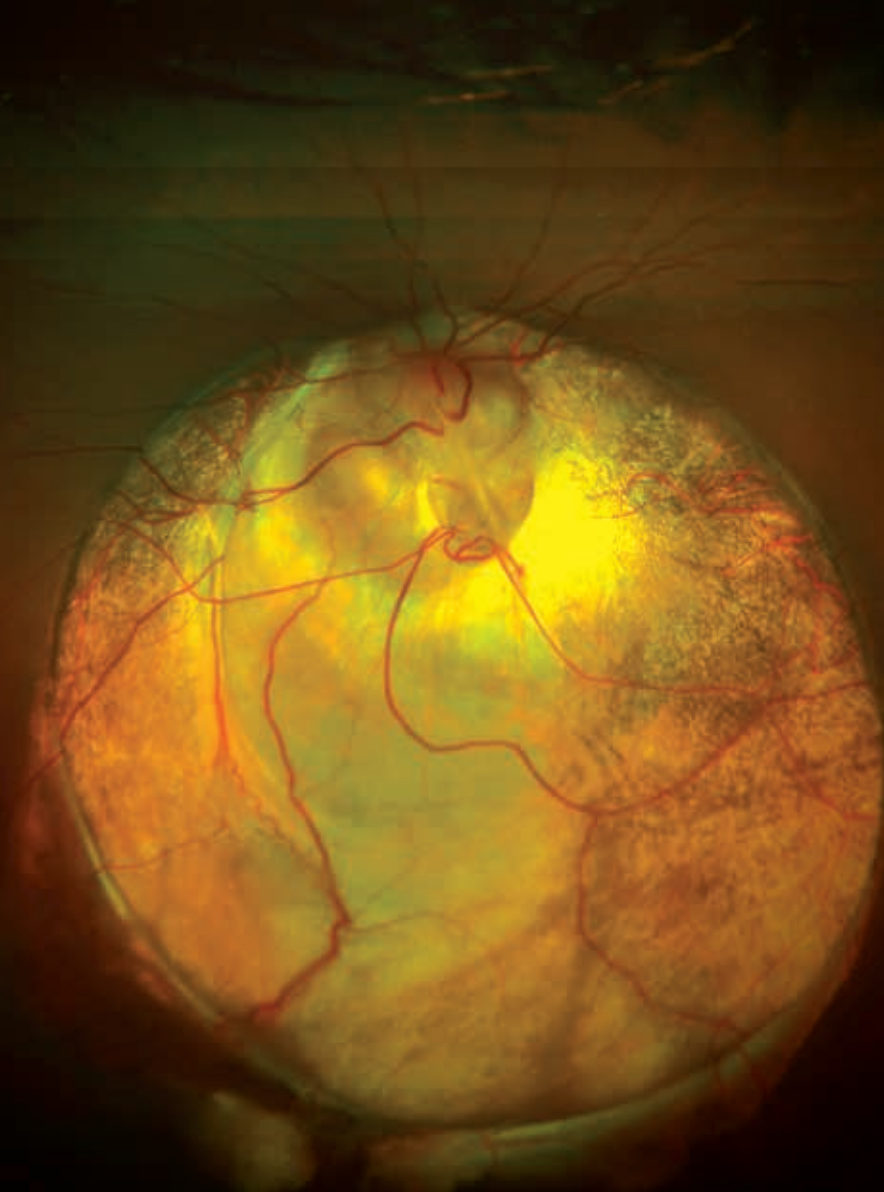




The Official Newsletter of the

VITREO RETINAL SOCIETY - INDIA

April 2017



Official Website : www.vrsi.in



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Original articles:

These include randomized controlled trials, intervention studies, studies of screening and diagnostic test, outcome studies, cost effectiveness analyses, case-control series, and surveys with high response rate. The text of original articles amounting to up to 3000 words (excluding Abstract, references and Tables) should be divided into sections with the headings Abstract, Key-words, Introduction, Material and Methods, Results, Discussion, References, Tables and Figure legends.

Case reports / Challenging case /Innovations / Instruments / Techniques

New, interesting, challenging, rare cases, innovations, instruments and techniques can be reported. They should be unique and providing learning point for the readers. Manuscripts with clinical significance or implications will be given priority. These communications could be of up to 1000 words (excluding Abstract and references) and should have the following headings: Abstract (unstructured), Key-words, Introduction, Case, Discussion, Reference, Tables and Legends in that order.

The manuscript could be of up to 1000 words (excluding references and abstract) and could be supported with up to 10 references. Case Reports could be authored by up to four authors.

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From the President's Desk

Dr. A. Giridhar

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Dear Members:

Greetings from the Vitreo Retinal Society-India!

This is the first issue of the newsletter after we assumed office in December 2016. The VRS-I newsletter was initiated a couple of years ago by our past president Dr S Natarajan as its first editor and it was envisaged on the lines of the Retina Times published by the American Society of Retina Specialists and a similar initiative by the European Vitreo Retina Society.

The purpose of the newsletter is primarily:

- To provide information regarding various activities of the society so as to keep the members informed;
- To provide an opportunity for its members to publish interesting cases, short case series, innovations, etc.;
- To create a platform for a better network among the members of the society.

This particular issue is being published with these objectives in mind. I request all members to utilise this opportunity and send interesting abstracts, scientific information relevant to our sub-speciality to the Editor so that there is broader participation and there are equal opportunities for all.

We are keen to convert this newsletter into a journal of vitreo retinal diseases in due course of time and if that has to happen, we need to get the full cooperation from all our members. Ours is a unique sub-speciality in ophthalmology where we have very large proactive set of members who are academically very conscious and very up to date in scientific information. Therefore it is not very difficult for us to move forward in due course of time with a journal pertaining to our sub-speciality in our country.

The initiative to start a journal was made a couple of years ago but it had to be shelved for various reasons. The situation now is different as we are a much larger organisation with a very strong membership base. Let us work together to improve the quality of our newsletter, give it a permanent name and convert it into a journal in a time bound manner.

With best wishes!



From the Honorary Secretary Desk

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Dear Members:

Greetings from the Vitreo Retinal Society-India!

I am delighted to know that the first issue of VRSI newsletter in 2017 is being published under the leadership of Dr. Vishali Gupta, Dr. Thomas Cherian, Dr. Anand Rajendran, Dr. Ramandeep Singh, and Dr. Jay Chhablani. I am sure that you will find the scientific information extremely valuable for your daily practice, and to provide the best care to your patients in the clinic. I take this opportunity to request you all to submit your interesting cases, articles and innovations to the VRSI newsletter, which will help improve the scientific knowledge base of our members.

VRSI is also holding the mid-term meeting at Palampur on June 16 and 17, under the stewardship of Dr. S.K. Sharma, Dr. Sudhir Salhotra, and Dr. Ramandeep Singh. The VRSI annual meeting will be held at Puri, Odisha from Nov 30 to Dec 3, 2017 under the leadership of Dr. S.T. Muralidhar, Dr. Santosh Mahapatra, and Dr. Umesh Behera. Dr. Vishali Gupta is creating a wonderful scientific program for us all, with numerous International and National faculty, to make it a memorable event. I request you all to participate enthusiastically in both the meetings.

I wish you a great year ahead.



From the Convenor Scientific Committee Desk

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Dear Members:

Greetings from the Vitreo Retinal Society-India!

It gives me great pleasure in writing this foreword for the first newsletter of Vitreo Retinal Society of India for the year 2017. Vitreoretinal Society of India continues to grow at a rapid pace with more than 50 young members joining us every year. The society remains committed to its goal of spreading the scientific knowledge as well as mentoring the young VR surgeons. At the same time, it is committed towards its senior members by providing a platform for the brainstorming and exchange of new ideas. The Mid-term VRSI has been started from this year and the first joint meeting of midyear VRSI with Retinal Imaging Symposium in the Himalayas (RISHI) shall be held on 15th and 16th of June 2017 at Palampur HP. This meeting aims to stimulate new ideas with free exchange of knowledge sharing the cutting edge technology as well as discussing the complex retinal and Vitreo-retinal issues. This will be a unique opportunity for the experts to interact with their peers (both national and international) and be up to date with the latest. The annual meeting of VRSI aims to be more inclusive, and keeping in view the wishes of our new president Dr. A Giridhar, aims to provide more exposure to fellows and residents in terms of surgical exposure, skill training, sessions focused on practice management and breakfast sessions with international experts. The current executive committee is working hard to provide the scientific stimulus to all the members of the society, giving a different flavor to both the meetings with minimal overlap in their scientific contents.

To keep our members updated with the new developments, we shall carry on the legacy of producing the scientific newsletter thrice a year. The young team comprising of Dr. Anand Rajinderan, Dr. Ramandeep Singh and Dr. Jatinder Singh have worked extremely hard to bring out this newsletter. They have formulated the guidelines for submission and these guidelines have been circulated to all the members in monthly VRSI newsletter brought out by our secretary Dr. Raja Narayan. In the current issues, there are case reports, original as well as review articles and we would like to thank our contributors for their hard work and look forward to their continued support. We have added the expert panel discussion where the experts would give their personal viewpoints about a common disease entity and share their experiences. We do hope that you enjoy reading this newsletter and look forward to your comments and suggestions for the improvement.

Idiopathic central serous chorioretinopathy (ICSC) Panelist

Dr. Amod Gupta, Prof Emeritus & Former head,
AEC, PGIMER, Chandigarh

Dr. Atul Kumar, Prof & Chief, RP center of
Ophthalmic sciences, AIIMS, New delhi.

Dr. Dhananjay Shukla, Senior Consultant &
Director, Retina-Vitreous Service,
Ratan Jyoti Netralaya, Gwalior.

Panel Questions

How will you manage Acute CSC?

(Amod Gupta) Once the diagnosis of acute CSC is established, I would suggest the following measures.

- I would like to rule out exposure to corticosteroids by any route. Unless this history is asked specifically, the patients are unlikely to volunteer the information. If the history is positive, get a physician's opinion whether steroids can be withdrawn and substituted with non-steroidal treatment. Remember, long term exposure to steroids may lead to adrenal insufficiency and hence always taper steroids. Avoid temptation to stop steroids all of a sudden once you spot the diagnosis of CSC.
- Specifically ask for any stressful situation at home or workplace. It is not a surprise given the association of Type-A personality with CSC, that majority of patients once probed will give history of stress. This is information unless probed shall not be forthcoming. Do not ignore stress in women who I saw increasingly presenting with CSC in the last few years.
- They need counselling that the disease is a self-resolving condition and they would improve if they change their life-style. I do not believe in the advice 'forget the disease and it will forget you'. Patients need to learn to cool down and take things easy.
- May advise them to join yoga classes.
- Advise them a follow-up after 4-6 weeks and demonstrate the resolution/decrease of SRF on the OCT to restore the confidence of the patient in your ability to deal with the disease.
- Keep in mind that in very rare instances secretory pituitary adenomas may present as CSC because of increased plasma cortisol levels.

(Atul Kumar) Acute CSC is self-limiting with typical visual and anatomical recovery between 1-4 months. Hence, observation may be considered as the 1st line of treatment in acute cases except in patients with recurrence, patients who require early rehabilitation for occupational purposes or one-eyed patients where the other eye has poor vision due to chronic CSC sequelae.

Initial treatment includes:

- Careful observation with close follow-up
- **Risk factor modification:** Correcting sleep disturbances, discontinuation of any forms of steroids, treatment of obstructive sleep apnoea, life style modification and psychological support etc.

(Dhananjay Shukla) Depends on what we call Acute. Chronological definitions label acute CSC as 1-3 months' old, and chronic as 6 months' or more. The intermediate period (>4 and <6 months) has not been specifically addressed except by Burumcek et al (Ophthalmol 1997;104:616-22), who called it "persistent." The second set of definitions is based on fluorescein angiography (FA): acute CSC displays pinpoint leaks (smokestack, inkblot etc.) and chronic is characterized by diffuse retinal pigment epithelial (RPE) decompensation. I take into account both definitions, and where there is dichotomy, bank on FA definition to decide on management. My second criterion for action (besides the acute/chronic aspect) is best-corrected visual acuity (BCVA), and the 3rd criterion is the site of leak. The 4th is patient's visual requirement. The 5th is the status of the other eye. If CSC is acute by clinical and angiographic definitions, BCVA is good ($\geq 6/12$), and the visual requirement is not acute, I wait for 3-4 months. I may treat persistent CSC (≥ 4 months) with 6/12 or worse vision if the other eye's course was less favorable. In all cases, I take a detailed history, and try to address aggravating behavior, diseases or drugs. I typically don't order indocyanine green angiography

(ICGA) until I decide to treat the patient (see below). Enhanced depth SD-OCT helps me to look at the predisposition of the other eye as well, and follow up on CSC resolution. Photodynamic therapy (PDT) is the treatment of choice on the rare occasions when treatment is indicated for acute CSC (see below).

