

Ayurvedic Management of a Case of Central Retinal Vein Occlusion

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ABSTRACT

Central Retinal Vein Occlusion (CRVO) is classified based on aetiology into ischaemic and non-ischaemic varieties. Treatment modalities of CRVO include intra-vitreous anti-Vascular Endothelial Growth Factor (anti-VEGF) injections, pan-retinal LASER photocoagulation, and pars plana vitrectomy. The case of a 31-year-old female with a two-month history of blurring and fogging of vision in her left eye (OS) and who was diagnosed previously with CRVO is presented here. Analysis of her symptoms using *Ayurvedic* diagnostics showed that she suffered from *Timiraor* blurring of vision. She underwent inpatient treatment in October 2014 and January 2015. Oral medicines such as *Kashaya* (decoctions), tablets, and *Sattva* (starch extract) were administered. External treatment included *Panchakarma* therapy and local therapies for the head and eye (*Kriyakalpa*). The Assessment was done using Distant Visual Acuity (DVA), posterior segment examination, and Optical Coherence Tomography (OCT), which showed improvement both at discharge and 2 subsequent follow-ups. This case illustrates that prompt and timely consultation and management brought about significant improvement in both her vision and well-being.

Keywords: Ayurveda medicine, *Kriyakalpa*, *Timira*

CASE REPORT

A 31-year-old female with a history of blurring of vision in her left eye since August 2014. The patient was apparently well before August 2014. Her symptoms started suddenly, prompting her to seek an ophthalmic consultation. She was diagnosed with CRVO with severe macular oedema. She underwent one intravitreal injection, which gave slight relief. She consulted Sreedhareeyam Hospital in October 2014 and was advised on Inpatient (IP) management. She was neither diabetic nor hypertensive, and she does not present with dyslipidemia. Her personal history was normal. Her immediate family members do not report similar complaints.

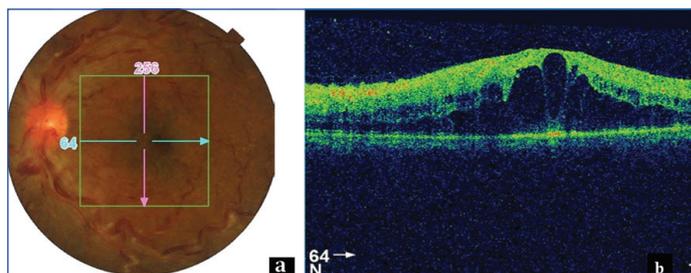
Distant Visual Acuity (DVA) was 6/6 in her right eye (OD) and 6/36 in her left eye (OS). Anterior segment examination was normal in both eyes.

Posterior segment exam OS showed haemorrhages, cotton-wool spots, tortuous blood vessels, and a dull foveal reflex indicating macular oedema [Table/Fig-1a]. OCT OS along the naso-temporal plane showed an elevation at the macular region with a hyporeflective area within the elevation [Table/Fig-1b].

The patient was provisionally diagnosed with CRVO and macular oedema based on history and investigations. The disease *Timira* (blurring of vision), a *DrshtigataRoga* (disease of vision) according to *Ayurveda*, was explored based on the symptom of blurred vision. She underwent 2 courses of inpatient treatment. The first course was for 25 days (October 4th, 2014 to October 28th, 2014), and the second course was for 14 days (January 15th, 2015 to January 28th, 2015).

Oral medicines included *Guducyadi Kashaya*, *Sudarsanam* Tablet, *Amrtottaram Kashaya*, *Guduci Sattva*, and *Triphala Guggulu*, *Punamavadi Kashaya*, *Dasamula Katutrayam Kashaya*, and a *Kashaya* prepared from *Kantakari*, *Tulasi*, and *Vasa* [Table/Fig-2] were administered over the course of the treatments.

