrase inhibitors [9], and in the recent years some authors found the inhibitors of the vascular endothelial growth factor (VEGF) to be effective [17]. In any case, many practitioners believe that carbonic anhydrase inhibitors are the mainstay of treatment [9]. These drugs stimulate the pumping mechanism of the retinal pigment epithelium [18]. Unfortunately, severe side effects could appear with oral administration of CAI (drowsiness, confusion, allergic reactions, paresis) [9]. These drugs stimulate the pumping mechanism of the retinal pigment epithelium [18]. Unfortunately, severe side effects could appear with oral administration of CAI (drowsiness, confusion, allergic reactions, paresis, myelosuppression, renal calculi, loss of potassium, or, with extended use, hyperchloremic metabolic acidosis). That is the reason why this treatment is not advised for any prolonged period of time. On the other hand, topical CAI is free from the adverse effects that are related to systemic administration and thus appropriate for prolonged use [19].

Ikeda et al. [7] found the dorzolamide to be an effective and safe treatment option for CME in RP patients, and consider it as the first treatment choice for CME. If the therapeutic efficacy is not sufficient, i.e. when CME does not completely resolve within six months, additional or change of the treatment could be required. They also believed that other therapeutic approaches such as intravitreal injections of corticosteroids, inhibitors of VEGF or vitrectomy are not standard therapy because of their potentially severe complications and because of the fact that safer and still effective alternative exists in the form of topical CAI [7].

Pacella et al. [19] believed that although topical CAI are less potent than systemic ones, because of their lacking in systemic adverse effects it could be a reasonable option for the treatment of this condition, particularly if it is necessary to be used continuously. The reduction of CME commonly results in visual acuity improvement [20]. However, Chung et al. [18] found that, occasionally, improvement in visual acuity did not match the degree of edema resolution shown by OCT. This limitation of treatment could be explained by irreversible functional impairment within the fovea, arising from either chronic macular edema or photoreceptor cell dysfunction. Moustafa and Moschos [17] reported only 10% improvement in BCVA after the treatment, despite the significant resolution of macular edema in OCT scan. They deem that reasonable explanation is that CME is only one factor that affects the vision, while atrophy of the retina (particularly of the photoreceptors) also has impact on the visual function. Although our patient had anatomical and functional improvement after the treatment with topical CAI, the attention must be paid to the pre-intervention anatomical changes of the retina (photoreceptors and retinal pigment epithelium band shown on OCT), which have prognostic significance for the efficacy of the treatment. Thus, timely diagnosis and prompt treatment of CME in patients with RP are necessary before permanent photoreceptor loss occurs [16].

In the presented case we investigate the six-month therapeutic efficacy of dorzolamide for management of the cystoid macular edema secondary to RP. Our patient showed an anatomical and functional improvement after topical CAI. There are various therapeutic options for this condition, but because of their safety and efficacy, topical CAI are considered as the first treatment choice by many authors. Treatment of CME should be rapid and effective before structural changes of photoreceptors occur.

**NOTE**

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**REFERENCES**