Any role of FFA in the era of OCT?

(Amod Gupta) Even if the OCT shows SRF, so many pathologies may show SRF especially patients with idiopathic CNVM or VKH disease may present with a similar SRF. To reach the definitive diagnosis, I would get an initial FFA to confirm the diagnosis of CSC. I do not think there is any need for repeating FFA in the follow up except in patients who are elderly (50+) where in the changing pattern of the FFA leak may point out the presence of CNVM rather than a CSC.

(Atul Kumar) FA is extremely helpful to confirm the diagnosis, and serves as a guide for CSC activity and for laser treatment of eccentric leaks.

With recent advances in OCT including SS-OCT and enhanced depth imaging, characteristic findings like neurosensory detachment, presence of pachychoroid (increased choroidal thickness), dilation of larger choroidal vessels and narrowing of choriocapillaries overlying areas of PED can provide additional supportive evidence of Pachychoroid spectrum in eyes with CSC.

(Dhananjay Shukla) OCT may replace FFA for observation and follow-up but not when treatment is required. I always order FFA when I consider treatment to check for site of leak, associated CNV or anastomotic channels. Rarely, in presence of subretinal fibrin, it helps rule out choroiditis and vitelliform lesions.

When will you order ICG angiography?

(Amod Gupta) In the past ICG was used to demonstrate the hyperpermeable choroid in CSC (even in the asymptomatic eye). Presently, there is no indication of ICG for straight forward cases of CSC. However, I would consider ICG if there is suspicion of underlying PCV lesions (PCV may complicate CSC!). If you see any exudates, or sub-RPE blood, I would order ICG.

(Atul Kumar) I often order it for eyes with chronic CSC. ICG angio is helpful in differentiating it from related conditions like CNV complicating CSC or PCV complicating chronic CSC, where I can view polyps and /or branching vascular network (BVN) on ICG-A.

In cases of chronic CSC, ICG angio also may be helpful to localize choroidal hyperpermeability and may be helpful for ICG guided PDT or recently, ICG guided diode laser treatment.

(Dhananjay Shukla) As mentioned before, I order ICGA in all cases of CHRONIC CSC to look for RAP (retinal angiomatous proliferation) and PCV (polypoidal choroidal vasculopathy is common in Indian population), and in selected cases of acute and persistent CSC where treatment is required, to delineate the total area of choroidal hyper-permeability requiring treatment.

Chronic ICSC - How do you decide choice of treatment?

(Amod Gupta) These are the most frustrating cases to treat. I would ask for an OCT angiography to rule out the underlying CNVM which is seen nearly 20-25% of the so called chronic CSC. If CNVM can be demonstrated, the treatment of choice is anti-VEGF therapy with gratifying results. However, in the absence of a demonstrable CNVM, I would consider low-fluence PDT which works by decreasing the choroidal thickness and hopefully reverse the hyperpermeability of choroid.

(Atul Kumar) Chronic CSC may be treated with one of the following options. Based on chronicity of CSC and persisting foveal detachment, reduced vision and associated metamorphopsia, reduced fluence PDT would be my first option.

Thermal laser photocoagulation in patients with SRD persisting ideally for over 4 months months with focal leak on FA located at least more than 500 microns away from the fovea. Laser treatment shortens the course of the disease and decreases the risk of recurrence for CSCR, but it does not appear to improve the final visual prognosis. I have additionally observed fresh leaks coming up in vicinity of the laser-treated focal areas sometimes too.

Various drugs for medical management has been described for CSC. e.g. Carbonic anhydrase inhibitors, beta blockers, imidazole (ketoconazole), glucocorticoid receptor antagonist (mifepristone) etc. With increasing evidence of association of mineralocorticoid pathway with CSC, mineralocorticoid receptor antagonist have been studied and described including spironolactone and Eplerenone. My personal experience with Tab Eplerenone 25mgs /50mgs OD has been quite equivocal ,with only a few patients showing reduction of SRF and improvement in symptoms.

(Dhananjay Shukla) The default treatment for CSC, acute, persistent or chronic is PDT, as mentioned previously. When CSC is defined as chronic by chronological (6 months or more) or fluorescein angiographic criterion (diffuse RPE decompensation) but still has focal leakage points, focal laser photocoagulation is a feasible but distinctly SECOND choice. Pharmacotherapy is discussed below.

If medical treatment, which one and why?

(Amod Gupta) I do not think any medical treatment works consistently in chronic CSC. Treatments in the long past have included intravenous injections of calcium gluconate (10ml X10 days) without any rationale. Anti-TB drugs have been used by some ophthalmologists in India especially in patients with multifocal leaks. Rifampicin has been used to treat chronic CSC. Rifampicin is supposed to work by activating the liver enzymes responsible for the metabolism of glucocorticoids and thus reducing the plasma corticoid levels. I do not endorse the use of this drug in the setting of high TB-endemic country like India where irrational use of such drugs may contribute to drug resistance TB, already a challenge in India.

More recently, Mifepristone 200mg daily for up to 12 weeks has been used in some patients with chronic CSC showing good outcome. Mifepristone is an oral glucocorticoid receptor blocker drug. In my experience it was not really very effective. A mineralocorticoid blocker drug Spironolactone used to treat hyperaldosteronism, congestive heart failure and hypertension has been used in chronic CSC with a view to block the expression of mineralocorticoid receptors that have been demonstrated in the RPE. Again, in my experience even the spironolactone has not worked consistently.

(Atul Kumar) Amongst the available medical treatment, with increasing evidence of activation of mineralocorticoid pathway oral mineral corticoid antagonists is a potential minimally invasive therapy for chronic CSC. I have been using Tab Eplerone 25 mgs OD with equivocal results. , for the last about 4-6 months. Monitoring of S. electrolyte (for hyperkalemia) is essential ,however it is clinically insignificant especially in patients with normal renal function. (Eplerone has lesser affinity for mineralocorticoid receptor (MR) than spironolactone, it has less hormonal side effects as compared to spironolactone since it is a selective MR antagonist)

(Dhananjay Shukla) Medical treatment is a distant fourth option after observation, PDT, and focal laser photocoagulation. Several options have been mentioned in the literature including oral acetazolamide, antitubercular treatment, eplenerone, spironolactone, as well as intravitreal anti-VEGF agents (esp. bevacizumab). I have personally tried eplenerone and bevacizumab, and have found both disappointing. I have no experience with other alternatives...and the list of alternatives is endless if we include single case-report publications. I prefer to make a candid admission of my inability to treat to the patient, rather than soldier on with a relentless battery of unproven treatments.

If Lasers – which one? How do you decide?

(Amod Gupta) There is no indication of laser photocoagulation of the CSC leaks. In the long past, argon green laser photocoagulation was done in non-resolving CSC. However, it carries a risk of inducing CNV formation at the site of laser spot due to rips in the Bruch's membrane, thus converting a benign condition into a sight-threatening disease. Already, the CSC eyes are predisposed to develop CNVM and any laser treatment may serve to aggravate the condition. I have personally seen this complication in several patients leading to irreversible vision loss.

(Atul Kumar) In eyes with chronic CSC with multiple active leaks or a single point leak within the arcade and close to the fovea , I use low or reduced –fluence PDT in eyes with chronic CSC with macula-off serous ,bullous detachment and reduced vision and have had very encouraging results.

Conventional thermal 532 frequency-doubled laser is my treatment option only in eyes with a single point leak located in the extra-foveal area. Leak on FA is located more than 500 microns away from the fovea. The risks of scotoma occurrence and secondary CNV formation however stay. Recently, sub threshold micropulse diode laser (810nm) se for CSC has also been described. The higher wavelengths would allow a better choroidal penetration while sparing the inner retina from the laser injury. I do not have any personal experience of using it.

(Dhananjay Shukla) When PDT was not available, we have tried green laser for focal photocoagulation of extrafoveal focal leaks like everyone else, with reasonable success (I don't have exact data).I also have successfully performed transpupillary thermotherapy for chronic CSC with predominantly extrafoveal lesions...and for acute persistent CSC with subfoveal leaks as well. However, it is worth reiterating repeat that PDT is the treatment of choice in both these situations, when the patient can afford it. I have read and heard about successful treatment with green and yellow micro-pulse lasers as well, but have no personal experience with it.

Current role of fundus autofluorescence in vitreoretinal disorders

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ABSTRACT

Fundus autofluorescence is a quick, non-invasive imaging modality that is gaining wide clinical applications in various retinal and choroidal disorders. Besides providing information about the retinal metabolism, the pattern of autofluorescence acts as a guiding tool for diagnosing and monitoring retinchoroidal diseases, especially those with involvement of the retinal pigment epithelium. We performed a MEDLINE search with a combination of key words: fundus autofluorescence, retina, choroid, and imaging, to present this review, which highlights the current role of fundus autofluorescence in retinal degenerations and dystrophies, and chorioretinal inflammations and infections.

Keywords: fundus autofluorescence, retina, choroid, imaging

Introduction

Fundus autofluorescence (FAF) is a non-invasive imaging technique that provides information on retinal metabolism. It is based on the detection of fluorophores (lipofuscin and melanolipofuscin) that are endogenous, hence, enabling a dyeless, non-invasive imaging technique.^[1] Stored as a metabolic by-product of the visual cycle comprising photoreceptor metabolism, the lipofuscin accumulates within the retinal pigment epithelial (RPE) cells.^[2,3] It absorbs (blue light, excitation wavelength of 470 nm) and emits (yellow-green light, emission wavelength of 600 nm) light of specific wavelength, giving rise to the fundus autofluorescence.^[4,5] Lipofuscin accumulation is suggestive of oxidative cellular damage in RPE, reflecting the retinal disease activity.^[6-8]

Methods

This review summarizes the current role of FAF in retinal

degenerations and dystrophies, and chorioretinal inflammations and infections. MEDLINE search was performed with a combination of key words: fundus autofluorescence, retina, choroid, and imaging. The search was limited to the literature pertaining to the English language and other-language publications with an English abstract. An emphasis was given, whenever possible, to the most recently published studies. Cross-referencing was also performed to retrieve the specific articles.

FAF imaging

The lipofuscin molecules have a broad range of excitation (300-600 nm) and emission spectra (480-800 nm). The absorption characteristics of ocular media, particularly the crystalline lens, restrict the transmission to and from the retina.^[9,10] Hence, the newer FAF systems are incorporated with some modifications to minimize the autofluorescence from the lens. The confocal scanning laser ophthalmoscope (cSLO) allows the excitation in the blue range of 488 nm, and emission between 500-700 nm for FAF detection, in contrast to the green spectrum (535-580 nm) of excitation and yellow-orange spectrum (615-715 nm) of emission by the conventional fundus camera (figure 1 a,b).^[11,12]

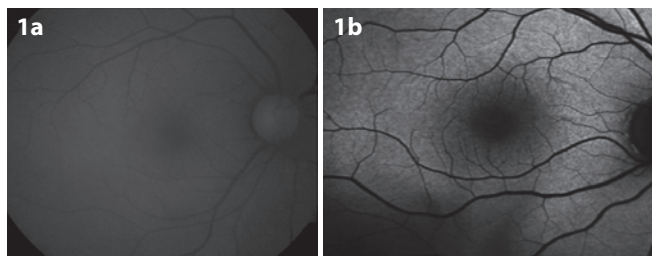


Figure 1: Fundus autofluorescence of a normal eye with conventional fundus camera (a) and with confocal scanning laser ophthalmoscope system (b).

Clinical application

A normal human fundus shows a diffuse FAF signal, with a marked hypoautofluorescence (lack of autofluorescent material) of the optic nerve head and the retinal blood vessels (absorption phenomena by blood contents).^[12,13] Absorption from lutein and zeaxanthin at the fovea, and decreased lipofuscin in RPE parafoveal cells leads to a decreased intensity of autofluorescence in these areas compared with that at the outer macula.^[1] An abnormally increased autofluorescence (hyperautofluorescence) results from an increased collection of lipofuscin, which is a mixture of pigments A2E, isomers of A2E and all-trans-retinal dimer.^[14-17] As a result of a chorioretinal disease, the impaired RPE phagocytic function, coupled with an increased photoreceptor outer segment shedding impairs the RPE cells' ability to recycle the metabolic by-products. This produces a state of hyperautofluorescence, which forms the basis of FAF-guided diagnosis of various chorioretinal diseases in their active stage. Following an irreversible loss of photoreceptors, the RPE cells undergo atrophy leading to a decreased lipofuscin content, producing a decrease or loss of autofluorescence (hypoautofluorescence). This FAF finding represents the stage of atrophy, scar, or fibrosis, and reflects the inactive (or healed) stage of the disease with significant RPE damage and photoreceptor loss.