External treatments comprised of *Kriyakalpa* (local ocular therapy), *Panchakarma* (purification), and therapies for the head. *Virechana*



[Table/Fig-1]: a) Fundus photograph OS showing haemorrhages, tortuous blood vessels, cotton-wool spots, and dull foveal reflex; b) OCT scan OS showing marked elevation at the macular region with a hyporeflective area within the elevation.

(therapeutic purgation), *Pratimarsa Nasya* (nasal medication), *Tala* (paste on a cotton gauze over the head), *Talapoticchil* (medicine on a plantain leaf over the head), *Anjana* (collyrium), *Purampada* (paste over the eyelids), *Lepa* (paste) over the forehead, and *Pindi* (poultice over the eyes) were administered during the first course of treatment. *Pratimarsa Nasya*, *Tala*, *Talapoticchil*, *Sirolepa* (paste over the head), *Takradhara* (irrigation of buttermilk over the head), *Seka* (irrigation), *Anjana*, and *NetraPicu* (cotton gauze with medicine over the closed eyes) were administered during the second course of treatment [Table/Fig-3].

All medicines prescribed were procured at Sreedhareeyam's own medicinal gardens and were manufactured at Sreedhareeyam Ayurvedic Medicines, Pvt. Ltd., the hospital's GMP-certified manufacturing unit.

DVA assessed on 28th October 2014 (25th day of the first course) was 6/6 OD and 6/18 OS. The same reading was reported on January 28th, 2015 (14th day of the second course).

The patient was administered *Guducyadi Kashaya* (15 mL with 45 mL boiled and cooled water before food), *Saptamrta Lauha* (1 tablet twice a day after food) [6], *Pathya Punamava Curna** (1 tablespoon of powder twice a day before food), *Candraprabha Vati* (1 tablet twice a day after food) [7], *Triphala Guggulu* (1 tablet twice a day after food), and *Netramrtam** (1 drop in both eyes twice a day) at discharge and was advised regular follow-ups.

Medicine	Preparation	Dosage	Duration
<i>Guducyadi Kashaya</i> (decoction of <i>Tinosporacordifolia</i> Miers., etc..) [1]	1 part of the ingredients are boiled in 4 parts of water and reduced to 1/4.	15 mL with 45 mL boiled and cooled water	04/10/2014-28/10/2014
<i>Sudarsanam</i> Tablet (tablet prepared from the powder of <i>Berberisaristata</i> DC., etc..)	The powder is prepared by mixing 1 part of each ingredient. This is then made into a tablet.	1 tablet twice a day after food	04/10/2014-28/10/2014
<i>BhunimbadiKashaya</i> (decoction of <i>Andrographispaniculata</i> (Burm f.) Wall. [2])	1 part of the ingredients are boiled in 4 parts of water and reduced to 1/4.	15 mL with 45 mL boiled and cooled water	04/10/2014-28/10/2014
<i>Amrtottaram Kashaya</i> (decoction of <i>Zingiberofficinale</i> Rosc., etc..) [3]	2 parts of <i>Zingiberofficinale</i> Rosc., 6 parts of <i>Tinosporacordifolia</i> Miers., and 4 parts of <i>Terminaliachebula</i> Retz. are added to 4 parts of water and reduced to 1/4.	60 mL twice a day before food	04/10/2014-28/10/2014
		10 mL with 30 mL boiled and cooled water at 6 am and 6 pm (with <i>PunarnavadiKashaya</i>)	15/01/2015-29/01/2015
<i>GuduciSattva</i> (starch extract of <i>Tinosporacordifolia</i> Miers.)	Starch extract is prepared by soaking stems in water overnight and draining them.	1 tablespoon at bedtime	04/10/2014-28/10/2014
<i>Triphala Guggulu</i> (tablets prepared from <i>Commiphoramuku</i> Linn., etc..) [4]	48 g of all ingredients taken separately are powdered and added to 240 g of purified extract of <i>Commiphoramuku</i> Linn. This is made into a paste and rolled into pills.	3 g twice a day after food	04/10/2014-28/10/2014
<i>Punarnavadi Kashaya</i> (decoction prepared from <i>Boerhaaviadiffusa</i> Linn., etc..) [5]	1 part of the ingredients are boiled in 4 parts of water and reduced to 1/4.	10 mL with 30 mL boiled and cooled water at 6 am and 6 pm (with <i>AmrtottaramKashaya</i>)	15/01/2015-29/01/2015
<i>DasamulaKatutrayaKashaya</i> (decoction of <i>Aeglemarmelos</i> Corr., etc..)	1 part of the ingredients are boiled in 4 parts of water and reduced to 1/4.	15 mL with 45 mL boiled and cooled water at 6 am and 6 pm	15/01/2015-29/01/2015
Decoction prepared from <i>Solanumxanthocarpum</i> Lam., <i>Ocimum sanctum</i> Linn., and <i>Adathodavasica</i> Nees.	1 part of the ingredients are boiled in 4 parts of water and reduced to 1/4.	15 mL with 45 mL boiled and cooled water at 6 am and 6 pm	15/01/2015-29/01/2015

