

# INTRAVITREAL DEXAMETHASONE IMPLANT IN RETINITIS PIGMENTOSA-RELATED CYSTOID MACULAR EDEMA

AHMAD M. MANSOUR, MD,\*† HUDA SHEHEITLI, MD,† CEM KUCUKERDONMEZ, MD,‡  
ROBERT A. SISK, MD,§ RAPHAEL MOURA, MD,¶ MARILITA M. MOSCHOS, MD,\*\*  
LUIZ H. LIMA, MD,†† LAILA AL-SHAAR, MS, MPH,‡‡ J. FERNANDO AREVALO, MD, FACS,§§  
MAURICIO MAIA, MD,¶¶ ROBERT E. FOSTER, MD,§ OZCAN KAYIKCIOGLU, MD,¶¶¶  
IGOR KOZAK, MD, PhD,\*\*\* SHREE KURUP, MD,††† HERNANDO ZEGARRA, MD,‡‡‡  
ROBERTO GALLEG0-PINAZO, MD, PhD,§§§ ROLA N. HAMAM, MD,† RIAD A. BEJJANI, MD,¶¶¶¶  
ESAT CINAR, MD,‡ ETHEM T. ERAKGÜN, MD,\*\*\*\* ALAN KIMURA, MD,††††  
ANDERSON TEIXEIRA, MD, MBA, PhD‡‡‡‡

**Purpose:** To report the clinical outcome after intravitreal dexamethasone implant in patients with retinitis pigmentosa and cystoid macular edema.

**Methods:** Multicenter retrospective case series of eyes with retinitis pigmentosa and cystoid macular edema that underwent intravitreal dexamethasone implant. Primary outcome measures were best-corrected visual acuity in LogMAR and central macular thickness. Statistical analyses used two-tailed comparison with Wilcoxon signed-rank test.

**Results:** There were a total of 45 eyes from 34 patients with a mean age of 32.7 years (range 16–57) and mean follow-up of 15.5 ± 13.0 months. At Month 3 after the first injection, mean initial best-corrected visual acuity improved from 0.61 ± 0.38 (20/81) to 0.37 ± 0.16 (20/47) ( $P = 0.012$ ), whereas mean central macular thickness ( $\mu\text{m}$ ) decreased from 506 ± 288  $\mu\text{m}$  to 311.7 ± 71.6  $\mu\text{m}$  ( $P < 0.001$ ) and mean intraocular pressure increased from 15.7 ± 2.3 mmHg to 19.8 ± 11.0 mmHg ( $P = 0.01$ ). Fourteen eyes had multiple injections (1–7 reinjections) at a mean interval of 6 months. Treatment effect was durable with multiple injections, but with seven eyes developing visually significant cataracts.

**Conclusion:** Best-corrected visual acuity improved up to 4 months in around half of the eyes. Eyes that benefited the most were pseudophakic, steroid nonresponsive, with large initial central macular thickness, and profuse fluorescein dye leakage.

RETINA 38:416–423, 2018

Retinitis pigmentosa (RP) refers to a group of inherited progressive retinal degenerations characterized by photoreceptor dysfunction involving primarily the rods with approximate worldwide prevalence of one in 3,000 or a total of 2 million affected individuals.<sup>1</sup> After visual field constriction and nyctalopia from death of the rods, cone photoreceptors degenerate resulting in visual acuity decline and eventual legal blindness. There is currently no cure for RP; however, considerable effort is devoted for rescue strategies to halt photoreceptor apoptosis. Cystoid macular edema (CME) is present in around 20% of patients with RP<sup>2–5</sup> and several treatment options are available for temporary visual success.<sup>6–16</sup> The intravitreal dexamethasone implant (IVDI) has been recently approved for the treatment of CME related to uveitis, diabetic maculop-

athy, and retinal vein occlusion.<sup>17</sup> In view of the evidence of the inflammatory nature of CME in RP,<sup>8–12</sup> this study explores the therapeutic efficacy of such an implant in CME from RP.

## Methods

We conducted a retrospective noncomparative multicenter study of the use of IVDI in eyes with CME from RP. The study adhered to the tenets of the Declaration of Helsinki, was approved by the institutional review board of all participating centers, and was registered on the National Clinical Trial website (NCT02804360). All patients signed an informed consent form after detailed review of the benefits and complications of this off-label therapy.

