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MANAGEMENT OF PROLIFERATIVE DIABETIC RETINOPATHY AND MACULAR EDEMA BY AN AYURVEDIC PROTOCOL - A CASE REPORT

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ABSTRACT

Proliferative Diabetic Retinopathy (PDR) is defined as the presence of newly formed blood vessels or fibrous tissue arising from the retina or optic disc and extending along their inner surfaces or into the vitreous cavity. Macular edema, which is defined as an area of retinal thickening at the region of the macula, is more prevalent in proliferative diabetic retinopathy than in non-proliferative diabetic retinopathy (NPDR). As modalities such as LASER photo-coagulation and injecting intravitreal anti-vascular endothelial growth factors (anti-VEGFs) may not always prove effective; an *Ayurvedic* approach may be explored. This condition may be compared to *Timira* according to *Ayur-veda.* The case of a 47-year-old male who presented with diminished vision in both eyes is presented here. His treatment plan consisted of oral medications such as *Kashaya* (decoction) and *Vati* (tablet), and external treatments for the eye and head. Results showed slight improvement in vision and significant improvement in fundus exami-nation and optical coherence tomography (OCT) scanning.

Keywords: *Anjanam*, Exudates, Case report, *Kriyakalpa, Pramehajanya Netra Roga, Timira*

INTRODUCTION

Diabetes Mellitus (DM) is a group of metabolic disor-ders that share the common phenotype of persistent hy-perglycemia over a prolonged period. It is classified into type 1 DM (insulin-dependent DM or IDDM), type 2 DM, (non-insulin-dependent DM or NIDDM), and gestational DM (GDM). An estimated 425 million peo-ple worldwide suffer from DM, with 90% of the cases made up of type 2 DM.

Complications of DM may be acute or chronic. Chronic complications result from micro-angiopathy, macro-vascular disease, and immune dysfunction. Microvas-cular complications affect all organs, especially the eye (retinopathy), kidneys (nephropathy), and nerves (neu-ropathy).

Diabetic Retinopathy (DR) is more common in type 1 diabetics than in type 2, with 10% of the population suffering from vision-threatening disease.[1] Risk fac-

tors include duration of diabetes, poor glycemic control, pregnancy, hypertension, hyperlipidemia, smoking, obesity, and anemia. The Early Treatment Diabetic Retinopathy Study (ETDRS) classifies DR into: [2]

- Non-proliferative DR (NPDR), which is characterized by micro-aneurysms, dot-and-blot hemorrhages, hard exudates, cotton-wool spots, venous changes, and intra-retinal microvascular anomalies (IRMA),
- Diabetic maculopathy or diabetic macular edema (DME), which affects the macula and is restricted to vision-threatening edema and ischemia,
- Proliferative DR (PDR), which is characterized by neovascularization, either at the optic disc (NVD) or elsewhere (NVE), and
- Advanced diabetic eye disease, which is characterized by tractional retinal detachment and neovascular glaucoma.

PDR is classified into mild-to-moderate and high-risk. Mild-to-moderate PDR is characterized by NVD and NVE that is insufficient to meet the high-risk criteria. High-risk PDR is characterized by NVD and NVE greater than the ETDRS standard and associated with pre-retinal or vitreous hemorrhage.

Diabetic macular edema (DME), the most common cause of visual impairment in diabetics, is divided into diffuse and focal edema. [3] Diffuse macular edema is characterized by extensive capillary leakage, and localized edema by focal leakage from microaneurysms. Cystoid macular edema results from further retinal thickening. Focal macular edema is characterized by a well-circumscribed area of thickening surrounded by rings of exudates. Clinically significant macular edema (CSME) is diagnosed based on 3 grades:

- Grade 1 is characterized by retinal thickening at or within 500μm of the fovea.
- Grade 2 is characterized by retinal thickening and exudates at or within 500μm of the fovea.
- Grade 3 is characterized by retinal thickening one-disc diameter or larger.

Diagnosis of PDR is made by fundus examination and OCT scanning. Management options involve LASER photocoagulation to treat maculopathy and anti-VEGF injections.