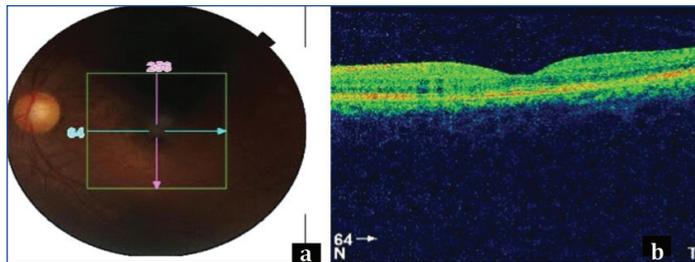
[Table/Fig-2]: Internal medicines.

Treatment	Medicine	Method of administration	Duration
<i>Seka</i>	<i>Kasyapam Kashaya*</i> (decoction prepared from <i>Terminaliachebula</i> Retz., etc..)	50 mL of the decoction was poured over the closed eyes in a thin streak.	• 15/01/2015 to 23/01/2015
<i>Anjana</i>	<i>Darsana</i> Drops* (sterile drops prepared from <i>Vitexnegundo</i> Linn., etc..)	1 drop of the medicine was instilled from a height of 2 Angula () in both eyes. The patient was asked to gently rotate the eyes while keeping them closed.	• 05/10/2014 to 06/10/2014
	<i>Nalikeranjana</i> (drops prepared from <i>Berberisaristata</i> D.C., etc..)		• 15/01/2015 to 22/01/2015
	<i>Candanadi Anjana</i> (drops prepared from <i>Santalumalbum</i> Linn., etc..)		
	<i>Netramrtam*</i> (sterile drops prepared from NaCl, etc..)		
<i>Tala</i>	<i>Kaccuradi Curma</i> (powder prepared from) and <i>Nimbamrtadi Eranda Taila</i> (castor oil processed with <i>Azadirachta indica</i> A. Juss, etc..)	A paste prepared from 60 g of the powder and 300 mL of decoction was put on cotton gauze and placed over the bregma.	• 06/10/2014, • 20/10/2014 to 27/10/2014 • 15/01/2015 to 16/01/2015
<i>Netra Picu</i>	<i>Vinayakanjana*</i> (semisolid prepared from <i>Cynodondactylon</i> Linn., etc..)	A piece of cotton was dipped in 15 mL of the medicine and applied to the closed eyes.	• 22/01/2015 to 29/01/2015
<i>Pratimarsa Nasya</i>	<i>Anutaila</i> (oil prepared from <i>Holostemmaadakodien</i> Schult., etc..)	2 drops of oil were instilled into each nostril.	• 6/10/2014, • 20/10/2014, • 22/10/2014 to 27/10/2014 • 16/01/2015 to 21/01/2015
<i>Purampada</i>	<i>MukkadiPurampada</i> (paste prepared from <i>Terminaliachebula</i> Retz., etc..)	A paste prepared from 9 tablets of the medicine was applied over the eyelid, obviating the lashes.	• 07/10/2014
<i>Talapoticchil</i>	<i>Adathodavasica</i> Nees., <i>Glychrrhyzaglabra</i> Linn., <i>Cyperusrotundus</i> Linn., <i>Asparagus racemosus</i> Linn., and <i>Emblicaofficinalis</i> Gaertn mixed with <i>VasaguducyadiKashaya</i> (decoction of <i>Adathodavasica</i> Nees., etc..)	A paste prepared by mixing 60 g of the powder and 300 mL of the decoction was applied on a plantain leaf, which was kept face down over the head, obviating a small circular hole in the center.	• 07/10/2014 to 11/10/2014, • 15/10/2014 to 17/10/2014