Table 1. BCVA and CMT Changes of Four Representative Patients at Baseline and Follow-Up Visits After a Single Intravitreal Dexamethasone Implant

Case No.	Eye	BCVA (CMT in $\mu\text{m}$ )				
		Preinjected	Week 1	Month 1	Month 3	Month 6
1	Left	20/50 (563)	20/50 (500)	20/50 (500)	20/50 (500)	20/50 (727)
2	Right	20/60 (436)	20/50 (279)	20/50 (270)	20/50 (270)	20/50 (400)
2	Left	20/60 (547)	20/30 (327)	20/30 (300)	20/30 (297)	20/50 (333)
3	Right	20/50 (510)	20/30 (335)	20/25 (385)	20/25 (381)	20/50 (532)
3	Left	20/30 (576)	20/25 (296)	20/25 (280)	20/25 (301)	20/50 (310)
4	Left	20/50 (560)	20/60 (363)	20/60 (360)	20/50 (304)	20/50 (520)

The RP eyes enrolled had the triad of bone-spicule pigment deposits, retinal vessel attenuation, and waxy pallor of the optic disk. In atypical forms of RP, it was confirmed by a family history of RP, a family screening for RP, electroretinography testing, and consistent clinical findings. Genetic testing for RP was not performed routinely in the current case series. Cystoid macular edema was defined as the presence of cystoid changes in the macula observed on linear scans of spectral domain optical coherence tomography and leakage on fluorescein angiography (to differentiate from retinoschisis). The primary outcomes were best-corrected visual acuity (BCVA) and central macular thickness (CMT).

This was a retrospective study with review of patient charts from January 2012 to December 2015. Inclusion criteria included both previously untreated and treated CME. Exclusion criteria included diabetes mellitus, vitreous hemorrhage, macular ischemia, macular scar related to subretinal fibrosis, corneal scar, uveitis,

infectious conjunctivitis, recent cataract or vitreous surgery, and history of herpetic eye disease. Patients who received previous intravitreal injections were allowed a washout period of 3 months before enrollment. Best-corrected visual acuity was assessed using Snellen charts. Central macular thickness measured the mean thickness in the central 1,000- $\mu\text{m}$  diameter area.

Intravenous fluorescein angiography was performed at the initial examination using standard protocol with visualization of the retinal midperiphery. Ocular examination, including lens status and intraocular pressure (IOP) by applanation tonometry, was performed at baseline and usually at Month 1, Month 2, Month 3, and thereafter.

The IVDI (Ozurdex; Allergan, Inc, Irvine, CA) contained 0.7 mg dexamethasone in a sustained-release drug delivery system. The implant was injected under sterile conditions using povidone iodine 5%, sterile eyelid speculum, and topical anesthesia. In a 9-year-old child, sedative agents were administered to achieve patient cooperation. The single-use applicator was injected into the midvitreal through a self-sealing scleral injection 3.5 mm posterior to the limbus at the superotemporal or inferotemporal area.

Statistical analyses were performed using SPSS version 23.0 software (IBM, Armonk, NY). Continuous variables were expressed as mean  $\pm$  SD, whereas categorical data were reported as counts and percentages when applicable. Measurements obtained before and after the injection were compared using both paired *t*-tests and Wilcoxon signed-rank tests for continuous variables and McNemar tests for categorical ones (such as IOP). Partial correlation analyses were conducted between the changes in the different vision parameters, after accounting to baseline measurements. *P* values  $<$  0.05 were considered statistically significant. Best-corrected visual acuity was converted into the logarithm of the minimal angle of resolution (LogMAR) for analysis. Because investigators used different spectral domain optical coherence tomography machines, we relied on the paired comparisons between preinjection and postinjection CMT, while

From the \*Department of Ophthalmology, Rafic Hariri University Hospital, Beirut, Lebanon; †Department of Ophthalmology, American University of Beirut, Beirut, Lebanon; ‡Department of Ophthalmology, Izmir University Faculty of Medicine, Izmir, Turkey; §Department of Ophthalmology, Cincinnati Eye Institute, University of Cincinnati, Cincinnati, Ohio; ¶Department of Ophthalmology, Universidade Federal de São Paulo, São Paulo, Brazil; \*\*Department of Ophthalmology, University of Athens, Athens, Greece; ††Department of Ophthalmology, Federal University of São Paulo, São Paulo, Brazil; ‡‡Vascular Medicine Program, American University of Beirut Medical Center, Beirut, Lebanon; §§Wilmer Eye Institute, Johns Hopkins University, Baltimore, Maryland; ¶¶Department of Ophthalmology, Celal Bayar University, Manisa, Turkey; \*\*\*Division of Vitreoretinal Diseases and Surgery, King Khaled Eye Specialist Hospital, Riyadh, Kingdom of Saudi Arabia; †††Department of Ophthalmology, Wake Forest University, Winston Salem, North Carolina; ‡‡‡Retina Associates of Cleveland, Beachwood, Ohio; §§§Department of Ophthalmology, University and Polytechnic Hospital La Fe, Valencia, Spain; ¶¶¶Department of Ophthalmology, Hotel Dieu de France, Beirut, Lebanon; \*\*\*\*Department of Ophthalmology, Ekol Eye Hospital, Izmir, Turkey; ††††Department of Ophthalmology, University of Colorado, Aurora, Colorado; and ‡‡‡‡School of Medicine, Catholic University Brasilia, Brasilia, Brazil.

None of the authors has any financial/conflicting interests to disclose.