Age-related macular degeneration (AMD)

Early AMD

The pathogenesis of age-related macular degeneration (AMD) is multifactorial, and the aged RPE cells play a key role in the disease process. The early non-neovascular AMD with pigmentary RPE disturbances and drusens seen clinically may not show exact correlation with FAF findings. Various possibilities of FAF findings exist in early AMD.^[1,18-21] While FAF might appear normal in eyes with small drusens, some have shown FAF alterations appearing before the clinically visible lesions.

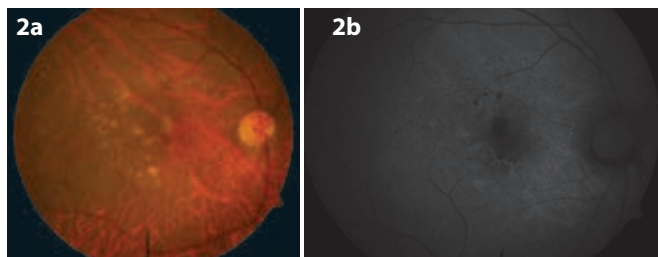


Figure 2: Large, soft drusens (a) appear hyperautofluorescent (b).

Abnormal patterns of FAF in early AMD have been classified as normal, minimal change, focal increased, patchy, linear, lacelike, reticular, and speckled patterns.^[21] Typical patterns may be seen in

specific types of drusens.^[22,23] Hypoautofluorescence is seen with cuticular and crystalline drusens. Large, soft confluent drusens, and drusenoid pigment epithelial detachments (PED) show hyperautofluorescence (figure 2a,b). Reticular drusens appear as round, elongated hypoautofluorescent spots, surrounded by a zone of hyperautofluorescence. The FAF characteristics of drusens provide important clues as a marker for disease progression.^[24]

Geographic Atrophy

Death of RPE cells and loss of lipofuscin content leads to progressive loss of autofluorescence. Geographic atrophy (GA) represents the advanced stage of "dry" AMD. The lesion is typically parafoveal with sharply demarcated borders and intense hypoautofluorescence (figure 3a,b).^[25-27] Presence of hyperautofluorescent edges around the area of GA is indicative of possible extension, and is classified as none, focal, diffuse, banded, and patchy.^[28,29] A higher risk of disease progression is reported with diffuse and banded phenotypes.

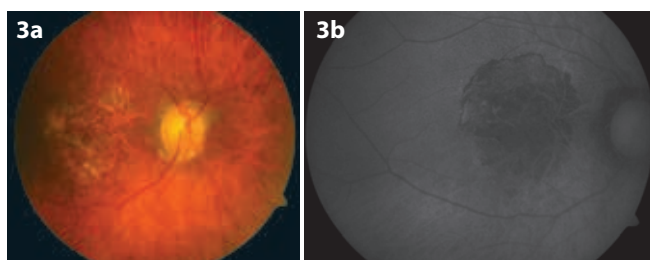


Figure 3: A large area of geographic atrophy (a) appearing hypoautofluorescent with large choroidal vessels appearing prominent (b).

Pigment epithelial detachment (PED)

Varying FAF patterns may be seen in PEDs. A PED often appears as a hyperautofluorescent lesion with a less autofluorescent border (figure 4a-b). Presence of subretinal fluid and RPE atrophy may give rise to hypoautofluorescence within the lesion.^[18,30]

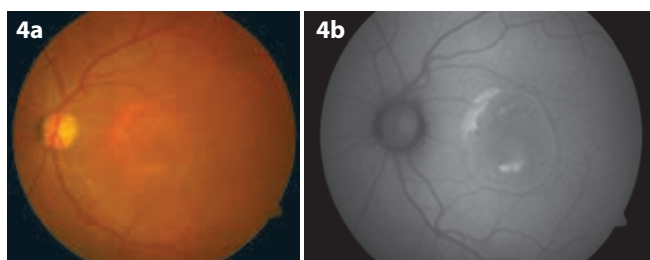


Figure 4: a large PED (a) showing hyperautofluorescence with a border of lesser hyperautofluorescence (b).

Choroidal neovascular membrane (CNV)

An early CNV secondary to AMD appears normal on FAF due to an intact and viable RPE.^[31,32] A decreased FAF underlying the CNVs is due to blockage of FAF by the growing vessels in early stage

(occult CNV), secondary to RPE alterations and atrophy later (classic CNV), and scarring in advanced stage. Presence of hyperautofluorescence adjoining the CNV is due to chronic subretinal fluid and phagocytized RPE remnants (figure 5 a,b). Progression from non-neovascular AMD to neovascular AMD may be predicted by certain FAF patterns.^[33,34] Patchy, linear and reticular patterns of early AMD have shown strong correlation with progression to CNV.

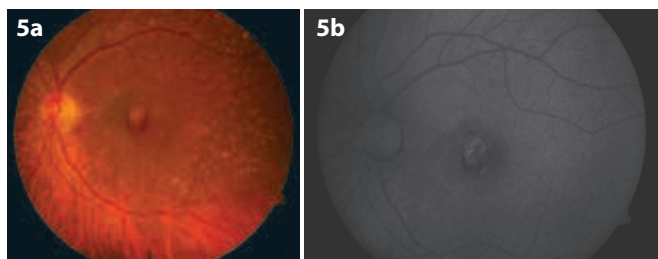


Figure 5: a case of neovascular AMD (a) with hyperautofluorescence corresponding to CNV, surrounded by hypoautofluorescence due to overlying hemorrhage (b).

RPE tears

Large fibrovascular PEDs may result into RPE tear spontaneously, or following anti-vascular endothelial growth factor (anti-VEGF) injection or photodynamic therapy. The FAF shows a well-defined area of intense hypoautofluorescence corresponding to the RPE tear (absent RPE), with adjacent area of intense hyperautofluorescence corresponding to the rolled RPE.^[35-37]

Macular Hole

FAF patterns vary with the stages of macular hole. A mild to moderate hyperfluorescence appears in the area of the hole in early stages (1 and 2) of macular hole.^[38] The central hyperfluorescence increases progressively in stage 3 and 4 full thickness macular hole, with stage 4 macular hole surrounded by a ring of hypoautofluorescence due to the cuff of subretinal fluid. This central hyperautofluorescence disappears following macular hole closure following surgery.

Central serous chorioretinopathy (CSR)

Varying patterns of autofluorescence have been reported in CSR.^[39-41] Hypoautofluorescence at focal leakage sites in acute stage has been attributed to reduced retinal metabolism at that site, and masking effect by subretinal fluid. Hyperautofluorescence in chronic cases is derived from accumulation of photoreceptor outer segments and chromophores. Chronic serous detachment leads to accumulation of photoreceptor debris, which collects at the inferior border of detachment and produces a granular hyperautofluorescence. Evidence of pre-existing long standing

subretinal fluid manifests as hypoautofluorescent gravitational tracts (figure 6a,b). Involvement of peripheral retina in CSR has been shown by ultra widefield FAF.^[42]

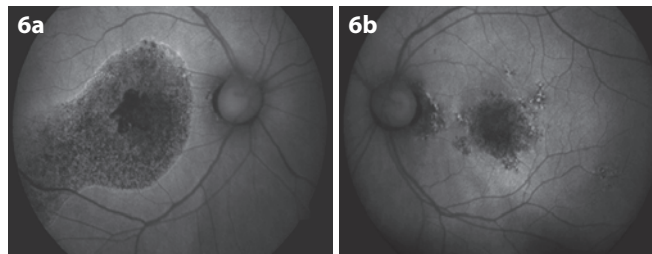


Figure 6: FAF of bilateral chronic CSR showing gravitational tract (a) and stippled autofluorescence (b).

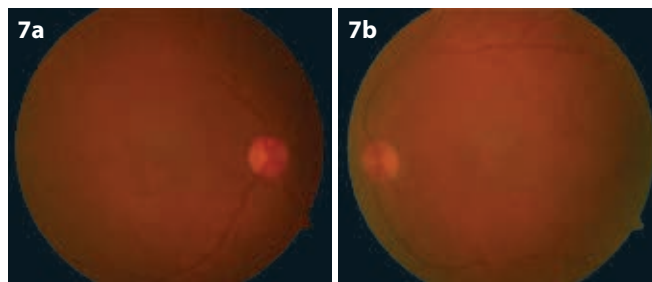
Diabetic retinopathy

Preferential involvement of the microglia instead of RPE for lipofuscin accumulation in diabetic retinopathy (DR) has restricted the studies of FAF in DR on diabetic macular edema (DME).^[43-46] A hyperautofluorescent edema has been linked with worse visual acuity and increased retinal thickness.

Retinal dystrophies

In Stargardt disease, an autosomal recessive mutation in the ABCA4 gene causes defective photoreceptor degradation, leading to lipofuscin accumulation. An initial hyperautofluorescence at the macula in the early stages is followed by macular hypoautofluorescence, surrounded by a hyperautofluorescent flecks, with typical peripapillary sparing.^[47,48]

Adult onset vitelliform dystrophy (AOVD) is characterized by bilateral, subfoveal vitelliform lesions that exhibit hyperautofluorescence. As RPE atrophy sets in, the lesion starts becoming hypoautofluorescent (figure 7 a-f).^[49-51] Different classifications with three stages have been proposed for FAF findings in AOVD. Best macular dystrophy has been reported to have six patterns on FAF: normal, multifocal, hyperautofluorescent, hypoautofluorescent, patchy and spoke-like.^[52,53] Though FAF characteristics are not very typical in other pattern dystrophies, a much more widespread disease is revealed by FAF than seen clinically.^[54]



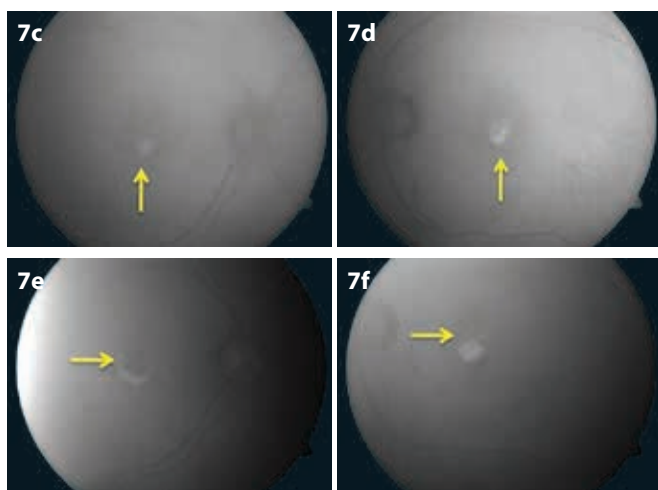


Figure 7: Both eyes (a,b) of adult onset vitelliform dystrophy, with subfoveal hyperautofluorescence (arrow) (c,d). 18 months later, hypoautofluorescence starts replacing hyperautofluorescence (e,f).

Retinitis pigmentosa may reveal a parafoveal hyperfluorescent ring on FAF, known as Robson-Holder ring.^[55-57] The ring denotes the junction of inner/outer segment disruption, encloses normal retina within, with complete loss of photoreceptors outside the ring. While few others may demonstrate an abnormal central hyperautofluorescence, some eyes show neither pattern. Presence of similar hyperautofluorescent rings on FAF in other retinal dystrophies (Best macular dystrophy, Bull's eye maculopathy, cone dystrophy, cone-rod dystrophy, etc.) indicates their common underlying mechanism.^[58]

In chloroquine/hydroxychloroquine toxicity, FAF imaging is more sensitive than funduscopy and FFA in detecting early RPE alterations.^[59,60] Early stages of toxicity reveal a pericentral ring of hyperautofluorescence, advanced stages typically show concentric rings of hyper- and hypo-autofluorescence in the parafoveal region, followed by a complete pericentral hypoautofluorescence in late stage.

Optic nerve head drusen

FAF imaging is valuable in distinguishing between optic disc edema and drusen. Drusens appear as round or oval brightly hyperautofluorescent deposits on the optic nerve head with irregular edges.^[61-63]

FAF imaging in uveitis

Chorioretinal inflammations

The multifocal choroidal lesions in various white dot syndromes exhibit different levels of autofluorescence, depending upon the stage of evolution of the disease. The FAF alterations reveal a more widespread disease than is evident on clinical examination,

enabling detection of subclinical disease.^[64,65] The sub-RPE nodules in punctate inner choroidopathy (PIC) appear hyperautofluorescent in initial active stages, turning hypoautofluorescent with resolution of inflammation, suggesting atrophy.^[65,66] A hyperautofluorescent halo persisting around PIC lesions has been reported to indicate an uncontrolled inflammation, which might cause reactivation.^[67]

The FAF in acute posterior multifocal placoid pigment epitheliopathy shows hypoautofluorescence due to masking by the subretinal fluid.^[68,69] As edema resolves, the placoid lesions start appearing hyperautofluorescent, which later become hypoautofluorescent as they develop into scars.