	<i>Emblicaofficinalis</i> Gaertn, <i>Adathodavasica</i> Nees., <i>Glychrrhyzaglabra</i> Linn., <i>Boerhaaviadiffusa</i> Linn., and <i>Terminaliachebula</i> Retz. mixed with <i>Vasa Triphaladi Kashaya</i> (decoction of <i>Adathodavasica</i> Nees., etc..)		• 16/01/2015 to 22/01/2015
<i>Lepa</i>	<i>Emblicaofficinalis</i> Gaertn and <i>Takra</i> (buttermilk)	A paste prepared with 60 g of the drug and 300 mL of buttermilk was applied over the forehead.	• 07/10/2014 to 11/10/2014, • 15/10/2014 to 27/10/2014
<i>Sirolepa</i>	<i>Glychrrhyzaglabra</i> Linn., <i>Symplocosracemosus</i> Roxb., <i>Adathodavasica</i> Nees., and <i>Cyperusrotundus</i> Linn.	60 g of the powdered ingredients are made into a paste with water and applied to the forehead.	• 27/01/2015 to 29/01/2015
<i>Takradhara</i>	<i>Vasaguducyadi Kashaya</i> (decoction of <i>Adathodavasica</i> Nees., etc..) and <i>Emblicaofficinalis</i> Gaertn. (for preparing the buttermilk) and decoction of <i>Emblicaofficinalis</i> Gaertn.	2 L of buttermilk was prepared from the 300 mL of the decoction and 60 g of the powder and was poured in a thin stream over the head. Afterwards, 1.5 L of the decoction of <i>Emblicaofficinalis</i> Gaertn. was poured over the head.	• 23/01/2015
<i>Pindi</i>	<i>Biophytumsensitivum</i>	10 g of the drug was made into a paste with <i>SukhoshnaJala</i> (lukewarm water) and placed on 2 pieces of Cora cloth. 2 pieces of cotton were kept over these and the cloth was folded inwards and kept over the closed eyes.	• 08/10/2014 to 13/10/2014, • 15/10/2014 to 27/10/2014
<i>Virechana</i>	<i>Avipattikara</i> Yoga (powder prepared from <i>Zingiberofficinale</i> Rosc., etc..)	6 g of the powder was given with warm water in the morning.	• 19/10/2014, 21/10/2014, • 23/10/2014, 25/10/2014, • 27/10/2014

[Table/Fig-3]: External therapies.

*Patented medicines of Sreedhareeyam Ayurvedic Eye Hospital and Research Center

The patient reported for two subsequent follow-ups. At the first follow-up, which was on August 25th, 2016, DVA was 6/6 in both eyes (OU). The same VA was reported at the second follow-up, on January 1st, 2018. Posterior segment examination OS showed resolution of haemorrhages and cotton-wool spots, reduction in tortuosity of blood vessels, and a newly-established foveal reflex [Table/Fig-4a]. OCT showed absorption of the subretinal fluid [Table/Fig-4b].