Reprint requests: Ahmad M. Mansour, MD, Department of Ophthalmology, American University of Beirut, Beirut, 113-6044 Lebanon; e-mail: ammansourmd@gmail.com

the calculated mean CMT was inaccurate; it is listed hereby to allow a gross comparison.

**Results**

A total of 45 eyes from 34 patients were collected. The clinical characteristics are summarized in Tables 1–5 (Figure 1). Mean ± SD of baseline values included IOP 15.7 ± 2.3 mmHg, BCVA 0.61 ± 0.38 (20/81), and CMT 506 ± 288 μm (Table 3). At month 1 after IVDI, mean values became IOP 17.1 ± 4.3 mmHg, BCVA 0.32 ± 0.23 (20/42), and CMT 292.0 ± 84.0 μm. At Month 3 after IVDI, mean values were IOP 19.8 ± 11.0 mmHg, BCVA 0.37 ± 0.16 (20/47), and CMT 311.7 ± 71.6 μm. The mean change using paired samples test was 216.5 ± 256.6 μm for CMT (*P* < 0.001), mean

Table 2. Clinical Characteristics of the Intervention Group Analysis of the Difference Between Preinjection and Postinjection of the First Intravitreal Dexamethasone Implant

Variables		Mean ± SD	Range	Missing
Age		32.7 ± 10.8	16–57	
Duration of RP, years		9.8 ± 8.8	1–33	
Length of follow-up, months		15.5 ± 13.0	1–48	
No. of IVDI		2.0 ± 1.9	1–8	
Refraction	Myopia	12	Emmetropia 12	Hyperopia 4
	Genetic type	Simplex 5	Recessive 2	Dominant 9
			Yes	No
Male sex		18	11	5
White race		26	0	8
Positive family history		13	17	4
Smoker		5	27	2
Positive systemic disease		8	26	0
Right eye		18	27	0
Hearing loss		2	43	0
Phakic		35	10	0
Uveitis		8	37	0
Bilateral CME		11	23	0
Good response to anti-VEGF intravitreal injections		2	9	NA
Good response to oral acetazolamide		2	17	NA
Good response to topical carbonic anhydrase inhibitor		6	7	NA
Good response to topical prostaglandin inhibitor		0	5	NA
OCT findings				
ERM		6	33	6
VMT		2	33	10
OS-IS intact		19	14	12

ERM, epiretinal membrane; NA, not assessed; OCT, optical coherence tomography; OS-IS, outer segment-inner segment; VEGF, vascular endothelial growth factor; VMT, vitreomacular traction.

Table 3. Clinical Response to One Injection of Dexamethasone Implant and Paired Comparison

Time	CMT	BCVA	IOP	No. Eyes
Initial (SD) [range]	506.0 (288.0) [182–1,713]	0.61 (0.38) [0.10–1.30] Snellen equivalent (mean 20/81; range 20/25–20/400)	15.7 (2.3) [11–22]	27
1–4 months after injection	284.3 (66.8) [174–500]	0.48 (0.36) [0.10–1.30] Snellen equivalent (mean 20/60; range 20/25–20/400)	20.1 (8.7) [12–46]	27
Time	ΔCMT	ΔBCVA	ΔIOP	No. eyes
First 4 months	222.8 (282.1) <i>P</i> = 0.000	0.10 (0.20) <i>P</i> = 0.011	4.7 (9.4) <i>P</i> = 0.011	27

BCVA, best-corrected visual acuity in LogMAR; Δ, change from baseline after intravitreal injection of dexamethasone implant.

Table 4. Change in IOP From Baseline Value With Each Intravitreal Injection of Dexamethasone Implant