Tubercular multifocal serpiginoid choroiditis (MSC) exhibits four stages of FAF findings, as the disease evolves.^[70-73] A hyperautofluorescent halo denotes a freshly appearing new lesion, which clinically appears as creamish-yellow, subretinal lesion with fuzzy borders (stage 1) (figure 8 a-d). As it heals, the lesion acquires a well-defined rim of hypoautofluorescence, and the central hyperautofluorescence becomes prominent (stage 2). An increasing hypoautofluorescence and decreasing hyperautofluorescence denotes stage 3, when the lesion appears stippled on FAF. A complete hypoautofluorescence represents a completely healed lesion with RPE atrophy (stage 4). The FAF has become an invaluable tool in diagnosing active MSC and monitoring the response to therapy. Without the need of invasive FFA or ICGA, FAF can easily detect any recurrences or paradoxical worsening.

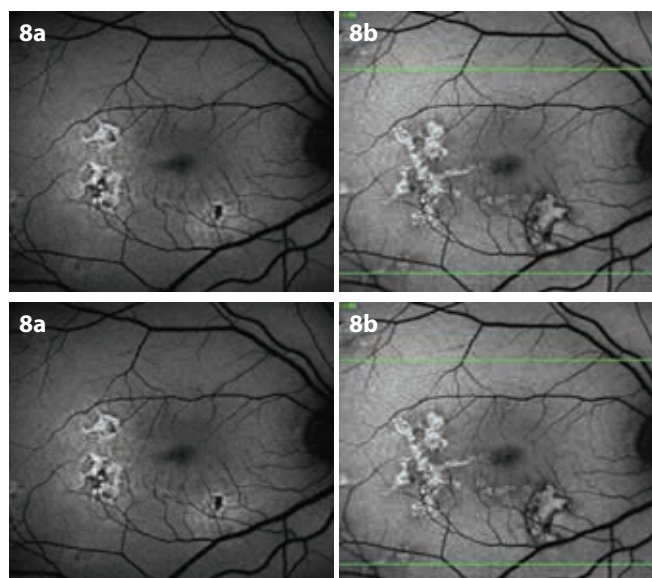


Figure 8: Stage 1 FAF of tubercular MSC showing hyperautofluorescent halo (a), surrounded by a hypoautofluorescent border as it heals (b). Stage 3 is seen by an increasing hypoautofluorescence and decreasing hyperautofluorescence (c), followed by a complete hypoautofluorescence in stage 4 (d).

In acute Vogt-Koyanagi-Harada (VKH) disease, the multilobular areas of dye pooling on FFA correspond to hypoautofluorescence on FAF due to masking of natural autofluorescence by serous detachments.^[74-75] Once the subretinal fluid resolves, these areas are replaced by granular dots of hypoautofluorescence, which correspond to window defects on FFA. Another study revealed two distinct patterns of FAF, depending upon the initiation of immunosuppressive therapy.^[76] In patients receiving an early aggressive immunosuppression, the mild hyperautofluorescence of initial stages decreased and returned to normal autofluorescence as the disease resolved (figure 9 a-h). Patients with delayed or no treatment revealed mixed spots of hyper- and hypoautofluorescence throughout the fundus. Chronic phase shows a normal autofluorescence as the sunset glow fundus represents loss of choroidal melanocytes, and not RPE.

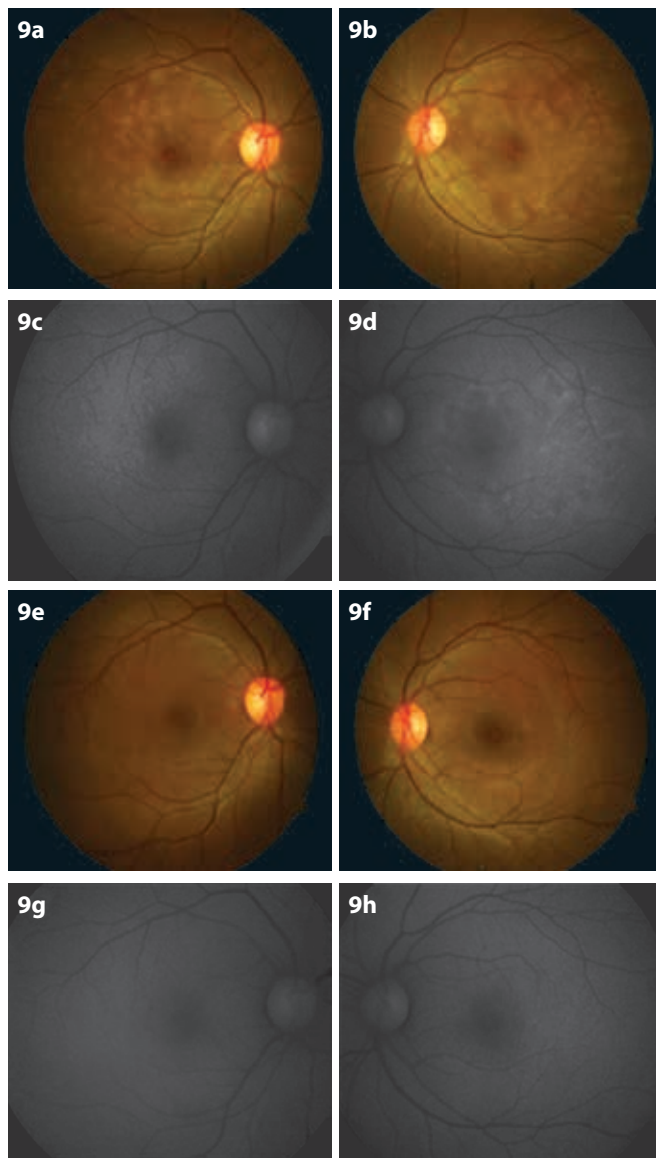


Figure 9: Bilateral serous detachments of acute VKH disease (a,b) showing hyperautofluorescence in posterior pole (c,d). 3 years following an intensive immunosuppressive therapy (e,f), the FAF looked normal (g,h).

Primary vitreoretinal lymphoma (PVRL)

An early diagnosis is essential in PVRL because of its fatal potential. Majority of eyes with active disease reveal a granular pattern of FAF (figure 10 a-c).^[77,78] The nodular hyperreflective sub-RPE spots on OCT indicate the lymphomatous infiltrates, which appear hyperautofluorescent on FAF. Lipofuscin accumulation adjacent to tumor cells cannot be ruled out. The granular FAF pattern provides important information, particularly when FFA fails to demonstrate the classical leopard spot pattern or when FFA is not possible.

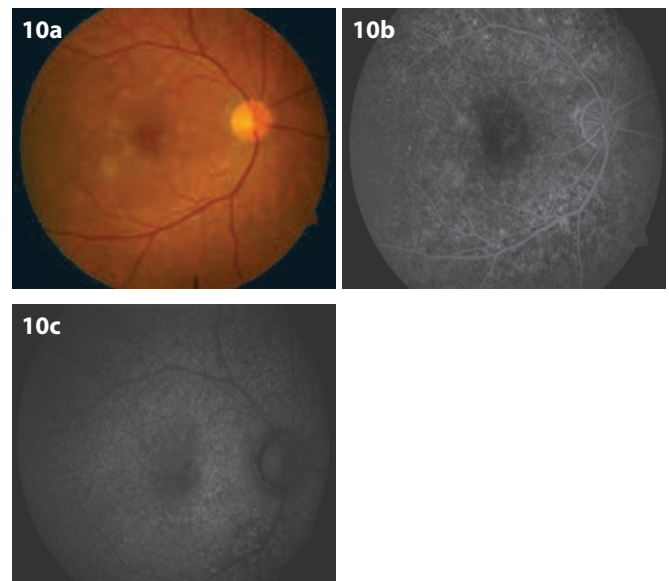


Figure 10: Subretinal deposits in primary vitreoretinal lymphoma (a), showing leopard spot appearance on FFA (b), and granular hyperautofluorescence on FAF (c).

Conclusion

Diseases of the retina and choroid involving alterations in the RPE and photoreceptors exhibit specific patterns on FAF imaging in active as well as healed stage. These phenotypic properties are utilized in analysis of FAF, which has emerged as a promising tool in routine clinical practice as it provides a quick, reliable, non-invasive method for diagnosing and monitoring these diseases.

References

- Schmitz-Valckenberg S, Holz FG, Bird AC, Spaide RF. Fundus autofluorescence imaging: Review and perspectives. *Retina* 2008;28:385-409.
- Bosch E, Horwitz J, Bok D. Phagocytosis of outer segments by retinal pigment epithelium: Phagosome-lysosome interaction. *J Histochem Cytochem* 1993;41:253-63.
- Herman KG, Steinberg RH. Phagosome movement and the diurnal pattern of phagocytosis in the tapetal retinal pigment epithelium of the opossum. *Invest Ophthalmol Vis Sci* 1982;23:277-90.
- Delori FC, Staurengi G, Arend O, Dorey CK, Goger DG, Weiter JJ. In vivo measurement of lipofuscin in Stargardt's disease – Fundus flavimaculatus. *Invest Ophthalmol Vis Sci* 1995;36:2327-31.
- Krebs J, Lois N, Forrester JV. Fundus autofluorescence. *Graefes Arch Clin Exp Ophthalmol* 2011;249:309.
- Wing GL, Blanchard GC, Weiter JJ. The topography and age relationship of lipofuscin concentration in the retinal pigment epithelium. *Invest Ophthalmol Vis Sci* 1978;17:601-607.
- Delori FC, Goger DG, Dorey CK. Age-related accumulation and spatial distribution of lipofuscin in RPE of normal subjects. *Invest Ophthalmol Vis Sci* 2001;42:1855-66.
- Sparrow JR, Nakanishi K, Parish CA. The lipofuscin fluorophore A2E mediates blue light-induced damage to retinal pigmented epithelial cells. *Invest Ophthalmol Vis Sci* 2000;41:1981-89.
- Eldred GE, Katz ML. Fluorophores of the human retinal pigment epithelium: separation and spectral characterization. *Exp Eye Res* 1988;47:71-86.
- Delori FC. Spectrophotometer for non-invasive measurement of intrinsic fluorescence and reflectance of the ocular fundus. *Appl Optics* 1994;33:7429-7452.
- Jorzik JJ, Bindewald A, Dithmar S, Holz FG. Digital simultaneous fluorescein and indocyanine green angiography, autofluorescence, and red-free imaging with a solid-state laser-based confocal scanning laser ophthalmoscope. *Retina* 2005;25:405-416.
- Rückmann AV, Fitzke FW, Bird AC. Distribution of fundus autofluorescence with a scanning laser ophthalmoscope. *Br J Ophthalmol*. 1995;79:407-412.
- Spaide RF. Fundus autofluorescence and age-related macular degeneration. *Ophthalmol* 2003;110:392-399.
- Delori FC, Dorey CK, Staurengi G, et al. In vivo fluorescence of the ocular fundus exhibits retinal pigment epithelium lipofuscin characteristics. *Invest Ophthalmol Vis Sci* 1995;36:718-729.
- Holz FG, Schmitz-Valckenberg S, Spaide RF, Bird AC. *Atlas of Fundus Autofluorescence Imaging*. Berlin: Springer, 2007.
- Fishkin NE, Sparrow JR, Allikmets R, Nakanishi K. Isolation and characterization of a retinal pigment epithelial cell fluorophore: an all-trans-retinal dimer conjugate. *Proc Natl Acad Sci USA*. 2005;102:7091-7096.
- Feeney L. Lipofuscin and melanin of human retinal pigment epithelium. *Invest Ophthalmol Vis Sci* 1978;17(7):583-600.
- Gabai A, Veritti D, Lanzetta P. Fundus autofluorescence applications in retinal imaging. *Indian J Ophthalmol* 2015;63:406-415.
- Hopkins J, Walsh A, Chakravarthy U. Fundus autofluorescence in age-related macular degeneration: An epiphenomenon? *Invest Ophthalmol Vis Sci* 2006;47:2269-71.
- Schmitz-Valckenberg S, Fleckenstein M, Scholl HP, Holz FG. Fundus autofluorescence and progression of age-related macular degeneration. *Surv Ophthalmol* 2009;54:96-117.
- Bindewald A, Bird AC, Dandekar SS, Dolar-Szczasny J, Dreyhaupt J, Fitzke FW, et al. Classification of fundus autofluorescence patterns in early age-related macular degeneration. *Invest Ophthalmol Vis Sci* 2005;46:3309-14.
- Delori FC, Fleckner MR, Goger DG, Weiter JJ, Dorey CK. Autofluorescence distribution associated with drusen in age-related macular degeneration. *Invest Ophthalmol Vis Sci* 2000;41:496-504.
- Spaide RF, Curcio CA. Drusen characterization with multimodal imaging. *Retina* 2010;30:1441-54.
- Lois N, Owens SL, Coco R, Hopkins J, Fitzke FW, Bird AC. Fundus autofluorescence in patients with age-related macular degeneration and high risk of visual loss. *Am J Ophthalmol* 2002;133:341-9.
- Holz FG, Bellman C, Staudt S, et al. Fundus autofluorescence and development of geographic atrophy in age-related macular degeneration. *Invest Ophthalmol Vis Sci* 2001;42:1051-1056.
- Khanifar AA, Lederer DE, Ghodasra JH, Stinnett SS, Lee JJ, Cousins SW, et al. Comparison of color fundus photographs and fundus autofluorescence images in measuring geographic atrophy area. *Retina* 2012;32:1884-91.
- Bearely S, Khanifar AA, Lederer DE, Lee JJ, Ghodasra JH, Stinnett SS, et al. Use of fundus autofluorescence images to predict geographic atrophy progression. *Retina* 2011;31:81-6.
- Bindewald A, Schmitz-Valckenberg S, Jorzik JJ, Dolar-Szczasny J, Sieber H, Keilhauer C, et al. Classification of abnormal fundus autofluorescence patterns in the junctional zone of geographic atrophy in patients with age related macular degeneration. *Br J Ophthalmol* 2005;89:874-8.
- Yung M, Klufas MA, Sarraf D. Clinical applications of fundus autofluorescence in retinal diseases. *Int J Retin Vitr* 2016;2:12 doi 10.1186/s40942-016-0035.
- Karadimas P, Bouzas EA. Fundus autofluorescence imaging in serous and drusenoid pigment epithelial detachments associated with age-related macular degeneration. *Am J Ophthalmol* 2005;140:1163-5.
- McBain VA, Townend J, Lois N. Fundus autofluorescence in exudative age-related macular degeneration. *Br J Ophthalmol* 2007;91:491-6.
- Vaclavik V, Vujosevic S, Dandekar SS, et al. Autofluorescence imaging in age-related macular degeneration complicated by choroidal neovascularization. A prospective study. *Ophthalmology* 2008;115:342-346.
- Batioglu F, Demirel S, Ozmert E, Oguz YG, Ozyol P. Autofluorescence patterns as a predictive factor for neovascularization. *Optom Vis Sci* 2014;91:950-5.
- Camacho N, Barteselli G, Nezgoda JT, et al. Significance of the hyperautofluorescent ring associated with choroidal neovascularization in eyes undergoing anti-VEGF therapy for wet age-related macular degeneration. *Br J Ophthalmol* 2015;99:1277-83.
- Sarraf D, Joseph A, Rahimy E. Retinal pigment epithelial tears in the era of intravitreal pharmacotherapy: risk factors, pathogenesis, prognosis and treatment (an American Ophthalmological Society thesis). *Trans Am Ophthalmol Soc* 2014;112:142-59.
- Nagiel A, Freund KB, Spaide RF, Munch IC, Larsen M, Sarraf D. Mechanism of retinal pigment epithelium tear formation following intravitreal anti-vascular endothelial growth factor therapy revealed by spectral-domain optical coherence tomography. *Am J Ophthalmol* 2013;156:981-8.e982.
- Mendis R, Lois N. Fundus autofluorescence in patients with retinal pigment epithelial (RPE) tears: an in vivo evaluation of RPE resurfacing. *Graefes Arch Clin Exp Ophthalmol* 2014;252:1059-63.
- Von Rückmann A, Fitzke FW, Gregor ZJ. Fundus autofluorescence in patients with macular holes imaged with a laser scanning ophthalmoscope. *Br J Ophthalmol* 1998;82:346-351.

