

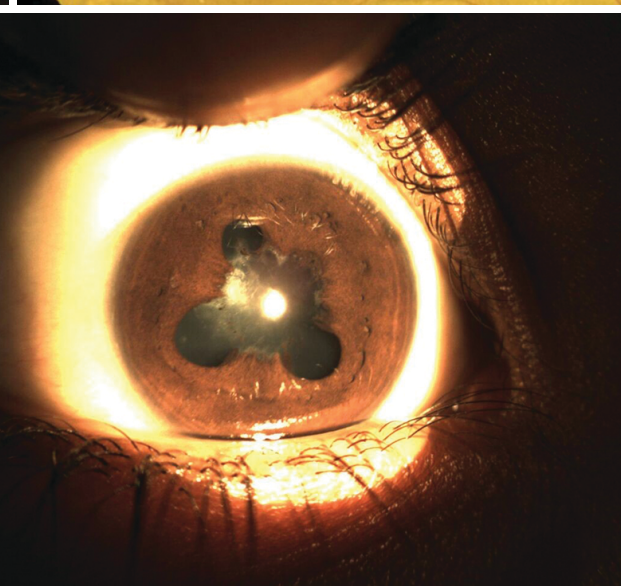
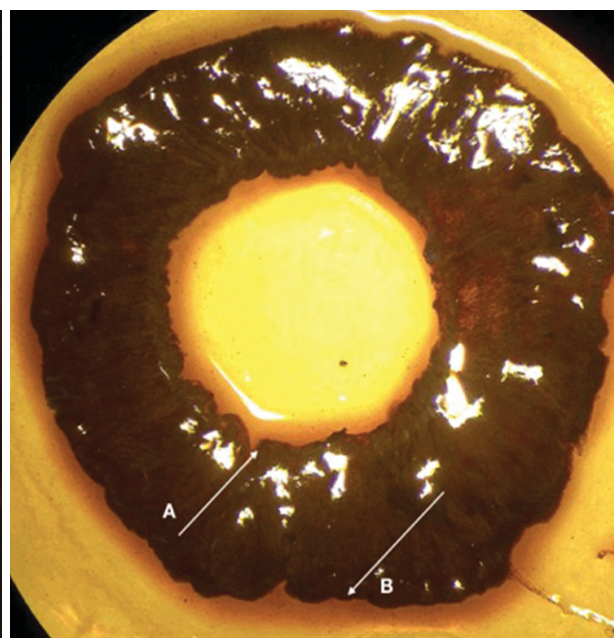
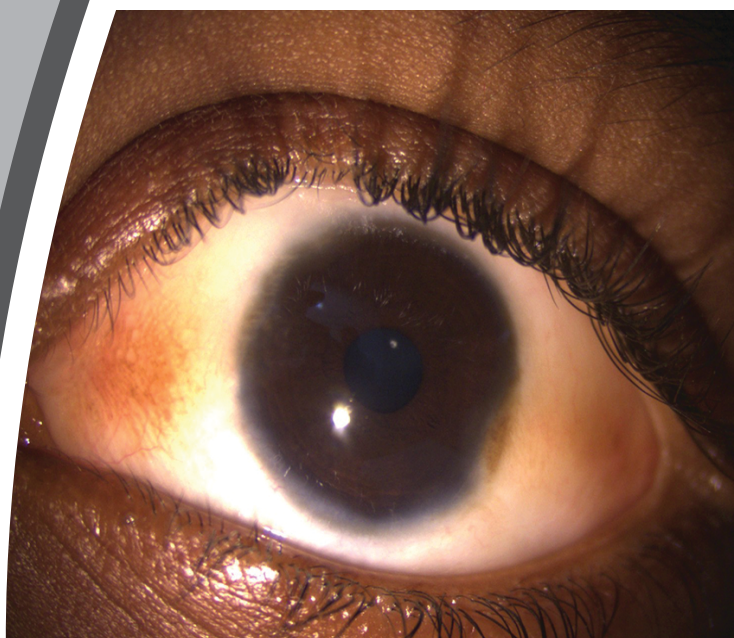


