Original Article

Role of Sub-Tenon Autologous Platelet Rich Plasma Injections in The Treatment of RP-Associated Cystoid Macular Edema: Interventional Case Series

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ABSTRACT

Purpose: Retinitis pigmentosa (RP)is a progressive degenerative disease that may develop complications such as cystoid macular edema (CME), epiretinal membrane (ERM), and cataracts. Our study aims to use platelet-rich plasma (PRP) to resolve the cystic spaces at the macula by healing the tissue damage done by RP disease and lowering tissue compliance to limit fluid accumulation.

Study Design: Interventional Case Series.

Place and Duration of Study: Ibrahim Eye Centre, Lahore from December 2024 to March 2025.

Methods: Seven patients (12 eyes) with retinitis pigmentosa–associated CME received three sessions of autologous sub-tenon PRP injections at 3-week intervals. Baseline evaluation included best-corrected visual acuity (BCVA), fundoscopy, optical coherence tomography (OCT), and intraocular pressure (IOP), all of which were repeated before each session. Final analysis compared pre-treatment findings with those obtained three weeks after the last injection.

Results: OCT demonstrated a statistically significant reduction in central foveal thickness (mean 289.50 ± 124.28 µm pre-treatment vs. 254.42 ± 111.67 µm post-treatment; p = 0.038). Visual outcomes showed improvement in 3 patients and stability in 4 patients, particularly in eyes with resolution of macular edema. No serious adverse events were observed; one patient developed transient IOP elevation.

Conclusion: Sub-tenon PRP is a safe and potentially effective option for reducing macular edema in RP. However, larger studies with longer follow-up are required to confirm efficacy, evaluate durability of response, and assess the risk of recurrence or progression.

Keywords: Optical Coherence Tomography, Edema, Cystoid Macular Edema, Retinitis Pigmentosa, Macular Edema, Platelet Rich Plasma.

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INTRODUCTION

Retinitis pigmentosa (RP) is an inherited neurodegenerative disease followed by progressive death of photoreceptor cells and Retinal pigment epithelium (RPE) atrophy. It initially disrupts the night vision, then daylight vision and eventually causes blindness.[1] RP prevalence is quite variable according to the regional or geographical locations; One in 750-9000 individuals is affected by the disease.[2] The disease is more prevalent in areas with family consanguinity. The disease is inherited in an autosomal dominant, autosomal recessive, X-linked, and mitochondrial manner.[3] Recently, ninety-three genes have been identified to be associated with RP,

mostly are linked with the phototransduction cascade, visual cycle, and photoreceptor structure.[4] In RP, the photoreceptor cell death is primarily due to oxidative stress, metabolic stress, and Endoplasmic Reticulum stress due to protein mutation and calcium regulation.[3]

RP is a progressive degenerative disease that may develop complications such as cystoid macular edema (CME), epiretinal membrane (ERM),vitreomacular traction syndrome, macular hole, and cataracts.[5,6] According to one report the prevalence of CME in RP patients is 10% to 15%.[7] The photoreceptor cells damage in RP leads to the inflammatory response and activation of innate immune cells of the retina, referred to as microglia. Most abundant type of microglial cells in the retina are Müller glial.[3] There are different mechanisms involved in the formation of CME in RP, such as Blood retinal barrier (BRB) breakdown, dysfunction of pumping mechanism in RPE, Muller cell edema, vitreous traction and antiretinal antibodies.[8] BRB maintains the ionic and metabolic gradients; its damage results in macular edema.[9]In a study it was found that cystic spaces are larger in advanced staged RP due to reduced structural stability and impaired RPE function.[10]

The main growth factors produced by platelets are PDGF, VEGF, FGF, IGF, EGF, and TGF-βwhich helps in regeneration or healing of the damaged tissues.[11]When autologous Platelet Rich Plasma (PRP) is obtained from the centrifuged whole blood, it is injected into the sub-tenon's space, the level of neurotrophic growth factors increase in the microenvironment space around the photoreceptors. Using this evidence, we used autologous PRP therapy to slow down the death of the photoreceptor cells and re-activate the cells in the dormant phase. PRP also heals the damaged BRB and controls the inflammatory response by its anti-inflammatory properties. Our study aims to use PRP to resolve the cystic spaces at the macula by healing the tissue damage done by RP disease and lowering tissue compliance to limit fluid accumulation and treat RP-associated CME.