39. Framme C, Walter A, Gabler B, et al. Fundus autofluorescence in acute and chronic-recurrent central serous chorioretinopathy. *Acta Ophthalmol Scand* 2005;83:161-167.
40. Spaide RF, Klancnik JM Jr. Fundus autofluorescence and central serous chorioretinopathy. *Ophthalmology* 2005;112:825-833.
41. Eandi CM, Ober M, Iranmanesh R, et al. Acute central serous chorioretinopathy and fundus autofluorescence. *Retina* 2005;25:989-993.
42. Pang CE, Shah VP, Sarraf D, Freund KB. Ultra-widefield imaging with autofluorescence and indocyanine green angiography in central serous chorioretinopathy. *Am J Ophthalmol* 2014;158:362-71.
43. McBain VA, Forrester JV, Lois N. Fundus autofluorescence in the diagnosis of cystoid macular edema. *Br J Ophthalmol* 2008;92:946-9.
44. Pece A, Isola V, Holz FZ, Milani P, Brancato R. Autofluorescence imaging of cystoid macular edema in diabetic retinopathy. *Ophthalmologica* 2010;224:230-5.
45. Vujosevic S, Casciano M, Pilotto E, Boccassini B, Varano M, Midena E. Diabetic macular edema: Fundus autofluorescence and functional correlations. *Invest Ophthalmol Vis Sci* 2011;52:442-8.
46. Chung H, Park B, Shin HJ, Kim HC. Correlation of fundus autofluorescence with spectral-domain optical coherence tomography and vision in diabetic macular edema. *Ophthalmology* 2012;119:1056-65.
47. Lois N, Halfyard AS, Bird AC, Holder GE, Fitzke FW. Fundus autofluorescence in Stargardt macular dystrophy-fundus flavimaculatus. *Am J Ophthalmol* 2004;138:55-63.
48. Burke TR, Duncker T, Woods RL, et al. Quantitative fundus autofluorescence in recessive stargardt disease. *Invest Ophthalmol Vis Sci* 2014;55:2841-52.
49. Chowers I, Tiosano L, Audo I, Grunin M, Boon CJ. Adult-onset foveomacular dystrophy: a fresh perspective. *Prog Retin Eye Res* 2015;47:64-85.
50. Furino C, Boscia F, Cardascia N, Sborgia L, Sborgia C. Fundus autofluorescence, optical coherence tomography and visual acuity in adult-onset foveomacular dystrophy. *Ophthalmologica* 2008;222:240-4.
51. Parodi MB, Iacono P, Pedio M, et al. Autofluorescence in adult-onset foveomacular vitelliform dystrophy. *Retina* 2008;28:801-7.
52. Duncker T, Greenberg JP, Ramachandran R, et al. Quantitative fundus autofluorescence and optical coherence tomography in best vitelliform macular dystrophy. *Invest Ophthalmol Vis Sci* 2014;55:1471-82.
53. Parodi MB, Iacono P, Campa C, Del Turco C, Bandello F. Fundus autofluorescence patterns in Best vitelliform macular dystrophy. *Am J Ophthalmol* 2014;158:1086-92.
54. Boon CJ, Jeroen Klevering B, Keunen JE, Hoyng CB, Theelen T. Fundus autofluorescence imaging of retinal dystrophies. *Vision Res* 2008;48:2569-77.
55. Murakami T, Akimoto M, Ooto S, et al. Association between abnormal autofluorescence and photoreceptor disorganization in retinitis pigmentosa. *Am J Ophthalmol* 2008;145:687-94.
56. Robson AG, Tufail A, Fitzke F, et al. Serial imaging and structure-function correlates of high-density rings of fundus autofluorescence in retinitis pigmentosa. *Retina* 2011;31:1670-9.
57. Greenstein VC, Duncker T, Holopigian K, et al. Structural and functional changes associated with normal and abnormal fundus autofluorescence in patients with retinitis pigmentosa. *Retina* 2012;32:349-57.
58. Fleckenstein M, Charbel Issa P, Fuchs HA, et al. Discrete arcs of increased fundus autofluorescence in retinal dystrophies and functional correlate on microperimetry. *Eye (Lond)* 2009;23:567-75.
59. Kellner U, Renner AB, Tillack H. Fundus autofluorescence and mfERG for early detection of retinal alterations in patients using chloroquine/hydroxychloroquine. *Invest Ophthalmol Vis Sci* 2006;47:3531-3538.
60. Duncker T, Tsang SH, Lee W, Zernant J, Allikmets R, Delori FC, et al. Quantitative fundus autofluorescence distinguishes ABCA4-associated and non-ABCA4-associated bull's eye maculopathy. *Ophthalmology* 2015;122:345-55.
61. Tugcu B, Ozdemir H. Imaging methods in the diagnosis of optic disc drusen. *Turk J Ophthalmol* 2016;46:232-236.
62. Sato T, Mrejen S, Spaide RF. Multimodal imaging of optic disc drusen. *Am J Ophthalmol* 2013;156:275-282.
63. Gili P, Flores-Rodriguez P, Yanguela J, Fernandez MLH. Using autofluorescence to detect optic nerve head drusen in children. *J Am Assoc Pediatr Ophthalmol Strabismus* 2013;17:568-571.
64. Furino C, Boscia F, Cardascia N, Alession G, Sborgia C. Fundus autofluorescence and multiple evanescent white dot syndrome. *Retina* 2009;29:60-3.
65. Spaide RF, Goldberg N, Freund KB. Redefining multifocal choroiditis and panuveitis and punctate inner choroidopathy through multimodal imaging. *Retina* 2013;33:1315-24.
66. Klufas MA, O'Hearn T, Sarraf D. Optical coherence tomography angiography and widefield fundus autofluorescence in punctate inner choroidopathy. *Retin Cases Brief Rep* 2015;9:323-6.
67. Turkuoglu P, Chang PY, Rentiya ZS, et al. Mycophenolate mofetil and fundus autofluorescence in the management of recurrent punctate inner choroidopathy. *Ocul Immunol Inflamm* 2011;19:286-292.
68. Spaide RF. Autofluorescence imaging of acute posterior multifocal placoid pigment epitheliopathy. *Retina* 2006;26:479-82.
69. Souka AA, Hillenkamp L, Gora F, Gabel VP, Framme C. Correlation between optical coherence tomography and autofluorescence in acute posterior multifocal placoid pigment epitheliopathy. *Graefes Arch Clin Exp Ophthalmol* 2006;244:1219-23.
70. Gupta A, Bansal R, Gupta V, Sharma A. Fundus autofluorescence in serpiginous like choroiditis. *Retina* 2012;32(4): 814-25.
71. Bansal R, Gupta A, Gupta V. Imaging in the diagnosis and management of serpiginous choroiditis. *International Ophthalmology Clinics* 2012;52:229-236.
72. Bansal R, Kulkarni P, Gupta A, Gupta V, Dogra MR. High-resolution spectral domain optical coherence tomography and fundus autofluorescence correlation in tubercular serpiginouslike choroiditis. *J Ophthalmic Inflamm Infect* 2011;1:157-163.
73. Bansal R, Gupta A, Gupta V, Dogra MR, Sharma A, Bamberg P. Tubercular serpiginouslike choroiditis presenting as multifocal serpiginoid choroiditis. *Ophthalmology* 2012 Nov;119(11):2334-42.
74. Samy A, Lightman S, Ismetova F, Talat L, Tomkins-Netzer O. Role of autofluorescence in inflammatory/infective diseases of the retina and choroid. *J Ophthalmol* 2014;2014:418193. doi: 10.1155/2014/418193. Epub 2014 Apr 1.
75. Koizumi H, Maruyama K, Kinoshita S. Blue light and near-infrared fundus autofluorescence in acute Vogt-Koyanagi-Harada disease. *Br J Ophthalmol* 2010;94:1499-1505.
76. Ayata A, Dogru S, Senol MG, Unal M, Ersanli D, Bilge AH. Autofluorescence findings in Vogt-Koyanagi-Harada disease. *Eur J Ophthalmol* 2009;19:1094-97.
77. Casady M, Faia L, Nazemzadeh M, Nussenblatt R, Chan CC, Sen HN. Fundus autofluorescence patterns in primary intraocular lymphoma. *Retina* 2014;34:366-372.
78. Ishida T, Ohno-Matsui K, Kaneko Y, et al. Fundus autofluorescence patterns in eyes with primary intraocular lymphoma. *Retina* 2010;30:23-32.

Current role of OCT angiography in vitreoretinal diseases

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Introduction

Technologies for multimodal digital imaging of vitreoretinal diseases have improved the accuracy of diagnosis and the depth of the knowledge of the mechanisms of disease and their response to treatments. Optical coherence tomography angiography (OCTA) is one such technology which uses a special processing algorithm developed for existing high speed OCT devices. It is an emerging and promising approach that provides non-invasive imaging of retinal and choroidal vessels at capillary level in a matter of few seconds.

OCT-A is a relatively new technology, but it carries the potential to significantly change the routine assessment and characterization of certain retinal and choroidal diseases. The aim of this review is to provide some general information about OCTA and to discuss about the current aspects of this technology in the diagnosis and management of vitreo-retinal diseases.