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Review Article

Co existent cataract and glaucoma – causes and management

Case Report

Encephalocraniocutaneous Lipomatosis (ECCL) – a rare neurocutaneous disorder

Expert Corner - Diabetic Retinopathy

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Abstract

Diabetic retinopathy (DR) continues to be a challenge both to clinicians and patients. The systemic variables involved, local mediators implicated, and the coexistence of other ocular conditions such as cataract requires careful planning and delivery of treatment. With the advent of antivascular endothelial growth factor agents, there has been a paradigm shift in the management of DR. Nevertheless, other treatment options such as retinal laser therapy, intravitreal steroids, and vitreoretinal surgery are equally important in selected clinical scenarios. We have a stellar panel of experts who are world-renowned experts in the field of DR. For the benefit of our readers, they distill the essence of evidence-based medicine and share their expertise with particular focus on real-world scenarios in DR.

Keywords: Diabetic macular edema, diabetic retinopathy, intravitreal injections, retinal laser therapy, vitreous hemorrhage

Q1. DR. MADANAGOPALAN. V. G: IN TODAY'S PRACTICE WHERE INTRAVITREAL ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR INJECTIONS ARE THE MAINSTAY OF TREATMENT, WHAT IS THE ROLE OF FUNDUS FLUORESCIN ANGIOGRAPHY IN DIAGNOSIS, MANAGEMENT, AND FOLLOW-UP OF DIABETIC MACULAR EDEMA?

Dr. R. Kim

Fundus fluorescein angiography (FFA) in diabetic macular edema (DME) is today restricted to those few cases which have very poor vision to look for ischemia and of course in severe nonproliferative diabetic retinopathy (NPDR) cases to rule out neovascularization elsewhere (NVE).

Dr. Atul Kumar

FFA stays as a baseline-imaging test to look for associated pathologies in the retina, e.g., retinal ischemia, neovascularization of disc, or NVE. For follow-up cases, optical coherence tomography (OCT) and even OCT angiography (OCTA) may suffice.

Dr. Rajiv Raman

It is preferable to have a baseline FFA in eyes with DME. If contraindicated, at least 7-field early treatment of diabetic retinopathy study (ETDRS) fundus pictures should be taken. FFA is definitely useful where vision loss is disproportionate to clinical picture (ischemic maculopathy), in cases where there is a suspicion of neovascularization, in cases of mixed retinopathy, and those who are nonresponders to treatment.

Dr. Raja Narayanan

I rarely use FFA in DME. I use quite often OCTA to look for macular ischemia. Wide-angle FFA is very useful in poor

response to antivascular endothelial growth factor (VEGF) injections. Targeted panretinal photocoagulation (PRP) to the periphery may be an option in cases of extensive peripheral ischemia.

Dr. Manish Nagpal

We typically use clinical diagnosis and usually would do a baseline OCT to check for edema or thinning to decide further intervention. We would do an FFA only in cases of unexplained visual loss to look for enlargement of the foveal avascular zone (FAZ) or if there is recurrent vitreous hemorrhage in eyes, which were already, lasered in the past. Follow-ups are usually done with OCT as per requirement.

Dr. Paisan Ruamviboonsuk

FFA is useful for nonresponders to anti-VEGF or cases with focal DME where focal laser to the leaking microaneurysms may be helpful.

Q2. DR. MADANAGOPALAN. V. G: DOES CLINICALLY SIGNIFICANT MACULAR EDEMA CRITERIA AS DEFINED BY THE EARLY TREATMENT OF DIABETIC RETINOPATHY STUDY STILL GUIDE DECISION-MAKING WHEN TREATING A PATIENT WITH DIABETIC MACULAR EDEMA? WHAT IS YOUR PREFERRED PROTOCOL FOR MANAGEMENT OF AN EYE WITH NEWLY DIAGNOSED DIABETIC MACULAR EDEMA?

Dr. R. Kim

For routine practice, the International Clinical Diabetic Retinopathy severity scale will be an easy guide to follow than the ETDRS guidelines. For a newly diagnosed center-involving

DME, after ruling out the contraindications, the first choice would be an anti-VEGF injection.