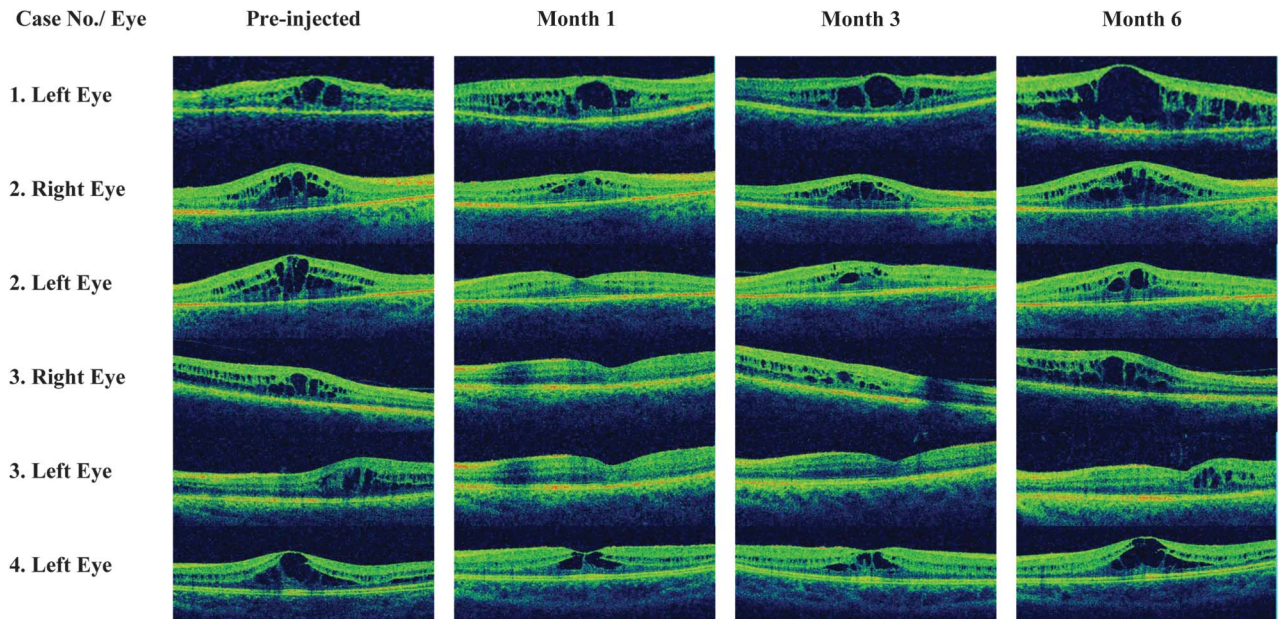
	ΔIOP After First Injection	ΔIOP After Second Injection	ΔIOP After Third Injection	ΔIOP After Fourth Injection	ΔIOP After Fifth Injection	ΔIOP After Sixth Injection
No. of eyes	28	10	9	7	5	4
Mean ± SD, mmHg	4.9 ± 9.4	4.9 ± 12.0	0.8 ± 4.9	2.6 ± 3.2	2.4 ± 4.3	-0.8 ± 1.0
Median, mmHg	1	2	2	2	3	-0.5
Range, mmHg	-5 to 33	-3 to 38	-7 to 6	0 to 9	-2 to 7	-2 to 0

Δ, change from baseline.

Table 5. Correlation Inner Segment (IS)–Outer Segment (OS) Status by Spectral Domain OCT and Visual Gain or Anatomic Improvement After a Single IVDI

Photoreceptor IS-OS	No. of Eyes	IOP Before IVDI	IOP After IVDI	ΔIOP	BCVA Before IVDI	BCVA After IVDI	ΔBCVA	CMT Before IVDI	CMT After IVDI	ΔCMT
Effaced IS-OS										
Mean	12	15.8	17.0	1.3	0.83 [20/135]	0.67 [20/94]	0.05	500.5	263.5	237.0
SD		2.2	3.1	2.5	0.52	0.44	0.24	402.1	54.4	391.9
Intact IS-OS										
Mean	14	15.6	21.0	5.4	0.52 [20/66]	0.37 [20/47]	0.15	529.2	304.5	224.6
SD		1.3	10.0	10.1	0.17	0.25	0.19	139.1	76.5	147.4
P value				0.18			0.11			0.17

OCT, optical coherence tomography; Δ, difference between initial values and values of the first 3 months after injection; vision is listed as LogMAR with values between brackets representing Snellen equivalents.



**Fig. 1.** Composite linear scans before and after injection of IVDI at Month 1, Month 3, and Month 6 in 6 eyes of 4 patients. The visual and anatomic responses (Table 1) reinforce the general finding of the duration therapeutic effect of 4 months.

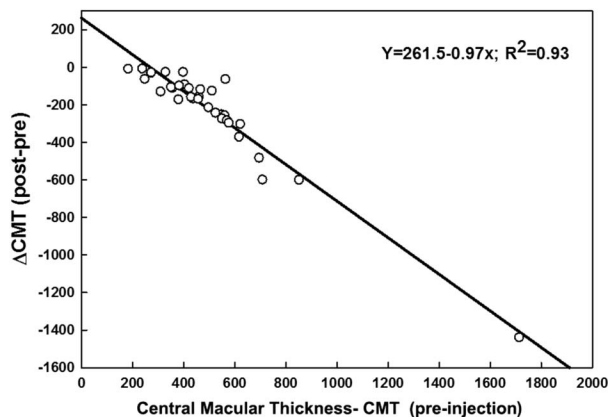
change of BCVA of  $0.11 \pm 0.25$  ( $P = 0.012$ ), and mean change of IOP of  $3.9 \pm 8.7$  mmHg ( $P = 0.01$ ). The amount of BCVA gain ( $P = 0.029$ ) and the reduction of macular thickness ( $P < 0.001$ ;  $n = 34$ ) after IVDI correlated positively with the initial macular thickness (Figure 2). There was no correlation between either duration of RP or inner retinal segment–outer retinal segment integrity and both anatomic improvement and visual gain (Table 5).