Principle of OCTA

The common principle OCTA uses to acquire the image is motion contrast detection. The device notes differences between multiple, rapidly repeated OCT B scans at each individual cross section of the retina and assumes them to be due to erythrocyte movement within blood vessels. These “decorrelation signals” create a vascular map called an OCT angiogram. [1-3] The various angiographic approaches can be roughly categorized into three groups: [4-6]

1. Angiography based on the phase of OCT signal- Speckle variance
2. Angiography based on the amplitude /intensity of OCT signal- split-spectrum amplitude decorrelation angiography (SSADA), OCT angiography ratio analysis (OCTARA), speckle variance

3. Angiography based on both the intensity and phase of OCT signal, i.e. complex signal- optical microangiography (OMAG)

OCTA requires higher imaging speeds in order to obtain a densely sampled volume which is possible only with Fourier domain OCT systems like spectral-domain (SD-OCT) [7,8] and swept-source OCT [9,10]. OCTA works by evaluating the difference between sequential OCT B-scans in the retina. Since the tissue structure does not change in this short interval, change is attributed to movement of erythrocytes within the blood vessel lumen. The signal is perceived in terms of changes in amplitude, intensity or combination of both (Complex) and the data is computed to form the final OCTA image. In a recent study, when all the above algorithms were compared, it was found that OMAG utilizing complex OCT signals to contrast retinal blood flow provided the best visual result for the imaging of retinal microvascular networks concerning image contrast and vessel connectivity. [5]

OCTA in normal eyes

As OCTA is a depth-resolved technique, precise axial segmentation of retinal layers is needed as to acquire important data on perfused structures simultaneously. The image is displayed as an enface map of the vasculature over the entire region of the scan in one image. To achieve this, several methods have been employed. An automated segmentation algorithm is provided by the majority of different OCTA devices [11-16] This algorithm is capable of providing an extremely fast way to delineate the presence of a decorrelation signal and to distinguish different retinal layers, from the inner limiting membrane (ILM) to the RPE. Second method is to do manual segmentation [17], where selection of C-scans at different depths is performed with either horizontal or variably shaped sections is done manually.

The superficial inner retina segmentation (Figure 1a) shows

vasculature in the retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL). Superficial capillary plexus (SCP) are arranged linearly which converge to fovea forming a web. (Fig 1a) The vascular plexuses at the border of the inner plexiform layer (IPL) and inner nuclear layer (INL) and the border of the INL and outer plexiform layer (OPL) are displayed by the deep retina segmentations (Fig 1b). The deep capillary plexus (DCP) is formed of fine interwoven vessels with thin horizontal and radial interconnections. The outer retina segmentation (Figure 1c) in normal eyes should show no blood flow between the OPL and Bruch membrane. A 10-µm slice directly below Bruch membrane is shown by the choriocapillaris segmentation (Fig 1d). [18]

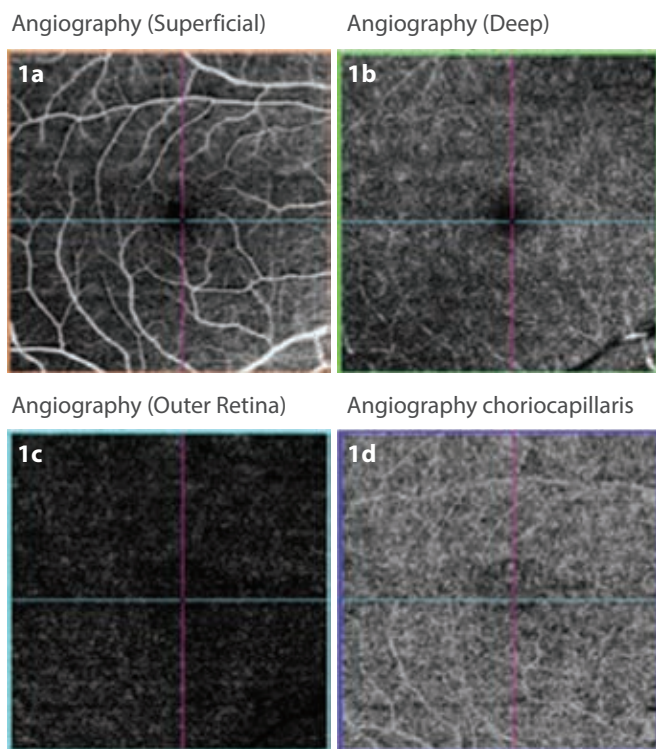


Fig 1 - Segmentation of different vascular layers using OCTA: superficial plexus (1a), deep plexus (1b) of the inner retina. Also shown are the outer retina (1c) and choriocapillaris (1d). Note the homogeneity of each plexus, the lack of blood flow in outer retina and small round foveal avascular zone (red arrow head).

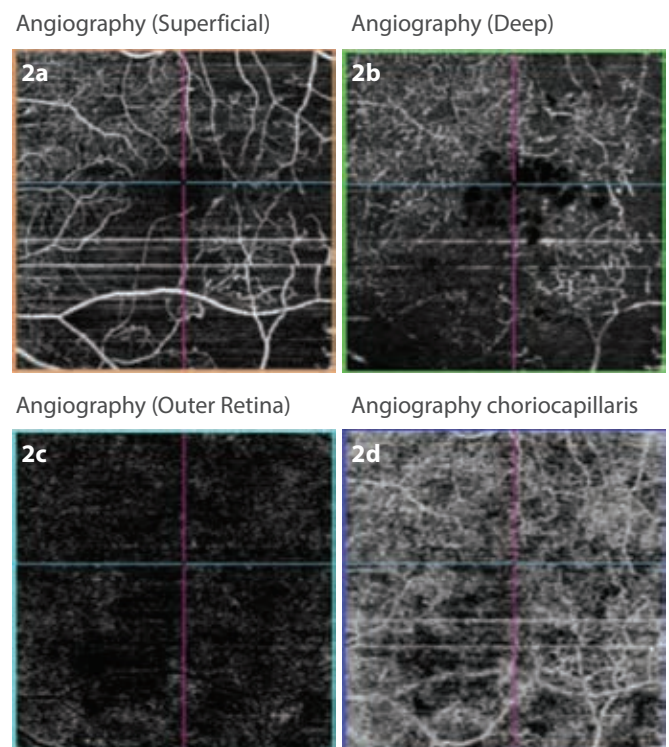
Update on clinical applications of OCTA

OCTA can detect changes in blood vessel flow in a variety of retinal vascular diseases. This may include, but is not limited to, idiopathic macular telangiectasia and diseases associated with choroidal neovascular membrane (CNV), such as occult central serous choroidopathy, myopic degeneration and age related macular degeneration. Additionally, OCTA may be particularly useful in the evaluation of vascular ischemic diseases, such as retinal vascular occlusive disease (retinal vein and artery occlusion) and diabetic retinopathy.

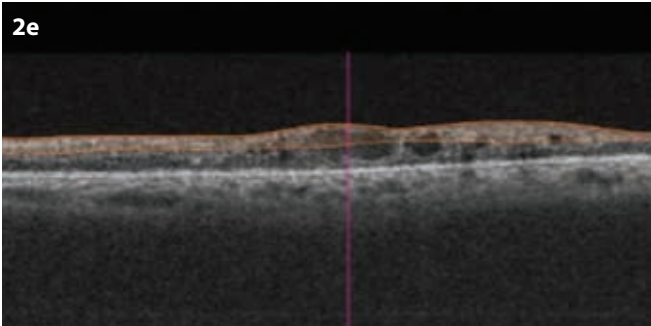
OCTA in diabetic retinopathy

Diabetic microangiopathy leading to capillary ischemia impairs the nutrition of the neuroglial tissues in the retinal parenchyma. The resultant hypoxia leads to angiogenic responses and increased vascular permeability^[20,21], causing ischemic maculopathy, proliferative diabetic retinopathy (PDR) and diabetic macular edema (DME). OCTA provides greater detail of most microvascular abnormalities, such as enlarged FAZ, capillary non perfusion areas (CNP) and intraretinal microvascular abnormalities.^[7]

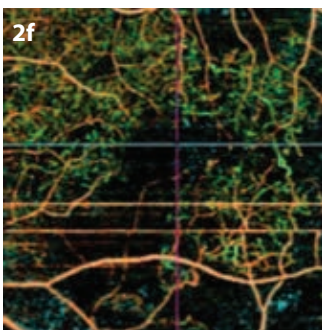
In a recent study conducted by Peres et al,^[22] where the authors compared the visualization of microaneurysms (MA) and the foveal avascular zone (FAZ) area using spectral-domain OCTA and FA. The different vascular plexuses can be segmented using OCTA for enhanced imaging to determine which plexus is more affected. OCTA images were automatically segmented into superficial (sOCTA) and deep (dOCTA) capillary plexuses. The study concluded that deep plexus OCTA can better identify microaneurysms compared to either sOCTA or FA. The FAZ area appeared larger on FA in contrast to OCTA of both plexuses. (Shown in fig. 2)



OCT B-Scan



Composite Angiography



Fundus

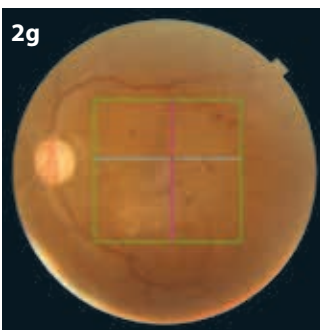


Fig 2a and 2b - An enlarged FAZ, capillary non-perfusion and other retinal microvascular abnormalities in a case of DR.

OCTA has the superior ability to delineate the vessels surrounding the foveal avascular zone. In contrast, perifoveal leakage of fluorescein dye may blur the FAZ margins, and thus FA is limited to primarily delineating the superficial vascular plexus. OCTA shows that the FAZ and perifoveal intercapillary areas are enlarged with each advancing stage of DR.^[23] Increased FAZ size has been correlated to reduced visual acuity prognosis in eyes with retinal vascular disease.^[24]

Also, neovascularization of the optic nerve, which can occur in proliferative DR and ischemic retinopathy, can be easily detected using OCTA (Fig 3) by viewing the inner retina/optic nerve surface at the most superficial level.^[25]

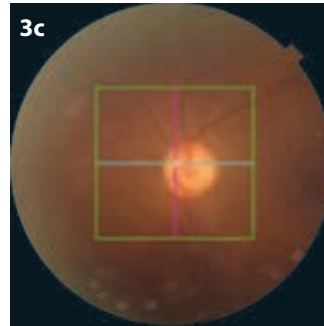
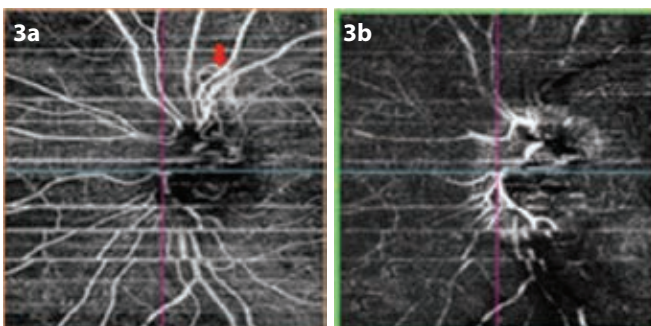


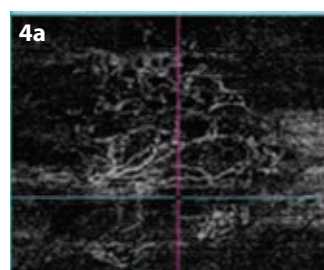
Fig 3- OCTA of the vitreous (3a) demonstrates some well-delineated, fine, abnormal vascular network. The red arrow point to the presence of the decorrelation signal on the vitreous interface, indicative of neovascularization flow.

OCTA in age related macular degeneration (AMD)

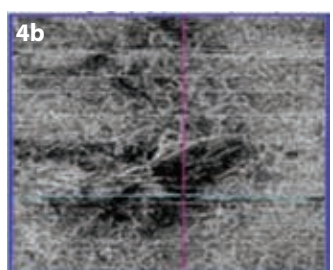
Segmentation allowing visualization of choriocapillaris together with outer retinal segmentation between the outer plexiform layer and Bruch's membrane enables detection of Choroidal neovascularization (CNV) and its feeder vessels with high sensitivity and specificity.^[26, 27] OCTA can be used to determine the location of the CNV, its morphology and its response to anti-VEGF therapy. Variety of CNV configurations have been described by the authors including well circumscribed "sea fan" or poorly defined "long filamentous" CNV. OCTA may be able to detect early CNV prior to visualization on FA. Because OCTA is noninvasive it can be repeated frequently to monitor treatment response by changes in subretinal and intraretinal fluid as well as CNV size and morphology.^[28]

The superior capability of OCTA to visualize finer vessels in the CNV network, it is gaining priority over FA in the follow-up after anti-VEGF therapy. In contrast, due to the leakage of the dye exact delineation of vascular net becomes cumbersome. A loss of fine vasculature of the CNV has been noted in patients who receive anti-VEGF therapy.