Dr. Atul Kumar

My preferred protocol is to differentiate the disease as “Center-involving DME” or “Noncenter-involving DME.”

Dr. Rajiv Raman

Clinically significant macular edema (CSME) is a form of DME that was precisely defined by the ETDRS. By definition, CSME exists if any of the following are present:

1. Any retinal thickening within 500 μm of the center of the macula
2. The presence of hard exudates at or within 500 μm of the center of the macula if associated with thickening of the adjacent retina (not residual hard exudates remaining after the disappearance of retinal thickening)
3. A zone, or zones, of retinal thickening 1 disk area or larger, any part of which is within 1 disc diameter (1 disc = 1500 μm) of the center of the macula.

In today's era of anti-VEGF agents, we define and treat DME based on “center-involving” or “noncenter-involving” status. Criterion 1 of the CSME definition is “center-involving,” and criterion 2 and 3 of CSME definition refers to “noncenter involving” DME.

Dr. Raja Narayanan

CSME was very useful in the laser era. As of today, I do an OCT to check whether DME is center involving, and we get a lot of additional information on the vitreoretinal interface as well as retinal structure. I treat noncenter DME with micropulse laser 5% duty cycle and center involved with vision <20/30 with injections. I am still conservative with vision 20/20 or 20/25.

Dr. Manish Nagpal

No, we are not using those guidelines to govern treatment protocols. We use OCT as a guide to inject anti-VEGF agents or to operate in case there is a tractional component. We clinically establish the diagnosis and use OCT to facilitate further treatment and use FFA only if visual loss is unexplained by our clinical findings.

Dr. Paisan Ruamviboonsuk

No. At present, the preferred protocols are from drcr.net studies.

Q3. DR. MADANAGOPALAN. V. G: WHAT IS THE ROLE OF SYSTEMIC COMORBID CONDITIONS (HYPERTENSION, HYPERLIPIDEMIA, ANEMIA, AND RENAL DYSFUNCTION) IN THE PATHOGENESIS AND PROGRESSION OF DIABETIC RETINOPATHY? IN AN EYE WITH DIABETIC RETINOPATHY, ARE THERE ANY SPECIFIC RETINAL FINDINGS THAT CAN ALERT THE CLINICIAN TO OTHER SYSTEMIC CONCERNS?

Dr. Atul Kumar

There is a definite role of systemic management for hypertension, hyperlipidemia, anemia, and renal dysfunction. Presence of extensive soft-exudates points to hypertensive

retinopathy. Extensive lipid deposits and retinal edema may signify renal dysfunction.

Dr. Rajiv Raman

Apart from plasma glucose levels, factors such as anemia, accelerated hypertension, dyslipidemia, renal abnormalities, and even pregnancy can influence the natural course of diabetic retinopathy (DR). Certain drugs can cause macular edema (Thiazolidinediones, fingolimod [used in MS], tamoxifen, taxanes, niacin, interferons, and prostaglandin analogs), and they should also be borne in mind.

Dr. Raja Narayanan

In India, we still see some patients for the first time with DR with systemic parameters off the charts, and they have no understanding of diabetes and its control. Delaying treatment of DME for a few weeks with injections does not harm, but the patients get the urgency to treat their systemic parameters. You may be surprised that some patients may never have visited their general physician in the last 6 months to 1 year, never checked their blood sugar in the last 6 months. They would “feel” that their sugar is under control (even if the last blood sugar was 300 mg%) because they take their daily medication, stopped eating rice, or never add sugar to their tea/coffee. These are the kind of patients who need extensive counseling before we start their ocular treatment. Hypertensive retinopathy can be picked up in fundus examination, and exudative retinal detachment or extensive subretinal fluid could indicate advanced nephropathy. Hard exudates can be seen in the so-called “normal range” lipid profile. The American Heart Association guidelines suggest a much lower “normal” level of cholesterol for patients with diabetes, compared to nondiabetics. I prefer cholesterol and triglyceride reduction with drugs to bring them as low as possible in DME. Some of the evidence comes from ACCORD trial, where fenofibrate was useful in controlling progression of DR.