[Table/Fig-4]: a) Fundus photograph OS showing reduction of tortuous blood vessels, resolution of haemorrhages and cotton-wool spots, and established foveal reflex; b) OCT scan OS showing absorbed subretinal fluid, resulting in a normal appearance of the macula.

A timeline of events of the complete course of treatment is provided [Table/Fig-5].

DISCUSSION

Vascular occlusions of the retina involve both central and branch arteries and veins. CRVO, enlisted as number 362.35 in the International Classification of Diseases, is the second most common retinal vascular pathology after diabetic retinopathy [8]. It is divided into ischaemic and non-ischaemic varieties. Its aetiology includes pressure on the vein by an atherosclerotic retinal artery, hypertension, diabetes mellitus, raised IOP, and local causes such as orbital tumours. The most common cause of defective or loss of vision in CRVO is macular oedema [9].

Its pathogenesis is believed to follow Virchow's triad of thrombosis, which involves stasis, vascular damage, and hyper-coagulation [10]. Occlusion is believed to be caused by a thrombus at or posterior to the lamina cribrosa. Another view is that arteriosclerosis of the central retinal artery causing turbulent venous flow and endothelial damage also plays a role. Another theory states that thrombosis is an end-stage phenomenon induced by a variety of primary factors such as inflammatory optic nerve or orbital problems, structural anomalies in the lamina cribrosa, and haemodynamic changes. [11] Haematological factors such as elevated erythrocyte sedimentation rate and increased haematocrit, homocysteine, fibrinogen, and blood viscosity levels may be associated with retinal venous occlusion, but their exact role in the pathogenesis of CRVO and whether they themselves can initiate venous occlusion remains obscure.

Timira, a condition that encompasses a range of symptoms starting from *Avyakta Rupa* (indistinct vision) to *Andhya* (blindness), occurs when the pathological *Doshas* (humours) lodge into the *Abhyantara Patalas* (interior layers) of the eye. It warrants immediate and comprehensive management as *Timiracan* progress to *Kaca* (diminished vision) and finally to *Linganasa* (complete blindness) if left untreated [12].

Involvement of *RaktaDhatu* (blood) was explored as CRVO involves the blood vessels of the retina. *Acakshushya Ahara* and *Vihara* (diet and lifestyle that are detrimental to eye health) caused *Pitta* (bile) and *Kapha* (phlegm) *Doshas* (humors) to increase. This factor, along with the *Asraya-AsrayiBhava* (homologous relationship) between *Pitta* and *Rakta*, caused *Rakta* to pathologically increase and lodge in the eye.

In this patient, *Mandagni* (impaired gastric fire) and the resultant increase of the *Doshas* (humors) resulted in compromised delivery of vital nutrients to the eye due to *Sanga* (obstruction) and *Vimarga Gamana* (diversion of flow to improper places) of the *Raktavaha Srotas* (channels transporting blood).