METHODS

An interventional case series using autologous sub-tenon PRP injections was conducted at Ibrahim Eye Center. The study was approved by the IRB (**ERB198/12/01-01-2026/AIMC/JHL**).Twelve eyes of 7 patients who were diagnosed with RP-associated CME were included. Detailed examination included clinical and family history, refraction, fundus examination, and Optical Coherence Tomography (OCT). Written informed consents of all the patients were obtained prior to every PRP injection.

A comprehensive eye examination was done on all patients. The best corrected visual acuity at distance was recorded using a standard Snellen chart. Intraocular pressure (IOP) was measured by anon-contact and contact tonometer, and fundus findings were observed after slit lamp biomicroscopy. Functional and structural findings of retinal layers and cystic spaces were assessed with OCT which included the assessment of inner segment/outer segment (IS/OS) continuity, outer retinal layers asymmetry, and central foveal thickness for the assessment of RP-associated CME prognosis.

After obtaining informed consent, patients were subjected to three PRP sessions with a gap of three weeks after each session. On the day of each session, the blood was taken out from the patient's antecubital vein into four 3.0 ml tubes containing tri-sodium citrate. After 8 min of centrifugation at 2500 rpm, 1.5 million to 4 million platelet counts were concentrated to ten times the normal concentration with the help of PRP kits. A total of 1.5 ml of PRP was taken out of the bottom layer with the help of a syringe and injected into the sub-tenon space of each eye under topical anesthesia.

During the injection, all the aseptic measurements were taken by the Ophthalmologist in the operation theater. A sterile drape was applied, and a speculum was placed in the patient's eye in supine position. The patient was asked to look superotemporally while 1.5 ml of PRP was injected at the inferonasal quadrant in the sub-tenon space with the help of a blunt curved Posterior Sub-tenon cannula. The same ophthalmologist did all the preparations and the procedure. After the injection, the patient's eye was patched for 2 hours and eyedrops (Tobramycin + Dexamethasone) and anti-glaucoma eye drops were prescribed. Before the first injection, all the baseline assessments (Visual acuity, fundoscopy, OCT, and IOP) were done and before every session, all measurements were repeated to assess the changes in the visual acuity readings and OCT imaging. The first examination before the first session and the final examination after three weeks of the last session were evaluated for the statistical analysis.

Table 1: *Effect of PRP on RP-associated cystoid macular edema.*

No. of Eyes	Central foveal thickness before injection	Central foveal thickness after injection	Cystic spaces at macula after injection
1	300 µm	333 µm	Increased
2	212 µm	212 µm	Resolved
3	266 µm	270 µm	Same
4	379 µm	258 µm	Resolved
5	137 µm	145 µm	Same
6	220 µm	170 µm	Resolved
7	266 µm	270 µm	Resolved
8	291 µm	179 µm	Reduced
9	625 µm	567 µm	Reduced
10	254 µm	208 µm	Resolved
11	187 µm	191 µm	Same
12	337 µm	250 µm	Resolved

Out of 12 eyes, one eye (8%) had an increase in foveal thickness, 2 eyes (17%) had a decrease in foveal thickness, 6 eyes (50%) had completely resolved edema, and 3 eyes (25%) had the same thickness edema.

Analysis was done by using SPSS version 21.0. P-value less than 0.05 was considered statistically significant.

RESULTS

Twelve eyes of 7 patients with RP were included. Best corrected visual acuity was recorded before and after PRP sessions. Four patients had stable vision, and 3 patients had improvement in vision after growth factor injections. Cystic spaces were measured by measuring changes in central foveal thickness with the help of OCT scans. Mean central foveal thickness before PRP was 289.50± 124.281 µm and after PRP was 254.42 ± 111.666 µm, which showed a significant decrease in mean central foveal thickness after PRP injections (P-value 0.038).

There were no side effects seen in patients during and after the three sessions. One patient had a transient increase in the intraocular pressure, which was later reduced by anti-glaucoma eye drops. Significant differences were noticed in the OCT scans before and after the treatment (Figure 1-4). Only one patient had a worsening effect on edema while the other patients' edema was either resolved or remained stable during and after the treatment.