Dr. Manish Nagpal

We encourage all these systemic conditions to be well controlled and advise the same to the patient. Accumulation of lipids at the macula would be a concern. We would specifically ask these patients to get their lipid profiles assessed and treated as per recommendation.

Dr. Paisan Ruamviboonsuk

I would still follow DCCT and UKPDS data to control blood sugar, lipid, and systemic hypertension. Patients with severe NPDR or worse can alert ophthalmologists that the patients may have other systemic conditions too.

Q4. DR. MADANAGOPALAN. V. G: WHEN TREATING DIABETIC MACULAR EDEMA WITH INTRAVITREAL AGENTS, HOW WOULD YOU DEFINE A “NONRESPONDER”? WHEN DO YOU PREFER TO CHANGE THE INTRAVITREAL AGENT BEING ADMINISTERED AND WHAT IS THE ROLE OF INTRAVITREAL STEROIDS IN MANAGEMENT OF DIABETIC MACULAR EDEMA?

Dr. R. Kim

Usually, if for two injections there is no response at all, then I would change the drug. In such instances, I would prefer to use the steroid, especially if the edema is very high.

Dr. Atul Kumar

A nonresponder in eyes with DME is when he not responding to 3–5 monthly anti-VEGF injections. At this juncture, I may like to switch to slow release biodegradable dexamethasone implant (Ozurdex) that is effective for intractable DME.

Dr. Rajiv Raman

If there is no improvement on OCT and no visual gain after 3 monthly injections consider angiogram and then plan rescue treatment. I would prefer to switch to another anti-VEGF agent. One can consider steroids in pseudophakic eyes after assessing glaucoma risk. Clinicians can also consider adding laser.

Dr. Raja Narayanan

This is quite a difference of opinion between DRCR protocols and practice in India. Most practitioners in India switch after 2 or 3 monthly injections if there has been an “inadequate” reduction of macular edema. I prefer to switch after two injections if there is no reduction of edema or a worsening of edema. However, I do not switch for recurrences, which is expected in DME. Regarding steroids, I never use them as primary treatment. However, I tend to use them for maintenance or as combined treatment after a minimum of three anti-VEGF injections. Protocol U had a lot of unanswered questions, including its methodology.

Dr. Manish Nagpal

There is usually never a nonresponder *per se*. Most cases would respond, some sooner and some later. In yet another group, the response may be transient. I would usually switch an agent only if it has not worked after giving 3 monthly doses. Steroids work extremely well in DME, and for all thick edemas, we would use them. Finally, if there were recurrence beyond three doses of anti-VEGF injections, the patient would do better with steroids.

Dr. Paisan Ruamviboonsuk

A “nonresponder” is when there is no change in best-corrected visual acuity and central subfield thickness (CSFT) on OCT for three consecutive visits. These criteria warrant change intravitreal agents. Intravitreal steroids may be used as the second choice or in conjunction with anti-VEGF when patients are pseudophakic.

Q5. DR. MADANAGOPALAN. V. G: IN ROUTINE CLINICAL PRACTICE, HOW OFTEN DO YOU ADVISE VITRECTOMY FOR DIABETIC MACULAR EDEMA? WHAT ARE THE CRITERIA TO BE SATISFIED IN ORDER TO ADVISE VITRECTOMY FOR DIABETIC MACULAR EDEMA?

Dr. R. Kim

I rarely advise vitrectomy for DME, unless there is a distinct vitreomacular traction (VMT) present.

Dr. Atul Kumar

I advise vitrectomy for DME when there is associated VMT, a thick epiretinal membrane (ERM) or early tractional retinal detachment (TRD) threatening the macula.

Dr. Rajiv Raman

Surgery is rarely performed for DME. However, few clinical scenarios warrant surgery. If there is focal VMT, vitrectomy is the choice. If broad vitreoretinal adhesions are present and if anti-VEGFs/rescue treatment have failed to resolve the macular edema and the ophthalmologist feels that there is a scope of improvement, vitrectomy can be considered. In eyes with diffuse DME, if desired outcomes are not obtained after primary and rescue treatment, vitrectomy with or without internal limiting membrane (ILM) peeling can be considered.