Nonparametric tests were concurrently conducted reflecting similar findings. Best-corrected visual acuity improved transiently in around half of the patients and was sustained until Month 4 with the recurrence of CME unless repeated injections were performed. The fovea recovered to its previous architecture up to 4

months after injection. In the first 4 months, both CMT and vision improved significantly (Table 3). In 11 patients who received bilateral injections, similar anatomic and visual results were found between the 2 eyes.

No significant ocular or systemic side effects were reported after a single IVDI. In addition, complications such as retinal detachment, endophthalmitis, and cataract development were not observed. Intraocular pressure during the first 4 months after the first injection was unchanged in 21 eyes, increased 1 mmHg to 5 mmHg in 13 eyes, 5.1 mmHg to 10 mmHg in 1 eye, and more than 10 mmHg in 6 eyes (data were missing in 4 eyes) (Table 4). Increased IOP was controlled medically. Seven eyes developed cataract after repeated injections. The study did not collect data on the number of eyes needing cataract surgery, especially with the relatively short follow-up.

Mean number of injections was 2.0 (SD = 1.9; range 1–8). Mean interval for retreatment was 6.0 months (range 2–14 months). A total of 31 eyes had a single IVDI while retreatment was performed in 14 eyes. The number of IVDI is described in ascending number: two (four eyes), three (three eyes), four (one eye), five (two eyes), six (one eye), seven (two eyes), and eight (one eye). With repeated injections, cataract developed in seven eyes, while IOP was unchanged, as all these eyes were steroid nonresponsive (Table 4). Retreatments resulted in quite a similar decrease in CMT and a similar BCVA gain to that noted after the first injection without loss of therapeutic effect according to the number of reinjections.



**Fig. 2.** Positive correlation graph between the initial CMT and anatomic response to IVDI or decrease in macular edema.

Table 6. Literature Review of Cases With Cystoid Macular Edema Related to Retinitis Pigmentosa Treated With Either an Intravitreal Dexamethasone Implant (IVDI) or Intravitreal Triamcinolone Acetonide (IVTA)

Author	Intravitreal Treatment	Study Design	No. of Eyes	Previous Treatment	Mean VA Before/After Treatment	Mean CMT Before/After Treatment, $\mu\text{m}$	Recurrence	Complication	Follow-Up in Month
Ahn et al <sup>12</sup>	IVDI	Case report	OU	AAA; IVTB	20/100–20/50 OD at 4 months; 20/150–20/60 OS at 4 months	631–218 OD at 4 months; 681–235 OS at 4 months	CME recurred at 6 months OU (IVDI reinjection performed OS)	IOP 23 mmHg	12
Patil et al <sup>16</sup>	IVDI	Case report	OD	AAA; DA; IVTB; IVTT; Orbital floor Depo-Medrone	20/200–20/155 at 6 weeks	559–271 at 6 weeks	No recurrence	No	10
Srour et al <sup>13</sup>	IVDI	Retrospective case series	4 eyes of 3 patients	AAA; NSAID; STT	Median 20/160–20/100 at 1 month to 20/125 at 3 months to 20/125 at 6 months	443 $\pm$ 185–234 $\pm$ 68 at 1 month to 332 $\pm$ 177 at 3 months to 305 $\pm$ 124 at 6 months	Recurrent CME was recorded in 2/4 eyes at 3 months	No	6
Saatci et al <sup>14</sup>	IVDI	Case report	OU	DA	20/100 OD to 20/50 OU at 1 week	NM	CME recurred at 2 months OS and 3 months OD	No	7
Alhassan et al <sup>15</sup>	IVDI	Case report	1 eye	AAA	20/40–20/30 at 1 month	538–294 at 1 month	No	No	1
Buchaim et al <sup>11</sup>	IVDI	Case report	OU	19 IVTA OD and 13 IVTA OS over 6 years with loss of effect	CF2m to 20/200 OD at 4 months; 20/100–2 to 20/80 OS at 4 months	NM	No	No	4
Barge et al <sup>18</sup>	IVTA	Case report	OU	AAA; NSAID	20/50–20/50 OD at 4 months; 20/100–20/50 OS at 4 months	643–623 OD at 4 months; 664–360 OS at 4 months	CME recurred at 5 months OD and 6 months OS	IOP 27 mmHg; OD 30 mmHg OS	11
Urban et al <sup>19</sup>	IVTA	Case report	1 eye	AAA	20/200–20/100 at 3 months	>1,000–600 at 3 months	NM	Endophthalmitis after the fourth injection	NM
Scorolli et al <sup>20</sup>	IVTA	Prospective, nonrandomized comparative trial	20 eyes of 20 patients	NM	Mean 20/90 unchanged at 1 and 6 months	456 $\pm$ 95–302 $\pm$ 82 at 1 month to 270 $\pm$ 64 at 3 months to 299 $\pm$ 76 at 6 months to 437 $\pm$ 95 at 12 months ( $P < 0.001$ )	NM	10 eyes (50%) developed IOP above 21 mmHg (2 eyes IOP 30–35 mmHg)	12
Wang et al <sup>21</sup>	IVTA	Retrospective study	Unspecified number of eyes	NM	Mean 20/140–20/100 ( $P < 0.05$ )	Mean 493–208 ( $P < 0.05$ )	CME recurred 2–5 months	IOP rise of 8 mmHg at 1–2 months	NM
Kim et al <sup>22</sup>	IVTA	Case report	OU	AAA; STT	20/80–20/80 OD at 3 months and 20/40 OD at 3 months after the second injection 1 year apart 20/125–20/125 OS at 3 months and 20/50 3 months after the second injection 1 year apart	590–143 OD at 3 months	CME recurred 11 months OU	NM	NM
Minnella et al <sup>23</sup>	IVTA	Case report	OS	AAA	20/70–20/45 at 6 months	620–149 at 6 months	No	IOP 33 mmHg at 6 months	6
Ozdemir et al <sup>24</sup>	IVTA	Prospective case series	5 eyes of 5 patients	AAA	Median 20/200 unchanged at 1, 3, and 6 months	Mean 418–224 at 1 month to 275 at 3 months to 312 at 6 months	CME recurred at 3 months in 1 patient and 6 months in 2 patients	No	6–8
Saraiva et al <sup>8</sup>	IVTA	Case report	OU	AAA	20/40–20/40 OD at 1 month; 20/80–20/50 OS at 18 days	CME resolved at 1 month OD and 6 weeks OS	CME recurred 6 months OS	NM	NM