The notion of metabolic disorders such as *Meha* (diabetes) being a cause of eye disease was put forth by the *Netra Prakashika,* an ancient text of ophthalmic care according to *Ayurveda.* [4] PDR *per se* does not have a direct correlation in *Ayurveda.* But, its symptom of diminished vision may be considered along the lines of *Timira* (blurring of vision), which is a *Drishtigata Roga* (disease of vision). The involvement of *Rakta* (blood) may also be explored, keeping in mind the neovascular status of PDR.

According to *Susruta, Timira* is characterized by *Drishti Vibhrama* (improper vision), *Mithya Padartha Darsana (*visualization of nonexistent objects), and *Indriyartha Vibhrama* (improper visualization of existing objects).

Management of *Timira* involves repeated administration of *Sneha* (intake of fats), *Asra-visravana* (bloodletting), *Reka* (therapeutic purgation), *Nasya* (nasal medication), *Anjana* (collyrium), *Murdha-basti* (retention of oil over the head), *Basti Kriya* (enema), *Tarpana* (retention of ghee in the eye), *Lepa* (application of pastes), and *Seka* (irrigation of the eye). [5]

Case Report

A 54-year-old diabetic and hypertensive male presented to the OPD of Sreedhareeyam Ayurvedic Eye Hospital and Research Center, Koothattukulam, Kerala, with a complaint of bilateral blurring of vision that was more in his right eye since 2014 associated with floaters and occasional flashes of light since 1 year.

The patient was apparently well before 2014. He developed blurring of vision with vertical distortion of the image in 2014, which prompted him to seek ophthalmic consultation. He was diagnosed with proliferative diabetic retinopathy and was advised intra-vitreal injections. He underwent 4 rounds of injection of Avastin (Accentrix and Ozurdex) in both eyes but got minimal relief. He consulted Sreedhareeyam Hospital in December 2017 for alternative options.

The patient has diabetes and hypertension for 18 years and renal problems for 1 year, for which he is currently under medication. The patient underwent cataract surgery in 2009 and 2013. He also underwent one round of LASER therapy.

The patient's bowel, appetite, and micturition are normal, and his sleep is sound. He is neither addicted to alcohol nor tobacco. His vital signs and general systemic examination are normal.

Table 1: Visual and External Ocular Examination at Admission

Parameters		**Right Eye (OD)**	**Left Eye (OS)**
Unaided Distant Visual Acuity		1/60 Snellen (LogMAR 1.778)	6/60 Snellen (LogMAR 1)
Aided Distant Visual Acuity		1/60 Snellen (LogMAR 1.778)	6/60 Snellen (LogMAR 1)
Near Visual Acuity		N36	N18
Cornea		Clear	Clear
Sclera		Normal	Normal
Iris		No rubeosis iridis	No rubeosis iridis
Pupil		Within normal limits	Within normal limits
Lens		Pseudophakia (posterior segment intra-ocular lens)	Pseudophakia (posterior segment intra-ocular lens)
Fundus	Media	Clear	Clear
	Optic Disc	Within normal limits	Within normal limits
	Background	Pale areas, edema, neovascularization **(Figure 1a)**	Hard exudates **(Figure 1b)**

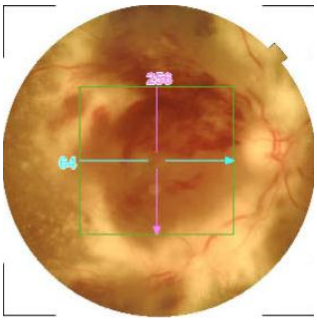

Figure 1a: Fundus examination OD at Admission

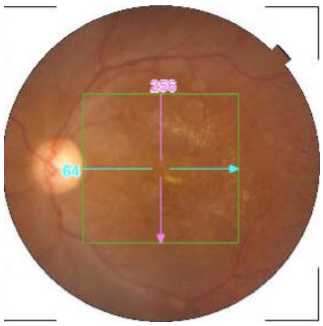

Figure 1b: Fundus examination OS at Admission

Ancillary Diagnostics

OCT scanning showed a dome-shaped elevation at the macula with a hyporeflective area within the dome OD **(Figure 1c)** and multiple, small cyst-like lesions within the macular region OS **(Figure 1d)**.