Angiography (Outer Retina)



Angiography choriocapillaris



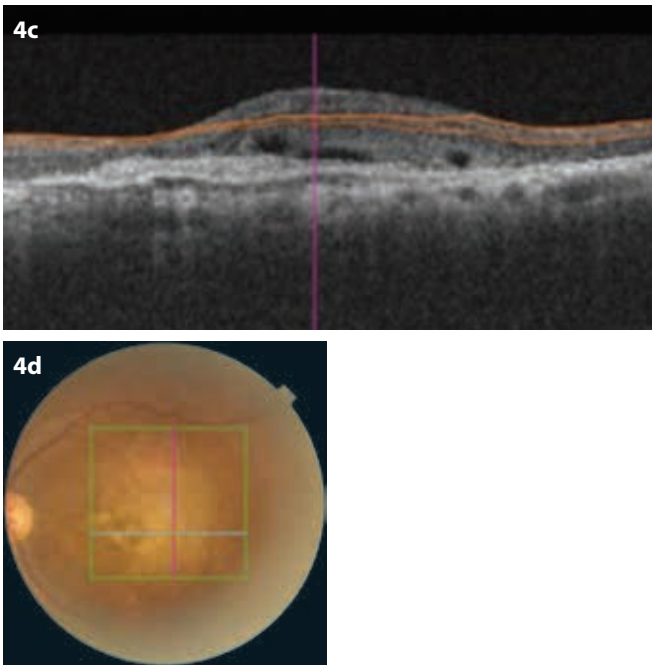


Fig 4 - OCT-A provides a superior visualization of the newly formed vessels and depth-resolved resolution of vascular perfusion – neovascularization is clearly visible in deeper layers (4a and 4 b)

Current research focuses on analysis of OCTA patterns of CNV and their potential correspondence to quiescent and progressive CNV characteristics. In a similar study, the investigators imaged CNV using OCTA and compared with the traditional multimodal imaging (FA and OCT).^[26] They graded it according to the presence or absence of the following features: well-defined CNV; presence of tiny capillaries; presence of anastomoses and loops; morphology of the vessels termini as opposed to a “dead tree” aspect; and presence of a hypo-intense halo surrounding the CNV. They found a 95-percent agreement between OCTA and the traditional multimodal imaging protocol for a “treatment required” decision in eyes with at least three out of the five features. There was a 91-percent agreement for “treatment not required” when patients presented with fewer than three features.

A recent study on type 1 CNV which included 105 eyes concluded that en face OCTA and structural OCT showed better detection of type 1 NV than either FA alone or en face OCTA alone. In this study, 51.3% of cases demonstrated a small or large dark ring around the type 1 NV on OCTA. ^[28] The possibility suggested was the lower flow rate occurring at the margins of certain neovascular lesions. Earlier studies conducted by Jia et al and McLeod had also suggested similar findings and they attributed the halo to be due to mechanical compression of the underlying choriocapillaris from the exudative changes leading to alterations in normal blood flow in the choriocapillaris and darkening on

OCTA imaging.^[29,30]

Swept-source OCT offers better penetration of choroid and visualization of the choriocapillaris owing to the use of longer-wave-length and higher scan speed. Earlier stages of dry AMD are found to be associated with patchy thinning of the choriocapillaris, while geographic atrophy is associated with loss of choriocapillaris lying under the area of geographic atrophy (GA) and asymmetric alteration of choriocapillaris at its margin as shown in fig 5a and 5b. ^[31, 32]

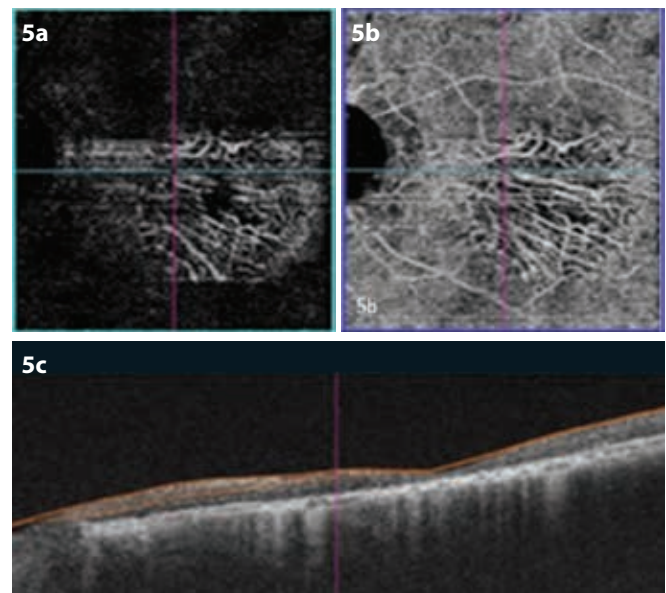


Fig 5a and 5b - En-face OCTA in Dry AMD demonstrating alteration of choriocapillaries in the area of GA. Larger choroidal vessels have been push inward into the area of choriocapillaris.

OCTA in polypoidal choroidal vasculopathy (PCV)

In PCV, optical coherence tomography angiography may inconsistently image the polyps when compared to indocyanin green angiography. However OCTA can the choroidal neovascular network even in such cases. ^[33]

OCTA in retinal dystrophies

The improved resolution of OCTA compared with FA allows for easier visualization of retinal changes in eyes with inherited diseases such as retinitis pigmentosa and Stargardt disease. They have progressive photoreceptor and RPE loss, OCTA shows overlying retinal thinning and increased intercapillary area, FAZ abnormalities and choriocapillaris loss or decreased perfusion below the absent RPE, similar to that seen in geographic atrophy. ^[34]

Conclusion

OCTA generates high-resolution images that are qualitatively similar to retinal vasculature imaged with conventional fluorescein angiography. As OCTA is completely non-invasive, it may be performed with greater ease and frequency than conventional fluorescein angiography. OCT holds promise for improving the detection and monitoring of other disorders involving the pathologic growth or condition of blood vessels in the inner retina, outer retina, and choriocapillaris.

References

- de Carlo TE, de Carlo TE, Bonini Filho MA, Chin AT, et al. Spectral-domain optical coherence tomography angiography of choroidal neovascularization. *Ophthalmology* 2015;122:1228.
- Jonathan E, Enfield J, Leahy MJ. Correlation mapping method for generating microcirculation morphology from optical coherence tomography (OCT) intensity images. *J Biophotonics* 2011;4:583-587.
- An L, Wang RK. In vivo volumetric imaging of vascular perfusion within human retina and choroids with optical micro-angiography. *Optics express* 2008;16:11438-11452
- Meng-Tsan T, Ting-Ta C, Hao-Li L, et al. Microvascular imaging using swept-source optical coherence tomography with single-channel acquisition. *Applied Physics Express*. 2011; 4: 097001.
- Zhang A, Zhang Q, Chen CL, Wang RK, Methods and algorithms for optical coherence tomography-based angiography: a review and comparison, *J Biomed Opt*, 2015.
- Leitgeb R, Schmetterer L, Drexler W., Fercher A., Zawadzki R., Bajraszewski T, "Real-time assessment of retinal blood flow with ultrafast acquisition by color Doppler Fourier domain optical coherence tomography," *Opt. Express* 11(23), 3116–3121 (2003).
- Wojtkowski M, Leitgeb R, Kowalczyk A, Bajraszewski T, Fercher AF. In vivo human retinal imaging by Fourier domain optical coherence tomography. *J Biomed Opt*. 2002; 7: 457–463.
- Nassif N, Cense B, Park B, et al. In vivo high-resolution video-rate spectral-domain optical coherence tomography of the human retina and optic nerve. *Opt Express*. 2004; 12: 367–376.
- Yun S, Tearney G, de Boer J, Iftimia N, Bouma B. High-speed optical frequency-domain imaging. *Opt Express*. 2003; 11: 2953–2963.
- Lee EC, de Boer JF, Mujat M, Lim H, Yun SH. In vivo optical frequency domain imaging of human retina and choroid. *Opt Express*. 2006; 14: 4403–4411.
- Starengi G, Cunha-Vaz J, Korobelnik JF, Optical coherence tomography angiography of the retinal microvasculature using the Zeiss AngioPlex, *European Ophthalmic Review*, 2015;9:147–56.
- Huang Y, Zhang Q, Thorell MR, et al., Swept-source OCT angiography of the retinal vasculature using intensity differentiation-based optical microangiography algorithms, *Ophthalmic Surg Lasers Imaging Retina*, 2014;45:382–9
- de Carlo ET, Bauml CR, *Advances in optical coherence tomography angiography*, *US Ophthalmic Review*, 2016;9:37–40.
- Coscas G, Lupidi M, Coscas F, Heidelberg Spectralis Optical Coherence Tomography Angiography: Technical Aspects. In: Bandello F, Souied EH, Querques G (eds), *OCT Angiography in Retinal and Macular Diseases*, *Dev Ophthalmol*, Basel: Karger, 2016;56:1–5.
- Stanga PE, Tsamis E, Papayannis A, et al., Swept-source optical coherence tomography angio™ (Topcon Corp, Japan): technology review, *Dev Ophthalmol*, 2016;56:13–7.
- Swept-Source OCT Angiography: SS OCT Angio™, 2015. Available at: www.topcon-medical.es/files/Local_TES/Estudios_clinicos/DRI_OCT_Triton_SS_OCT_Angio_Whitepaper_E_201511.pdf.
- Coscas G, Lupidi M, Coscas F. Image Analysis of Optical Coherence Tomography Angiography. In: *OCT Angiography in Retinal and Macular Diseases*. Karger Publishers (2016).
- Chalam K V, Sambhav K. Optical coherence tomography angiography in retinal diseases. *J Ophthalmic Vis Res* 2016;11:84-92

OCTA in DR

- de carlo TE, Moulton E, Choi W, et al. *Clinical OCT angiography Atlas*, 1st Edition. New delhi, India.
- Aiello, L. P. et al. Vascular endothelial growth factor in ocular fluid of patients with diabetic retinopathy and other retinal disorders. *N Engl J Med* 331, 1480–1487 (1994).
- Antonetti, D. A., Klein, R. & Gardner, T. W. Diabetic retinopathy. *N Engl J Med* 366, 1227–1239 (2012).
- Peres MB, Kato RT, Kniggendorf VF, Cole ED, Onal S, Torres E, Louzada R, Belfort R Jr, Duker JS, Novais EA, Regatieri CV. Comparison of Optical Coherence Tomography Angiography and Fluorescein Angiography for the Identification of Retinal Vascular Changes in Eyes With Diabetic Macular Edema. *Ophthalmic Surg Lasers Imaging Retina*. 2016 Nov 1;47(11):1013-1019.
- Parodi MB, Visintin F, Della Rupe P, et al. Foveal avascular zone in macular branch retinal vein occlusion. *Int Ophthalmol* 1995;19:25-28.
- Salz DA, de Carlo TE, Adhi M, et al. Select features of diabetic retinopathy on swept-source optical coherence tomographic angiography compared with fluorescein angiography and normal eyes. *JAMA Ophthalmol* 2016;134:644-650.
- de Carlo TE, Bonini Filho MA, Bauml CR, et al. Evaluation of preretinal neovascularization in proliferative diabetic retinopathy using optical coherence tomography angiography. *Ophthalmic Surg Lasers Imaging Retina* 2016;47:115-119.

OCTA in AMD

- Coscas GJ, Lupidi M, Coscas F, et al. Optical coherence tomography angiography versus traditional multimodal imaging in assessing the activity of exudative age-related macular degeneration: A new diagnostic challenge. *Retina* 2015;35:2219.
- Bandello F, Souied EH, Querques G (eds): *OCT Angiography in Retinal and Macular Diseases*. *Dev Ophthalmol*. Basel, Karger, 2016, vol 56, pp 91-100.
- Waheed NK, Moulton EM, Fujimoto JG, Rosenfeld PJ. Optical Coherence Tomography Angiography of Dry Age-Related Macular Degeneration. *Dev Ophthalmol*. 2016;56:91-100.
- Jia Y, Bailey ST, Wilson DJ, et al. Quantitative optical coherence tomography angiography of choroidal neovascularization in age-related macular degeneration. *Ophthalmology*. 2014; 121: 1435–1444.
- McLeod DS, Grebe R, Bhutto I, et al. Relationship between RPE and choriocapillaris in age-related macular degeneration. *Invest Ophthalmol Vis Sci*. 2009; 50: 4982–4991.
- Bandello F, Souied EH, Querques G (eds): *OCT Angiography in Retinal and Macular Diseases*. *Dev Ophthalmol*. Basel, Karger, 2016, vol 56, pp 91-100.
- Waheed NK, Moulton EM, Fujimoto JG, Rosenfeld PJ. Optical Coherence Tomography Angiography of Dry Age-Related Macular Degeneration. *Dev Ophthalmol*. 2016;56:91-100.
- Kim JY, Kwon OW, Oh HS, You YS. Optical coherence tomography angiography in patients with polypoidal choroidal vasculopathy. *Graefes Arch Clin Ophthalmol*. 2016; 254: 1505-1510.
- de Carlo TE, Adhi M, Salz DA, et al. Analysis of choroidal and retinal vasculature in inherited retinal degenerations using optical coherence tomography angiography. *Ophthalmic Surg Lasers Imaging Retina*. 2016;47:120-127.