AAA, acetazolamide 500 mg daily; DA, dorzolamide hydrochloride drops; IVTB, intravitreal bevacizumab; IVTT, intravitreal triamcinolone; NM, not mentioned; NSAID, nonsteroidal anti-inflammatory drops; OD, right eye; OS, left eye; OU, both eyes; values after  $\pm$  refer to SD; STT, subtenon triamcinolone.

Discussion

This study shows IVDI to have a short-lasting anatomic and functional improvement of few months with ocular hypertension being the major complication (Table 4). This is the largest study on IVDI in RP-related CME (Table 6)<sup>8,18–24</sup> and the only analysis of repetitive injection of the implant in such disorder. In RP eyes that are steroid nonresponsive and pseudophakic, repeated injections did not lead to loss of clinical effect, and no complications were encountered. Cataract surgery can help also in clearing media opacity and allows repetitive injection in eyes that need multiple injections.

The role of intravitreal corticosteroids in managing RP-related CME was previously addressed by few case reports using IVDI and two case series using intravitreal triamcinolone (Table 6).<sup>8,18–24</sup> In a recent study, IVDI was administered in a 13-year-old boy with refractory CME from RP and Coats'-like exudative retinopathy; 6 weeks after IVDI, CMT decreased from 559 μm to 271 μm with persistent resolution of the exudative response 10 months after the injection.<sup>16</sup> In one prospective study of intravitreal triamcinolone (4 mg), all 20 treated eyes showed an anatomical improvement at 3 months after injection: median CMT decreased significantly from 459.9 μm to 272.8 μm, whereas mean LogMAR BCVA improved marginally from 0.66 (20/91) to 0.59 (20/78).<sup>20</sup> Another study treated 5 eyes with intravitreal triamcinolone and resulted in anatomic improvement in all eyes (median CMT decreased from 418 to 275 μm at 3 months), but BCVA improvement was discrete in 2 eyes and unchanged in 3 eyes.<sup>24</sup> An additional study demonstrated that one eye treated with intravitreal triamcinolone resulted in decrease of CMT from 590 μm to 143 μm without change in vision<sup>22</sup>; the dissociation between CME resolution after IVDI or intravitreal triamcinolone and lack of BCVA recovery is explained by either chronicity of CME and/or the presence of injury at the photoreceptor layer that is variable according to the pattern of genetic abnormality.

The pathogenesis of CME in RP is unclear and may be multifactorial with the proposed main mechanisms being (Figure 3) 1) breakdown of blood-retinal barrier from accumulation of apoptosis metabolic by-products<sup>3–5</sup>; 2) retinal pigment epithelium pump failure<sup>2</sup>; 3) autoimmunity<sup>25</sup> (leakage of retinal antigens from an abnormal blood-retinal barrier, followed by sensitization of the immune system; ending in production of antiretinal antibodies); 4) chronic low-grade inflammation<sup>26</sup>; 5) epiretinal membrane formation.<sup>1</sup> Corticosteroids are usually effective in resolving CME