Time	Event
08/2014	<ul style="list-style-type: none"> Experiences a sudden onset of blurring of vision Seeks ophthalmic consultation and is diagnosed with central retinal vein occlusion and severe macular oedema Undergoes one intravitreal injection, which gives slight relief
03/10/2014	<ul style="list-style-type: none"> Consults at Sreedhareeyam Hospital and is advised IP management DVA: 6/6 OD and 6/36 OS Fundus examination OS: cotton-wool spots, tortuous blood vessels, and a dull foveal reflex OCT scanning OS: elevation at the macula with a hyporeflective area within the elevation
First course of treatment (04/10/2014 - 28/10/2014)	
04/10/2014	<ul style="list-style-type: none"> Oral medicines (<i>GuducyadiKashaya</i>, <i>SudarsanamTablet</i>, <i>BhunimbadiKashaya</i>, <i>AmrtottaramKashaya</i>, <i>GuduciSattva</i>, and <i>TriphalaGuggulu</i>) are started
05/10/2014	<ul style="list-style-type: none"> <i>Anjana</i> with <i>DarsanaDrops*</i> and <i>Nalikeranjana</i> is started
06/10/2014	<ul style="list-style-type: none"> <i>Anjana</i> is stopped <i>Tala</i> with <i>KaccuradiChurna</i> and <i>NimbamrtadiErandaTaila</i> is done <i>PratimarsaNasya</i> with <i>Anutailais</i> done
07/10/2014	<ul style="list-style-type: none"> <i>Talapoticchil</i> with <i>Vasa</i>, <i>Yashtimadhu</i>, <i>Musta</i>, <i>Satavari</i>, and <i>Amalaki</i> mixed with <i>VasaguducyadiKashaya</i> is started <i>Lepa</i> with <i>Amalaki</i> and <i>Takrais</i> started <i>Purampada</i> with <i>MukkadiPurampadais</i> done
08/10/2014	<ul style="list-style-type: none"> <i>Pindi</i> with <i>Biophytumsensitivum</i> is started
11/10/2014	<ul style="list-style-type: none"> <i>Talapoticchil</i> and <i>Lepa</i> are stopped
13/10/2014	<ul style="list-style-type: none"> <i>Pindi</i> is stopped
15/10/2014	<ul style="list-style-type: none"> <i>Lepa</i>, <i>Talapoticchil</i>, and <i>Pindi</i> are restarted
17/10/2014	<ul style="list-style-type: none"> <i>Talapoticchil</i> is stopped
19/10/2014	<ul style="list-style-type: none"> <i>Virechana</i> with <i>Avipattikara</i> Yoga is done
20/10/2014	<ul style="list-style-type: none"> <i>Tala</i> and <i>PratimarsaNasya</i> are restarted
21/10/2014	
23/05/2014	<ul style="list-style-type: none"> <i>Virechana</i> is done
25/05/2014	
27/10/2014	<ul style="list-style-type: none"> <i>Virechana</i>, <i>Pratimarsa Nasya</i>, <i>Tala</i>, <i>Lepa</i>, and <i>Pindi</i> are stopped
28/10/2019	<ul style="list-style-type: none"> Oral medicines are stopped Patient is discharged. DVA: 6/6 OD and 6/18 OS
Second course of treatment (15/01/2015 - 29/01/2015)	
15/01/2015	<ul style="list-style-type: none"> Oral medicines (<i>Amrtottaram Kashaya</i>, <i>Punamavadi Kashaya</i>, <i>Dasamula Katutraya Kashaya</i>, and a decoction of <i>Kantakari</i>, <i>Tulasi</i>, and <i>Vasa</i>) are started <i>Seka</i> with <i>Kasyapam Kashaya*</i> is started <i>Anjana</i> with <i>Candanadi Anjana</i> and <i>Netramrtam*</i> is started <i>Tala</i> with <i>Kaccuradi Churna</i> and <i>Nimbamrtadi ErandaTaila</i> is started
16/01/2015	<ul style="list-style-type: none"> <i>Tala</i> is stopped <i>Pratimarsa Nasya</i> with <i>Anutaila</i> is started <i>Talapoticchil</i> with <i>Amalaki</i>, <i>Vasa</i>, <i>Yashtimadhu</i>, <i>Punarnava</i>, and <i>Haritaki</i> mixed with <i>Vasa Triphaladi Kashayais</i> started
21/01/2015	<ul style="list-style-type: none"> <i>PratimarsaNasyais</i> stopped
22/01/2015	<ul style="list-style-type: none"> <i>Anjanais</i> stopped <i>Talapoticchilis</i> stopped <i>NetraPicu</i> with <i>Vinayakanjana*</i> is started
23/01/2015	<ul style="list-style-type: none"> <i>Sekais</i> stopped <i>Takradhara</i> with <i>VasaguducyadiKashaya</i> and <i>Amalaki</i> is done
27/01/2015	<ul style="list-style-type: none"> <i>Sirolepawith Yashtimadhu</i>, <i>Lodhra</i>, <i>Vasa</i>, and <i>Mustais</i> started
29/01/2015	<ul style="list-style-type: none"> <i>Sirolepais</i> stopped <i>NetraPicuis</i> stopped Oral medicines are stopped DVA: 6/6 OD and 6/18 OS
25/08/2016	<ul style="list-style-type: none"> DVA: 6/6 OU
01/01/2018	<ul style="list-style-type: none"> DVA: 6/6 OU Fundus examination OS: reduction in cotton-wool spots and tortuous blood vessels, and re-establishment of the foveal reflex OCT scanning OS: absorption of subretinal fluid