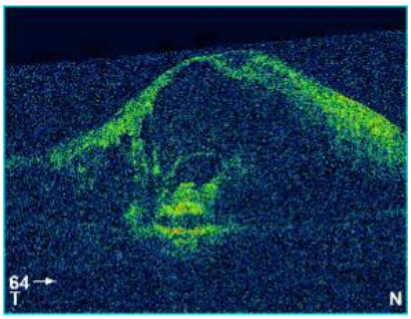

Figure 1c: OCT scanning OD at Admission

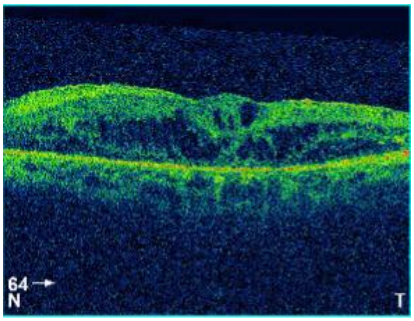

Figure 1d: OCT scanning OS at Admission

Diagnosis

The patient was diagnosed with proliferative diabetic retinopathy with macular edema. The condition *Timira* was explored based on the patient's symptoms, along with *Dushita Rakta Dhatu* (pathological blood). The *Samprapti Ghataka* (factors for pathogenesis) was determined as follows:

Dosha: *Pitta, Kapha;* ***Dushya:*** *Rasa, Rakta;* ***Agni:*** *Mandagni;* ***Rogamarga:*** *Madhyama;* ***Srotas:*** *Rasavaha, Raktavaha;* ***Srotodushti:*** *Atipravrtti, Sanga*

Therapeutic intervention

Table 2: Oral Medicines

Medicine	Dose	*Anupana*	Time	Duration
*Samirapancakam Kashaya**	60mL	Lukewarm water	6 am and 6 pm	16/12/2017 - 31/12/2017
Candraprabha Vati	1 tablet			
Vara Churna	10g	Lukewarm water	Bedtime	
*Pathya Punarnavadi Churna**				
Amrtadi Kashaya	60mL	Lukewarm water	6 am and 6 pm	
Drakshadi Kashaya				
*Vasti Rasayana**	1 tablet	Lukewarm water	Twice a day after food	

Table 3: External Therapies

Treatment	Medicine	Procedure	Duration
Netradhara	*Mrdvikadi Kashaya**	Patient lay supine and the medicine was poured in a thin stream over the eyes. The patient was asked to blink during the procedure.	16/12/2017 - 31/12/2017
Anjana	Eye Plus Drops*	One drop of the medicine was poured into the inner canthus. The patient was asked to slowly move the eyeballs with closed lids.	
Ascyotana	Drops prepared from *Sahadevi*		26/12/2017 - 31/12/2017
Siroveshtana	*Vasalakshadi Churna* and *Vasaguducyadi Kashaya*	30g of *Churna* was mixed with 60mL of *Kashaya* to prepare a paste. This was placed on a Cora cloth and tied around the patient's head.	16/12/2017 - 31/12/2017
Purampada	*Mukkadi Purampada* and *Karutta Gutika*	A paste prepared from the ingredients was applied over the eyelids, obviating the lashes.	18/12/2017 - 31/12/2017

Outcome Measures and Results

The patient was assessed for visual acuity, fundus examination, and OCT findings. Both unaided and aided DVA was 1/60 OD and 6/60 OS at discharge. Fundus examination showed reduction in hemorrhages and neovascularization OD and reduction in exudates OS. OCT scanning showed absorption of edema OD and reduction in cyst-like lesions OS.

He was discharged on 31st December 2017 with medicines **(Table 4)** and was advised to report for regular follow-ups.

He reported for 2 subsequent follow-ups. VA was maintained at the first follow-up and showed improvement at the 2nd follow-up **(Table 5)**. Fundus examination and OCT scanning were done at the 2nd follow-up, and those results are shown in **Table 6.**

Table 4: Discharge Medicines

Medicine	Dosage	*Anupana*	Time
Laksha Churna, *Yashti Churna*, and *Haritaki Churna*	5g each is mixed with castor oil into a paste and applied over the forehead and temporal region	-	1 hr daily
Guggulu Tiktakam Kashaya	15mL	Lukewarm water (45mL)	Twice a day before food
Triphala Guggulu	1 powdered tab with *Kashaya*		

Vasti Rasayana Tablet*	1 tab	Lukewarm water	Twice a day after food
Pathya Shadangam Tablet	1 tab		Twice a day after food
*Netramrtam**	1 drop in both eyes	-	Twice a day
Aloe syrup	30 ml	-	Morning

**Patented medicines of Sreedhareeyam Ayurvedic Eye Hospital and Research Center*

Ingredients of all medicines were procured at Sreedhareeyam's own herbal gardens. The medicines were manufactured at Sreedhareeyam Ayurvedic Medicines, Pvt. Ltd., the hospital's GMP-certified drug manufacturing unit.