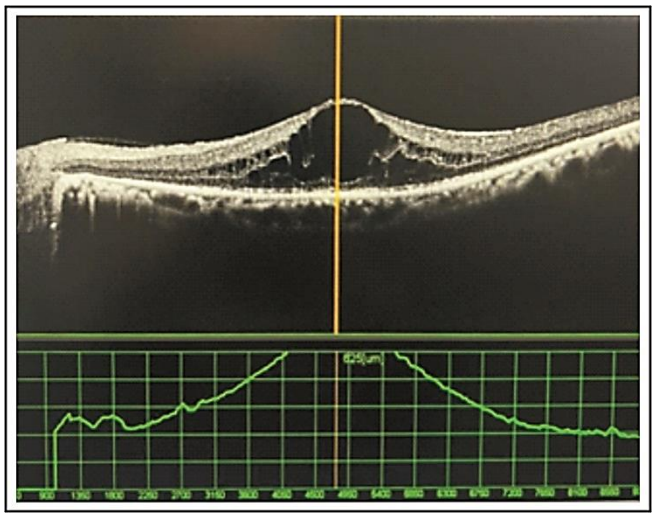

Figure 1: Central foveal thickness before PRP injection.

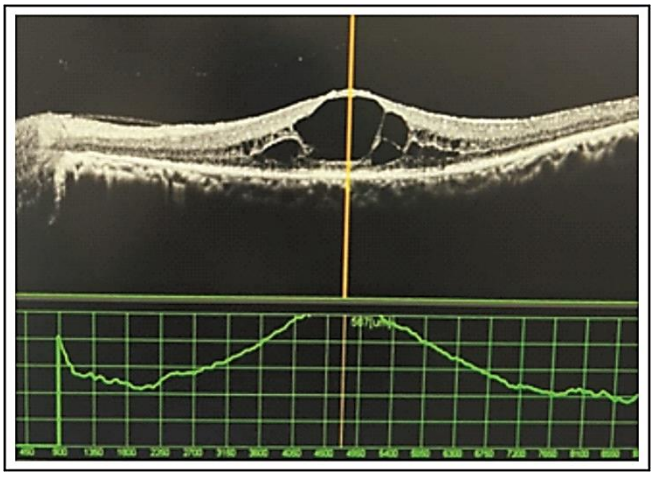

Figure 2: Same patient as in figure 1. Central foveal thickness after PRP injection (central foveal thickness is reduced).

DISCUSSION

Retinitis pigmentosa is a neurodegenerative disease caused by the death of photoreceptor cells and retinal pigment epithelium atrophy.[1] The disease is diagnosed

based on the presence of bony spicules or intraretinal hyperpigmentation, while on OCT it is diagnosed based on the images of the sensory retina and ellipsoid zone. OCT helps in quantifying the loss of the ellipsoid zone as well as the thickness of cystoid macular edema.[13] RPE atrophy and photoreceptor cells death lead to an increase in inflammatory response and fluid accumulation, forming cystic spaces at the macula. The components of PRP are beneficial in reducing the inflammatory response, tissue regeneration, and activation of the cells in a dormant phase. It may also resolve the cystic spaces and provide overall benefit to the RP patients.

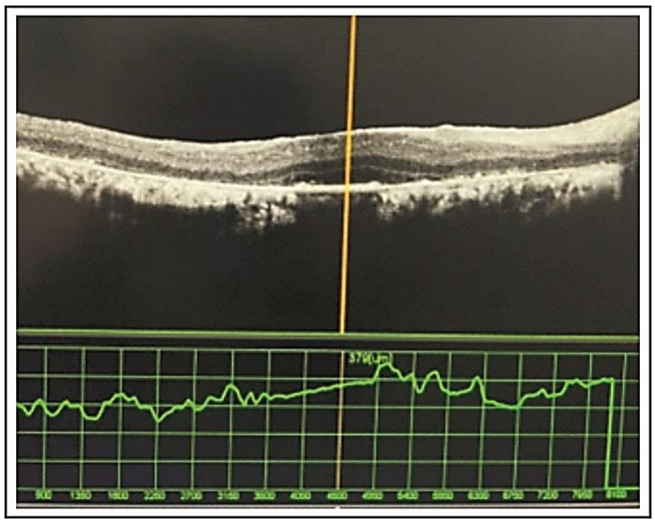

Figure 3: Central foveal thickness before PRP injection.

Umut Arslan et al. first conducted the trial of sub-tenon autologous platelet-rich plasma on retinitis pigmentosa patients, and they observed a significant improvement in visual functions and retinal structural findings on OCT.[14] They did not include RP patients who had other complications, such as cataracts, cystoid macular edema, and epiretinal membrane and could not explain the effect on resolving macular edema associated with RP disease.