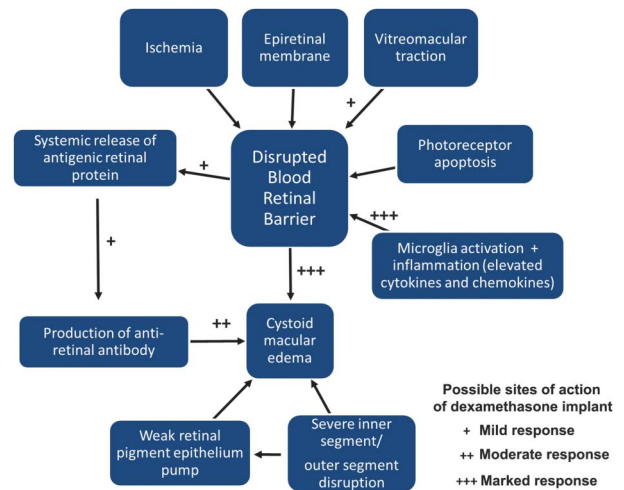


Fig. 3. Proposed pathophysiology of CME in RP and the possible sites of action of dexamethasone implant.

through several mechanisms<sup>11–16</sup>: 1) reduction in proinflammatory cytokines; 2) reduction of vascular endothelial growth factor levels<sup>6</sup>; 3) restoration of blood-retinal barrier<sup>8</sup>; 4) suppression of autoimmune processes<sup>7</sup>; and 5) improvement of RP phenotype by inhibition of activated microglia and possibly slowing retinal degeneration.<sup>9,10,27</sup> Carbonic anhydrase inhibitors are currently the preferred therapy for CME in eyes with RP.<sup>2</sup>

The role of inflammation in the pathogenesis of RP is still unclear. For the past four decades, researchers have detected the presence of retinal autoantibodies in the serum of human RP patients and in animal models of RP.<sup>25</sup> Recently, slit-lamp biomicroscopic detection of immune system cells in the anterior vitreous cavity of RP was reported.<sup>26</sup> Moreover, recent studies highlighted the occurrence of microglial activation and consequent inflammatory cytokine production in the outer retinas of rodent models of RP at the time of photoreceptor death.<sup>28</sup> In all cases, systemic immunotherapy delayed photoreceptor cell loss in Royal College of Surgeons' rats,<sup>27</sup> and it is unknown if IVDI would play an immune-modulatory effect in experimental models of RP and in patients with RP.<sup>27</sup> Interestingly, stem cell transplantation caused resolution of CME in one case of RP.<sup>7</sup>

The limitations of this study are the relatively low number of subjects, absence of a control group, retrospective nature of the study, absence of a uniform standard protocol for treatment and follow-up, and loss to follow-up. Another major drawback is the lack of microperimetry, visual fields, and electroretinographic studies after injection to evaluate the potential benefit of corticosteroids on the overall retinal function. Moreover, this study did not analyze

Downloaded from http://journals.lww.com/retinajournal by BhdMf6Pfkav1zEoun1tQIN4a+KkLhEZqbslH04XWf0 hCywCX1AWnYVqplllOCHD313D00DFy71TVSFAc3JC1yOabggQZXdMwfkZBvYtws= on 08/29/2024

the clinical response according to genetic pattern of the disease.

In conclusion, the anatomical resolution of CME in RP after IVDI supports the hypothesis, at least in part, of an underlying inflammatory response involved in its pathogenesis. Intravitreal dexamethasone implant may be considered for CME refractory to medical treatment. Special subsets of patients with RP suited for IVDI treatment include steroid nonresponsive eyes, pseudophakic eyes, profuse leakage on fluorescein angiography, and large CMT. However, an important drawback is the temporary response and the need for reinjection, resulting in a risk of ocular hypertension and cataract formation.