Table 5: Visual Acuity at 2 Subsequent Follow-Ups

Parameters		**23/03/2018**		**26/05/2018**	
		OD	**OS**	**OD**	**OS**
Unaided Distant Visual Acuity	**Snellen**	1/60	6/60	2/60	6/60
	LogMAR	1.778	1	1.477	1
Aided Distant Visual Acuity	**Snellen**	1/60	6/60	2/60	6/60
	LogMAR	1.778	1	1.477	1
Near Visual Acuity		N18	N18	N18	N18

Table 6: Fundus Examination and OCT Scanning at the 2nd Follow-Up

Parameter	**26/05/2018**	
	OD	**OS**
Media	Clear	Clear
Optic Disc	Within Normal Limits	Within Normal Limits
Background	Complete resolution of pale areas, hemorrhages, and neovascularization **(Figure 2a)**	Complete reduction of exudates **(Figure 2b)**
OCT Scanning	Resolution of edema **(Figure 2c)**	Resolution of cyst-like lesions **(Figure 2d)**

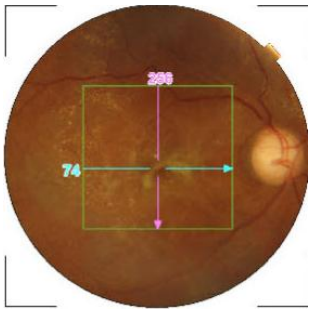

Figure 2a: Fundus examination OD at the 2nd follow-up

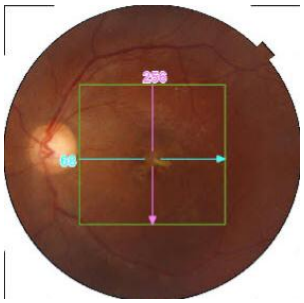

Figure 2b: Fundus examination OS at the 2nd follow-up

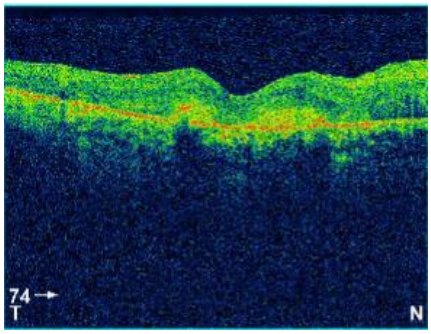

Figure 2c: OCT scanning OD at the Second Follow-up

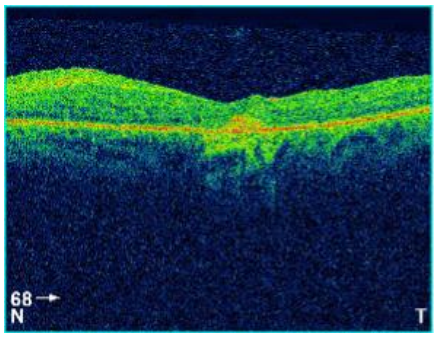

Figure 2d: OCT scanning OS at the Second Follow-up

DISCUSSION

Neovascularization, the hallmark feature of PDR, is caused by capillary non-perfusion to an estimated 1/4 of the retina leading to hypoxia. The predilection of NVD is thought to be caused by the absence of the internal limiting membrane at the optic nerve head. New blood vessels originate as endothelial proliferations from the retinal veins. These pass through ILM defects to lie in the potential plane between the posterior vitreous cortex and the retina. [5]

Timira occurs when the *Doshas* invade the 3rd *Patala* (layer) of the eye according to *Susruta*, and the 2nd *Patala* according to *Vagbhata*. Symptoms observed include false perception of flies, mosquitoes, gnats, flags, rings, and hairs; seeing small objects as large and vice versa; seeing distant objects as near and vice versa; and blurring of the visual field based on the position of the *Doshas* in the *Drishti*.[6] *Timira* if not treated on time, progresses to *Kacha* (diminished vision) and *Linganasa* (loss of vision). [7]

Meha is included among the eight grave conditions according to *Ayurveda* (*Ashta Mahagada*), *viz.*, *Vatavyadhi* (neurological diseases), *Asmari* (renal calculus), *Kushta* (skin disorders), *Meha* (metabolic disorders including diabetes), *Udara* (enlargement of the abdomen), *Bhagandara* (fistula-in-ano), *Arsas* (hemorrhoids), and *Grahani* (irritable bowel disease).