[Table/Fig-5]: Timeline of complete course of treatment.

*Patented medicines of Sreedhareeyam Ayurvedic Eye Hospital and Research Center

Oedema and tortuous blood vessels were a direct result of *Sanga* and *Vimarga Gamana*, in which the retinal blood vessels became pathologically affected and leak serum into the retina. Cotton-wool

spots are caused by *Sanga* in the fact that the inadequate supply of nutrients caused by obstruction results in hypoxia, which leads to infarction of the tissue.

The first line of management was to enhance the *Jatharagni* (gastric fire) by *AmaPacana* (digestion of toxic products) using internal medicines. This helped to clear up the obstruction in the Srotas and allow nutrition to reach both the retina and the eye as a whole. The external treatments corrected the vascular pathology in the retina and absorbed the excess subretinal fluid from the macula. Lepa (application of paste) to the forehead and Tala (application of semisolid paste) to the head facilitated vasodilation, which allowed faster absorption of toxins and resolution of oedema. An identical mode of action at the ocular level was observed with Pindi and Purampada. Takradhara facilitated absorption of the subretinal fluid and cooling down of the body.

Virechana expelled *Pitta* and *Kapha* out of the body, thus enabling absorption of the subretinal fluid and correction of vascular pathology. It also prevented the *Doshas* from moving upwards to the head. *Nasya* prevented excess *Kapha* from accumulating in the head, with *Anutaila* being an excellent oil for bestowing strength to the sense organs [13]. *Anjana* allowed penetration of minute particles that had the affinity to pass through the barriers of the eye and hence reach the target tissues.

Darsana Eye Drops is made from Nirgundi (*Vitexnegundo* Linn.), *SaindhavaLavana* (rock salt), and *Tankana* (borax), and is indicated in *Timira*. *KasyapamKvatha*, prepared from *Triphala* (*Terminaliachebula*Retz., *Terminaliabellerica*Linn., *Emblicoefficialis*Gaertn.), *Vasa* (*Adathodavasica*Nees.), *Bhrngaraja* (*Ecliptaalba*Linn.), and *Candana* (*Santalumalbum*Linn.), is useful in all eye diseases. *Vinayakanjana*, prepared from *Durva* (*Cynodondactylon*Linn.), goat's milk, and goat's ghee, provides strength to the eyes and is a healing medicine. *PathyaPunarnavaChurna* (a powder prepared from *Terminaliachebula*Retz. and *Boerrhaaviadiffusa*Linn.) prevents collection of fluid and permits smooth flow of nutrients to the target tissues.

The discharge medicines helped maintain *Agni*, prevent formation of oedema, and promote vision. In the end, the VA improved to 6/6 and was maintained through the follow-ups. This shows that the

Ayurvedic protocol not only targets the disease, but also aims to bring the body back to normal activity.

CONCLUSION

The *Ayurvedic* treatment protocol for the present study patient resulted in improved DVA and retinal images both at discharge and after 2 follow-ups because of early and timely management. This case can be a stepping stone for future research in that the results may be validated by conducting large-scale sample trials.

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