**Key words:** cystoid macular edema, dexamethasone implant, intraocular pressure, retinitis pigmentosa.

### References

- Milam AH, Li ZY, Fariss RN. Histopathology of the human retina in retinitis pigmentosa. *Prog Retin Eye Res* 1998;17:175–205.
- Liew G, Moore AT, Webster AR, Michaelides M. Efficacy and prognostic factors of response to carbonic anhydrase inhibitors in management of cystoid macular edema in retinitis pigmentosa. *Invest Ophthalmol Vis Sci* 2015;56:1531–1536.
- Chung H, Hwang JU, Kim JG, Yoon YH. Optical coherence tomography in the diagnosis and monitoring of cystoid macular edema in patients with retinitis pigmentosa. *Retina* 2006;26:922–927.
- Kim YJ, Joe SG, Lee DH, et al. Correlations between spectral-domain OCT measurements and visual acuity in cystoid macular edema associated with retinitis pigmentosa. *Invest Ophthalmol Vis Sci* 2013;54:1303–1309.
- Sandberg MA, Brockhurst RJ, Gaudio AR, et al. The association between visual acuity and central retinal thickness in retinitis pigmentosa. *Invest Ophthalmol Vis Sci* 2005;46:3349–3354.
- Artunay O, Yuzbasioglu E, Rasier R, et al. Intravitreal ranibizumab in the treatment of cystoid macular edema associated with retinitis pigmentosa. *J Ocul Pharmacol Ther* 2009;25:545–550.
- Siqueira RC, Messias A, Voltarelli JC, et al. Resolution of macular oedema associated with retinitis pigmentosa after intravitreal use of autologous BM-derived hematopoietic stem cell transplantation (letter). *Bone Marrow Transplant* 2013;48:612–613.
- Saraiva VS, Sallum JM, Farah ME. Treatment of cystoid macular edema related to retinitis pigmentosa with intravitreal triamcinolone acetonide. *Ophthalmic Surg Lasers Imaging* 2003;34:398–400.
- Sacchetti M, Mantelli F, Merlo D, Lambiase A. Systematic review of randomized clinical trials on safety and efficacy of pharmacological and nonpharmacological treatments for retinitis pigmentosa. *J Ophthalmol* 2015;2015:737053.
- Guadagni V, Novelli E, Piano I, et al. Pharmacological approaches to retinitis pigmentosa: a laboratory perspective. *Prog Ret Eye Res* 2015;48:62–81.
- Buchaim G, Rezende MP, Maia M. Implante intravítreo de liberação crônica de dexametasona (Ozurdex®) para o tratamento de edema macular por retinose pigmentar: relato de caso [in Portuguese]. *Arq Bras Oftalmol* 2013;76:377–379.
- Ahn SJ, Kim KE, Woo SJ, Park KH. The effect of an intravitreal dexamethasone implant for cystoid macular edema in retinitis pigmentosa: a case report and literature review. *Ophthalmic Surg Lasers Imaging Retina* 2014;45:160–164.
- Strour M, Querques G, Leveziel N, et al. Intravitreal dexamethasone implant (Ozurdex) for macular edema secondary to retinitis pigmentosa. *Graefes Arch Clin Exp Ophthalmol* 2013;251:1501–1506.
- Saatci AO, Selver OB, Seymenoglu G, Yaman A. Bilateral intravitreal dexamethasone implant for retinitis pigmentosa-related macular edema. *Case Rep Ophthalmol* 2013;4:53–58.
- Alhassan M, Quintyn JC. Unilateral intravitreal dexamethasone implant for bilateral retinitis pigmentosa-related macular edema. *Graefes Arch Clin Exp Ophthalmol* 2013;251:2827–2828.
- Patil L, Lotery AJ. Coat's-like exudation in rhodopsin retinitis pigmentosa: successful treatment with an intravitreal dexamethasone implant. *Eye (Lond)* 2014;28:449–451.
- Haller JA, Bandello F, Belfort R Jr, et al. Dexamethasone intravitreal implant in patients with macular edema related to branch or central retinal vein occlusion twelve-month study results. *Ophthalmology* 2011;118:2453–2460.
- Barge S, Rothwell R, Sepúlveda P, Agrelos L. Intravitreal and subtenon depot triamcinolone as treatment of retinitis pigmentosa associated cystoid macular edema. *Case Rep Ophthalmol Med* 2013;2013:591681.
- Urban KE, Quiram PA, Trese MT. Subretinal triamcinolone acetonide associated with improvement of cystoid macular edema in a patient with retinitis pigmentosa. *Retin Cases Brief Rep* 2009;3:47–49.
- Scorolli L, Morara M, Meduri A, et al. Treatment of cystoid macular edema in retinitis pigmentosa with intravitreal triamcinolone. *Arch Ophthalmol* 2007;125:759–764.
- Wang C, Hu J, Bernstein PS, et al. Intravitreal injection of triamcinolone acetonide for macular edema due to retinitis pigmentosa and other retinal diseases. *Adv Exp Med Biol* 2006;572:309–314.
- Kim JE. Intravitreal triamcinolone acetonide for treatment of cystoid macular edema associated with retinitis pigmentosa. *Retina* 2006;26:1094–1096.
- Minnella AM, Falsini B, Bamonte G, et al. Optical coherence tomography and focal electroretinogram evaluation of cystoid macular edema secondary to retinitis pigmentosa treated with intravitreal triamcinolone: case report. *Eur J Ophthalmol* 2006;16:883–886.
- Ozdemir H, Karacorlu M, Karacorlu S. Intravitreal triamcinolone acetonide for treatment of cystoid macular oedema in patients with retinitis pigmentosa. *Acta Ophthalmol Scand* 2005;83:248–251.
- Heckenlively JR, Jordan BL, Aptsiauri N. Association of anti-retinal antibodies and cystoid macular edema in patients with retinitis pigmentosa. *Am J Ophthalmol* 1999;127:565–573.
- Yoshida N, Ikeda Y, Notomi S, et al. Clinical evidence of sustained chronic inflammatory reaction in retinitis pigmentosa. *Ophthalmology* 2013;120:100–105.
- Adamus G, Wang S, Kyger M, et al. Systemic immunotherapy delays photoreceptor cell loss and prevents vascular pathology in Royal College of Surgeons rats. *Mol Vis* 2012;18:2323–2337.
- Kohno H, Chen Y, Kevany BM, et al. Photoreceptor proteins initiate microglial activation via Toll-like receptor 4 in retinal degeneration mediated by all-trans-retinal. *J Biol Chem* 2013;288:15326–15341.