Dr. Raja Narayanan

I rarely perform vitrectomy for pure DME not associated with ERM or VMT. I have performed vitrectomy with ILM peeling in patients who have frequent recurrences despite excellent control of systemic parameters. I rule out obstructive sleep apnea in frequent recurrences over a prolonged period.

Dr. Manish Nagpal

Surgery is advised only if there is traction or membranes are noted on OCT. Vitreoretinal surgery and ILM peeling are very rarely used for nonresponsive edema without traction. I would make sure that the patient has a healthy FAZ on FFA or OCTA before deciding on surgery.

Dr. Paisan Ruamviboonsuk

Rarely, in the presence of obvious VMT, diabetic membrane, or concurrent idiopathic epimacular membrane that is believed to be the cause of the edema, I would perform vitreoretinal surgery.

Q6. DR. MADANAGOPALAN. V. G: A 62-YEAR-OLD DIABETIC MAN HAD UNDERGONE UNEVENTFUL CATARACT SURGERY IN BOTH EYES 45 DAYS AGO. HIS RECORDS SHOW THAT HE WAS DIAGNOSED TO HAVE SEVERE NONPROLIFERATIVE DIABETIC RETINOPATHY BEFORE CATARACT SURGERY AND NO DIABETIC MACULAR EDEMA WAS DOCUMENTED. AT PRESENT, VISUAL ACUITY IN BOTH EYES IS 6/18, N10 WITH GROSS MACULAR EDEMA IN BOTH EYES. THE EXTENT AND INTENSITY OF BACKGROUND NONPROLIFERATIVE DIABETIC RETINOPATHY APPEARS TO BE STABLE. WHAT IS THE BEST APPROACH TO THIS PATIENT?

Dr. R. Kim

I would first reevaluate his systemic status and would observe him with nonsteroidal anti-inflammatory drug eye drops for a month.

Dr. Atul Kumar

The treatment of choice is intravitreal anti-VEGF agents in both the eyes.

Dr. Rajiv Raman

Differentiating pseudophakic edema from DME in the presence of DR is important. A diffuse petalloid type of leakage with disc leakage on the FFA with very few aneurysms, and no hard exudates around the macula is suggestive of pseudophakic macular edema. On the other hand, if there is no component of Irvine–Gass syndrome, and only DME is present, treat as center-involving macular edema. However, if compliance is an issue, one can initiate the treatment with intravitreal steroids.

Dr. Raja Narayanan

I will proceed with anti-VEGF injections in this case.

Dr. Manish Nagpal

At this stage, he needs anti-VEGF injections and follow-up. Later, one could consider PRP as per the protocol once the edema settles.

Dr. Paisan Ruamviboonsuk

Anti-VEGF injections of both eyes are needed.

Q7. DR. MADANAGOPALAN. V. G: A NEWLY DIAGNOSED 46-YEAR-OLD DIABETIC PATIENT HAS COME FOR ROUTINE OPHTHALMIC EXAM. VISUAL ACUITY IS 6/6, N6 IN BOTH EYES. MILD NONPROLIFERATIVE DIABETIC RETINOPATHY IS DIAGNOSED WITH FEW SCATTERED MICROANEURYSMS. OPTICAL COHERENCE TOMOGRAPHY SHOWS DEFINITE LOSS OF FOVEAL CONTOUR AND FOVEAL THICKENING. CAN THIS PATIENT BE OBSERVED OR IS INTRAVITREAL ANTI-VEGF THERAPY NEEDED?

Dr. R. Kim

Again the systemic status has to be evaluated. Also, if the patient is asymptomatic, I will observe for 2–3 months and treat him if there is any change in the vision or in OCT.

Dr. Atul Kumar

As foveal contour and center-involving DME are apparent (foveal thickening), even with vision of 6/6, an anti-VEGF agent should be administered intravitreally.