An appraisal of the *Samprapti* (pathogenesis) of DR reveals that *Srotobhishyanda* (pathological oozing of fluid from *Srotas*) and *Raktavaha Sroto Dushti* (pathological activity of the *Raktavaha Srotas*) are prime factors in the pathogenesis of the disease. *Acakshushya Ahara* and *Vihara* (diets and activities that are non-conducive to eye health) aggravate the *Doshas*, with *Pitta Dosha* being dominant. *Pitta* aggravates *Rakta* as the two share *Asraya-Asrayi Bhava* (homologous connection) with each other. These two traverses the *Urdhvavaha Sira* (vessels of the upper extremity) and lodge in *Netra.* [8]

The pathogenic factors of DR are due to the *Kleda* (moisture) and *Kapha* in *Prameha*, which cause *Srotorodha* (obstruction of the channels) in the retinal vasculature. This *Srotorodha* results in *Atipravrtti* (increased flow) of already-increased *Doshas*, which may be compared to neovascularization. Macular edema is due to *Sanga* (obstruction) of the *Srotas* in that serum is leaked into the retina as a result of vascular pathology.

The oral medicines treat *Prameha* and help to correct the pathological changes internally. *Candraprabha Vati* is indicated in all types of *Prameha*, and because of its cooling nature, checks *Pitta* and is good for the eyes. *Vara Churna* corrects both *Prameha* and the retinopathy by directly acting on the *Tridoshas*. *Drakshadi Kashaya* is indicated in *Urdhvaga Raktapitta*, and its direct action on *Vata* and *Pitta* makes it useful in the management of neovascularization and hemorrhages.

Netra Dhara and *Purampada* make direct contact with the lids and help to correct the ocular pathology by stimulating the peripheral nerve endings and enabling faster mobilization and expulsion of obstructive toxins. The medicines used for both conditions relieve *Vata* and *Pitta*, relieve *Sotha*, and purify *Rakta Dhatu*. *Ascyotana* and *Anjana* enable absorption of the medicine by

such parameters as height and temperature. The medicines employed for *Ascyotana* and *Anjana* are *Drishtiprasadana* (promoting eyesight) and *Kapha-Pitta Samaka* (pacify *Kapha* and *Pitta).*

Siroveshtana, a unique treatment practiced in *Sreedhareeyam* Hospital, is the application of paste over the head using a Cora cloth. It has the affinity to reach the target tissues by absorption through the hair follicles and its property of bypassing the barriers of the head and eye.

Samirapancakam Kashaya is prepared from *Musta, Triphala,* and *Yava* and is indicated in diabetic retinopathy and other *Raktaja* disorders of the eye. *Pathya Punarnavadi Kvatha,* with its *Sothahara* (relieves edema) and *Kapha-Pitta Samaka* (relieves *Kapha* and *Pitta*) properties, relieves hemorrhage and absorbs edema from the macula. *Vasti Rasayana* has *Gokshura* and *Abhraka Bhasma* as its main ingredients and is indicated in all urinary tract disorders, especially those related to the kidneys. *Gokshura* is a potent diuretic, and it helps to relieve *Vata* and *Pitta*. *Netramrtam* is prepared from *Sphatika, Saindhava Lavana,* and distilled water, and is indicated in all eye disorders, especially *Pitta*-related eye disorders. It also acts as a good *Rakta Prasadana* (purifying blood) in case of *Netra*. The ingredients of Eye Plus eye drops are *Ropana* (healing) *Pitta-Kaphahara* (relieving *Pitta* and *Kapha*), and *Sothahara* (relieving edema).

CONCLUSION

Maintenance of vision was the biggest challenge in this case. Although the condition improved after 2 follow-ups to an extent where the macula almost returned to normal, VA was maintained in the left eye, while it improved in the right eye. The results of this study may be validated using large-scale sample trials.

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