Grover S. et al. conducted a clinical trial of topical dorzolamide, which was used three times a day for at least four weeks on 15 RP-associated macular edema patients. Thirteen patients showed a significant decrease in their foveal thickness in both eyes during four weeks, and five patients had improvement in one eye. Four patients who initially showed improvement showed worsening with continued treatment. However, this treatment showed a decrease in foveal thickness and foveal zone thickness, but with continued treatment, some patients had a rebound phenomenon, which required extra care or monitoring of the drug dosage while administering it.[15]

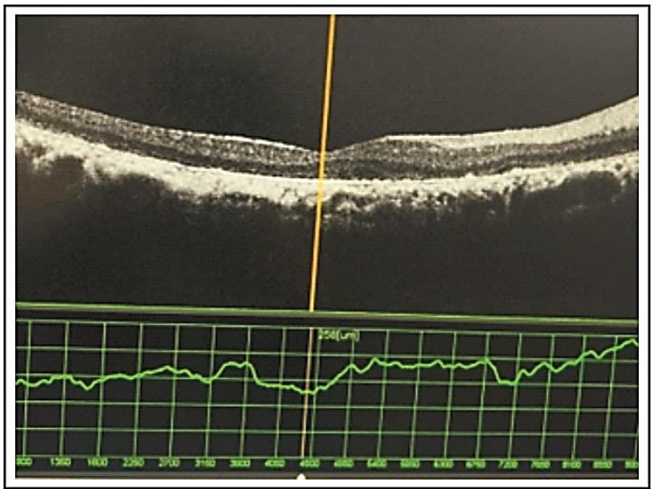

Figure 4: Same patient as in figure 3. Central foveal thickness after PRP injection.

Another study was done by Ozgur Artunay in which they used intravitreal ranibizumab injections for the treatment of chronic cystoid macular edema in RP patients. Thirty eyes of 30 patients were included who were treated with acetazolamide for 6 months. Among 30 patients, 15 were given 0.5 mg intravitreal Ranibizumab injections. Significant resolution of central foveal thickness was seen in the treated group after a single injection. The other 15 who had acetazolamide infusion showed no significant decrease in foveal thickness in 6 months. The mean central foveal thickness was 272 ± 65 µm after 6 months of injection, which was 478 ± 88 µm before the treatment. No side effects occurred during and after the treatment.[16]

In another study to compare the clinical outcome of oral acetazolamide and intravitreal dexamethasone implants in treating RP-associated cystoid macular edema, 2 groups with 30 eyes each were included.[17] One group was given intravitreal dexamethasone, and the other group was given oral acetazolamide. After 12 months, a significant decrease in central retinal thickness was observed in patients with intravitreal dexamethasone. Another study was done in which 11 children with RP underwent sub-tenon injection of triamcinolone for cystoid macular edema, refractory to local carbonic anhydrase inhibitor. One to eleven

injections were given, with an average of 3 in each patient. In 10 cases central retinal thickness was decreased with the improvement in BCVA in two eyes, and 12 eyes had no significant change in edema. Ocular hypertension occurred in two children; the rest of them did not have side effects after the treatment.[18]

In all the treatments described above, improvements in visual acuity were noticed partially in the patients. Some of the patients' edema was resolved, while some patients' edema remained stable. Most of the treatments were done with the other systemic approach. The rebound phenomenon or recurrence and worsening of edema occurred in the patients treated with topical dorzolamide. All the treatments were long-term and required additional dosages with multiple applications of topical treatment per day. In our study, patients who underwent PRP sessions had improvement in edema after the first injection, and a 6-month follow-up period showed no recurrence.

One of the limitations of our study was that only 7 patients underwent treatment. We need to include a larger sample size of patients with RP-CME to evaluate its effectiveness. There was a short follow-up of six months only. Lack of macular function tests to evaluate further macular stability after the treatment was another limitation.

CONCLUSION

Significant improvement in central foveal thickness was noticed on OCT scans after sub-tenon PRP injection. No ocular adverse events occurred. This treatment can be used for resolving macular edema or cystic spaces in RP patients. More data is required to confirm its efficacy on the resolution and stability of the cystic spaces or fluid accumulation in RP patients.

Funding: This study was not funded by any organization.

Patient's Consent: Researchers followed the guidelines set forth in the Declaration of Helsinki.

Conflict of Interest: Authors declared no conflict of interest.

Ethical Approval: The study was approved by the Institutional review board/Ethical review board **(ERB198/12/01-01-2026/AIMC/JHL)**.

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Muhammad Irfan Karamat; Medical Director: *Concepts, Design.*

Gul-e-Lala; Optometrist: *Literature Search, Data Acquisition, Data Analysis, Statistical Analysis.*

Zaigham Abbas; Professor: *Manuscript Review.*