Dr. Rajiv Raman

A visual acuity of 6/6, N6 does not convey the entire picture. Quality of vision is not conveyed to the examiner with Snellen's acuity alone. I will revisit the patient's complaints and enquire about what brings him to visit the ophthalmologist. Often, subtle visual symptoms that warrant treatment are present even in these "6/6" patients. In the event that this was a routine ophthalmic examination, I would explain that the disease is present and will see the patient in 2 months. In the meantime, I would advise the patient to visit his physician and have a strict systemic control.

Dr. Raja Narayanan

I would not give anti-VEGF injections to this patient at the first visit. I would recommend a thorough systemic workup and do micropulse laser. I would discuss anti-VEGF injections here but would not consider doing them at the first visit. However, if edema persists or worsens over the next few months, I would certainly consider anti-VEGF injections with the patient, even if he has good vision. Discussing long-term plan with patients is important at baseline, so that there are no surprises for the patient if the macular edema worsens.

Dr. Manish Nagpal

Yes, I would always treat such patients with a few injections of anti-VEGF and follow-up.

Dr. Paisan Ruamviboonsuk

I would prefer to observe at this time.

Q8. DR. MADANAGOPALAN. V. G: A 55-YEAR-OLD GENTLEMAN IS AWAITING LEFT EYE CATARACT SURGERY. ON EXAM, HE IS NOTED TO HAVE A VISION OF 6/18 AND IS ALSO DIAGNOSED TO HAVE SEVERE NONPROLIFERATIVE DIABETIC RETINOPATHY ALONG WITH DIABETIC MACULAR EDEMA (OPTICAL COHERENCE TOMOGRAPHY SHOWS LOSS OF FOVEAL CONTOUR, GENERALIZED THICKENING, CENTRAL SUBFIELD THICKNESS OF 350 μm, NO DISCRETE CYSTS). WHAT IS THE BEST COURSE OF ACTION?

Dr. R. Kim

I will place him on anti-VEGF and then take him for cataract surgery after 2 weeks if the cataract is significant.

Dr. Atul Kumar

It is best to defer cataract surgery. Control of blood sugar, hypertension, and lipids is essential. A mild scatter laser 400–650 spots will also help. As DME is spongiform, anti-VEGF injection can be deferred for the time being.

Dr. Rajiv Raman

As long as there is a clear enough view to see DME clinically, and on OCT, I treat DME according to the protocol. Once macular edema is treated, one can plan cataract surgery. Ideally, we can wait for 3 months for cataract surgery. However, if the view is not good enough to treat DME, cataract surgery can be done either along with intravitreal anti-VEGFs or 2 weeks after surgery and subsequent protocol continued. If the view is clear and treatment initiated, but even after three to four injections, the edema has not resolved and during this time cataract has worsened, cataract surgery can be planned and treatment of DME continued thereafter. One can consider concurrent intravitreal injection or injection postsurgery based on logistics.

Dr. Raja Narayanan

Treat the macular edema, stabilize it, and then proceed for cataract surgery after 3–6 months. Visual acuity of 6/18 with CSFT of 350 microns gives an impression that the cataract surgery can be deferred. I would certainly discuss cataract at baseline, and that there would be a need for a surgery in the next few months.

Dr. Manish Nagpal

I would advise the patient to take anti-VEGF along with the cataract surgery in same sitting and then review for any other treatment on follow-up.

Dr. Paisan Ruamviboonsuk

Cataract surgery with anti-VEGF either 1 week before or concurrent with the surgery.

Q9. DR. MADANAGOPALAN. V. G: A 52-YEAR-OLD WOMAN PRESENTS WITH VISUAL ACUITY OF 6/18 AND 6/24 IN RIGHT EYE AND LEFT EYE, RESPECTIVELY. A DIAGNOSIS OF SEVERE NONPROLIFERATIVE DIABETIC RETINOPATHY IS MADE. CLUMPS OF HARD EXUDATES ARE PRESENT UNDER THE FOVEA WITH MILD CENTER INVOLVING DIABETIC MACULAR EDEMA (CENTRAL SUBFIELD THICKNESS: 346 μ M AND 378 μ M, RESPECTIVELY). WHAT IS AN APPROPRIATE TREATMENT PLAN FOR THIS PATIENT?

Dr. R. Kim

I will treat with anti-VEGF injection.

Dr. Atul Kumar

If patient is pseudophakic, then a dexamethasone implant would be the best. It may help to dissolve the central hard exudates. If patient is phakic, an anti-VEGF injection followed by mild scatter laser can be done.

Dr. Rajiv Raman

If the patient has not received anti-VEGF injections in the past, it would be appropriate to start with them. If there is a history of multiple injections, one may consider steroid injections after assessing the risk for glaucoma. Control of systemic status (serum lipids) and referral to physician to initiate lipid-lowering drugs is important. Laser may aggravate subfoveal deposits and should be avoided.

Dr. Raja Narayanan

Know your patient completely, not just the retina. Review their systemic control. Discuss with their diabetologist any potential concerns, and consider statins with fenofibrate. “Normal” lipids should be brought down even lower in diabetics. All facts considered, I would start with anti-VEGF injections.

Dr. Manish Nagpal

First of all, I shall explain the guarded visual prognosis to the patient. The likelihood of gaining good vision is less since the deposits are under the fovea. In these cases, I prefer to treat using steroids instead of anti-VEGF agents as the first line.

Dr. Paisan Ruamviboonsuk

The CSFT in each eye is quite thick although the subfoveal hard exudates may give poor visual prognosis; I still think anti-VEGF could somehow have a role in this case.

Q10. DR. MADANAGOPALAN. V. G: A 63-YEAR-OLD MAN WHO HAS HAD NO OCULAR TREATMENT IN THE PAST PRESENTS WITH DEFECTIVE VISION IN THE RIGHT EYE FOR 1-WEEK DURATION. ON EXAMINATION, VISUAL ACUITY IS 1/60 IN RIGHT EYE AND 6/12 IN LEFT EYE. THE RETINA IS VISIBLE ONLY IN THE SUPERIOR QUADRANT OF RIGHT EYE AND THE REMAINING FUNDUS IS OBSCURED BY VITREOUS HEMORRHAGE. THE LEFT EYE SHOWS NEOVASCULAR FRONDS AT THE SUPERIOR ARCADE. WHAT WOULD BE AN APPROPRIATE PLAN OF ACTION FOR THIS PARTICULAR PATIENT?

Dr. R. Kim

For the right eye, I will do an ultrasonogram and if there is no TRD, I will observe. For the left eye, I would plan for laser PRP in 2–3 sittings. If associated with DME, inject first followed by PRP.

Dr. Atul Kumar

This patient has fresh vitreous hemorrhage in the right eye. In the visible superior area, extensive scatter laser needs to be done and patient asked to stay propped up when sleeping for about 1 month. The left eye requires PRP.

Dr. Rajiv Raman

An ultrasound examination of the right eye should be done to look for TRD. In the absence of TRD, I would prefer to observe for a month to look for spontaneous clearance of hemorrhage. Laser photocoagulation needs to be done to the visible retina in the right eye and to the entire retina in the left eye.

Dr. Raja Narayanan

My standard practice would be to perform PRP in the left eye and observe for 3–4 weeks in the right eye before deciding the next course. Discuss in detail with the patient about Plan A and Plan B for both eyes. Right eye may improve spontaneously, and the left eye may bleed even after laser, which may need surgery. Never proceed with a treatment without discussing all possible outcomes, and further treatment options if the outcomes are not as expected. I would stress the importance of honest discussion with the patient along with clinical treatment. Setting the right expectations at the beginning goes a long way in retaining the patient's trust.

Dr. Manish Nagpal

I would do an ultrasound for the right eye. If there is no detachment, I will wait for 1 month and consider vitrectomy if the hemorrhage is nonresolving. If the hemorrhage clears, one could perform retinal laser and administer injections. For the left eye, I would recommend two sittings of PRP along with anti-VEGF injections and follow-up.

Dr. Paisan Ruamviboonsuk

I would try anti-VEGF injection in the right eye first. I would then follow the patient to see if the bleeding clears up with 2–3 injections. If the bleeding still persists, I recommend vitrectomy with PRP. PRP may be applied to the left eye now. However, if the new vessels in the left eye are aggressive, anti-VEGF can be injected first followed by PRP later.

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