Vitreotomy with silicone oil tamponade in rhegmatogenous retinal detachment following acute retinal necrosis: Clinical outcomes and prognostic factors

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Abstract

Purpose

To report the prognostic factors and outcomes of vitrectomy (PPV) with silicone oil tamponade in rhegmatogenous retinal detachment (RRD) secondary to acute retinal necrosis (ARN).

Methods

This retrospective, non-randomized, interventional comparative study included 38 eyes of 38 patients. All cases underwent PPV with silicone oil tamponade. The main outcome measure was improvement of final visual acuity relative to the presenting visual acuity and factors affecting the same. Group A included eyes with improved vision and Group B included eyes with no improvement of vision.

Results

Factors predicting favorable treatment outcome

Factor predicting favorable outcome	Odds ratio	95% C.I. for the odds ratio	P value
RD developing later than at presentation with ARN	8.4	1.53-46.1	0.01
Administration of systemic steroids	5.2	1.14-23.54	0.03
Usage of valcyclovir instead of intravenous acyclovir	4.33	1.05-17.84	0.04
Non-occurrence of recurrent RD	6.25	1.37-28.5	0.01

Group A included 16 eyes (42.10%), group B included 22 eyes (57.89%). In Group A, 2 eyes out of 16 (12.5%) and in Group B, 12 eyes out of 22 (54.54%) had RRD at presentation ($p=0.02$, 95% C.I.

for the difference 7.88%-65.78%). The time interval between first presentation and development of RRD in Group A was 30.94 ± 38.8 days (median 30 days) whereas that in Group B was 10.81 ± 11.73 days (median 8 days) ($p = 0.02$). The odds of visual improvement post vitrectomy when RRD occurred later was 8.4 ($p = 0.01$, 95% C.I. 1.53-46.1). The usage of systemic steroids (odds 5.2, $p=0.03$, 95% C.I. 1.14-23.54) and oral valacyclovir (Odds 4.33 $p=0.04$, 95% C.I. 1.05-17.84) were associated with odds favoring a good visual outcome. Recurrent RRD was noted in 3/16 eyes (18.75%) in Group A and 13/22 eyes (59.09%) in Group B ($p=0.03$).

Conclusion

Delayed occurrence of RRD after ARN is a good prognostic factor. Usage of systemic steroids and oral valacyclovir are associated with a favorable visual outcome.

Manuscript

Introduction

Acute retinal necrosis (ARN) is a relatively rare retinal infection which is caused by varicella zoster (VZV) and herpes simplex viruses (HSV).^[1,2] The disease can be unilateral or bilateral with a guarded visual prognosis. The course is often complicated by a secondary rhegmatogenous retinal detachment (RRD). RRD is known to occur in 25%-75% of eyes following viral retinitis.^[3-6] The propounded mechanism for development of RRD is traction on the necrotic retina due to the inflamed vitreous and inflammatory membranes.^[7] Till date the optimal approach to RRD following ARN is unclear. Due to rarity of the condition there is paucity of literature on the long term outcomes of PPV for RRD in ARN in a large cohort of patients. Factors predicting better outcomes and those predicting worse prognosis are also not clear. In the current study we describe the long-term visual and anatomic outcome of vitreous surgery for RRD in ARN.

Materials and Methods

This was a retrospective, non-randomized, interventional comparative case series. The study was conducted at a tertiary eye care center in Southern India after taking appropriate institutional review board approval. Case records of all patients diagnosed with RRD following ARN from January 2000 to December 2015 which underwent PPV were reviewed. The diagnosis of ARN was based on the criteria described by the American Uveitis Society.^[8] Cases were diagnosed by the presence of one or more foci of retinal necrosis with discrete borders located in peripheral retina, rapid circumferential spread of the disease, evidence of occlusive vasculopathy and a prominent inflammatory panuveitis. Demographic and clinical data noted included age, gender, duration of symptoms, vision at presentation, interval between presentation and development of RRD, usage of systemic steroids, final visual acuity, anatomic outcome and associated complications. A favorable visual outcome was defined as final visual acuity of 20/400 or more.^[9,10]

Treatment

All cases of ARN were diagnosed clinically. The patients were started on systemic antivirals (oral valacyclovir or intravenous acyclovir) as per the treating physician's preference and the economic considerations on a case to case basis. Oral valacyclovir was given in a dosage of 1 gram three times per day whereas intravenous acyclovir was given as 6mg/kg 3 times per day. Oral steroids were added to control the inflammation in a dose of 1mg/kg body weight per day. Topical steroids and cycloplegics were prescribed as per the inflammation in the anterior chamber.

Retinal detachment was managed by a sutureless pars plana vitrectomy, endolaser of the breaks and injection of 5000 centistokes silicone oil. In case of concurrent ARN with detachment, retinal detachment repair was deferred till the inflammation was reasonably controlled (7-10 days).

Statistical analysis

The data was arranged on an excel spread sheet for statistical analysis. The data was arranged on an Excel spread sheet. Relevant statistical analysis was done using MedCalc ver 12.2.1.0. for statistical analysis, vision was converted from Snellen to logMAR equivalents. Mean and standard deviations were computed for all continuous variables. In case of non-parametric distribution, median was calculated. Pre and post operative data was compared using the paired t test in parametric data and Wilcoxon rank sum test in non parametric data. Odds ratio were computed for the possible risk factors with appropriate confidence intervals. Simple logistic regression formula was used

to assess co-relation between continuous independent variables and the dichotomous outcome variable. A p value of <0.05 was assigned as statistically significant.

Results

Demographic characteristics of Group A and Group B

	Improved (16 eyes)	Not Improved (22eyes)	P value
Males	75%	68.2%	0.9
Age	27.5±12.23	33.31±12.03	0.15
Vision at presentation logMAR	1.42±0.8	1.4±0.7	0.9
Vision in logMAR at last visit	1.02±0.54	1.58±0.92	0.03
IOP at presentation	12.56±6.05	11.8±3.24	0.62
RD at presentation	2, (12.5%)	12, (54.54%)	0.02
Interval between presentation and development of RD	10.81±11.73 (8)	30.94±38.8 (30)	0.02
Oral steroids given	12.56±6.05	11.8±3.24	0.62
Initial PPV	2, (12.5%)	12, (54.54%)	0.02
SOR done	12.56±6.05	11.8±3.24	0.62
Recurrent RD	2, (12.5%)	12, (54.54%)	0.02

The study included 38 eyes of 38 patients which underwent PPV for RRD secondary to ARN. Males accounted for 75% of the patients. The outcome groups were divided into two for analysis. Group A included eyes which had a favorable visual outcome (16 eyes) and Group B included eyes which had a non-favorable outcome (22 eyes). The mean age at presentation in Group A was 27.5±12.23 years while that in Group B was 33.31±12.03 years (p=0.15). The mean presenting vision in logMAR (Snellen acuity) was 1.42±0.8 (20/526) in Group A and 1.4±0.7 (20/256) in Group B (p=0.9). RRD at presentation was seen in 2/16 eyes (12.5%) in Group A and in 12/22 eyes (54.54%) in Group B (p=0.02). The mean final visual acuity in logMAR (Snellen Acuity) was 1.02±0.54 (20/209) in Group A and 1.58±0.92 (20/760) in Group B (p=0.03). The interval between presentation and development of RRD was 10.81±11.73 days (median = 8) in Group A and 30.94±38.8 days (median =30) in Group B (p=0.02). The total follow up noted was 34.81±44.27 months (median 16 months, range 1 - 180 months). Recurrent RRD was noted in 3/16 eyes (18.75%) in Group A and 13/22 eyes (59.09%) in Group B (p=0.01). Silicone oil removal (SOR) was done in 9 eyes (56.25%) in Group A and in 6 eyes (27.27%) in Group B (p=0.13). Among the 15 eyes that underwent SOR anatomical good outcome was achieved in 6 eyes (27.27%). Among the remaining 9 eyes, 1 developed phthisis bulbi, 3 developed hypotony and 5 developed recurrent retinal

detachment. All recurrences were re-operated and were finally attached. Optic neuropathy was seen in 10/38 eyes (26.31%) of which 4 were in Group A and 6 in group B ($p=0.87$). The cases which developed optic neuropathy along the follow up had a poorer final visual acuity as compared to the presenting visual acuity. In this subset, the visual acuity decreased from a median of logMAR 1.12 to logMAR 1.53. Vitreous biopsy was positive for viral DNA in only one case.

On analyzing the factors predicting outcome, RRD developing later than at presentation had odds of 8.4 for a favorable visual outcome ($p=0.01$, 95% C.I. 1.53-46.1). Administration of systemic steroids had odds of 5.2 for a favorable visual outcome ($p=0.03$, 95% C.I. 1.14-23.54). Usage of valacyclovir instead of intravenous acyclovir had an odds of 4.33 ($p=0.04$, 95% C.I. 1.05-17.84) for a favorable outcome. Occurrence of a recurrent RRD had odds of 6.25 for a non-favorable final visual outcome ($p=0.01$, 95% C.I. = 1.37-28.5). Other factors like gender, age at presentation, intraocular pressure at presentation, duration of complaints did not have any association with the final outcome.

Discussion

In the current study, 42.1% (16/38 eyes) undergoing PPV with silicone oil tamponade for RRD following ARN had a mean final visual acuity of 20/200. Occurrence of RRD later along the follow up, prompt administration of systemic steroids and usage of oral valgancyclovir had a greater odds of a favorable visual outcome whereas occurrence of recurrent retinal detachment had a greater odds of a non-favorable visual outcome. Though many studies^[11,12,13] show a high viral PCR positivity from the ocular fluids in cases of ARN, in our series only 1/38 eyes had PCR positive for viral DNA. Hillenkamp J, et al^[14] in a retrospective series of 27 eyes with ARN, describe that occurrence of optic nerve involvement is a poor prognostic factor for final visual outcome. In the current series, optic nerve involvement was seen in 26.31% of all cases. There was no difference between the favorable and the non-favorable groups with regards to occurrence of optic neuropathy, but all these cases had relatively poorer final visual acuity as compared to presenting acuity.

The overall final visual acuity achieved over both the groups in this study was a mean of 1.25 logMAR (Snellen acuity 20/355). This was commensurate with previously noted visual outcome.^[4,15] The most frequent cause of vision loss has been macular pucker and optic neuropathy in past literature.^[16,17] In the present study, 8 eyes developed macular pucker and 10 eyes had optic neuropathy. The role of oral valacyclovir and oral famcyclovir has been well established in literature.^[18,19,20] It allows for a convenient dosage regime, does not require hospitalization and close

monitoring of the patient and reduces the risk of systemic side effects. The effect of oral valacyclovir as compared to intravenous acyclovir has not been studied in acute retinal necrosis treatment before. In the current study, we found a greater odds of a favorable visual outcome in cases where oral valacyclovir was used as compared to intravenous acyclovir. To the best of our knowledge, this is the first study of its kind which objectively elicits factors affecting the final visual outcome.

This study has its limitations. The retrospective nature of the study did not allow the two groups to be completely comparable. The sample size was small due to the relative rarity of the condition. The small sample size reflects statistically in the wide confidence intervals associated with the factors which otherwise are statistically significant. As the viral PCR was largely negative in the study, it was not possible to judge the effect of various viruses on the overall visual outcome. In conclusion this study shows that occurrence of retinal detachment late in the course of ARN, administration of systemic steroids and usage of oral valacyclovir are associated with a favorable visual outcome. Conversely, occurrence of recurrent retinal detachment augurs a non-favorable outcome. A multi-centric prospective trial could be attempted to validate these results.

References

1. Geux-Crozier Y, Rochat C, Herbort CP. Necrotizing herpetic retinopathies: a spectrum of herpes virus induced diseases determined by the immune state of the host. *Ocul Immunol Inflamm* 1997; 5: 259–65.
2. Ganatra JB, Chandler D, Kuppermann B, Margolis TP. Viral causes of the acute retinal necrosis syndrome. *Am J Ophthalmol* 2000; 129: 166–72.
3. Sims JL, Yeoh J, Stawell RJ. Acute retinal necrosis: a case series with clinical features and treatment outcomes. *Clin Experiment Ophthalmol*. 2009;37:473–477.
4. Lau CH, Missotten T, Salzmann J, Lightman SL. Acute retinal necrosis features, management, and outcomes. *Ophthalmology*. 2007;114:756–762.
5. Meghpara B, Sulkowski G, Kesen MR, Tessler HH, Goldstein DA. Long-term follow-up of acute retinal necrosis. *Retina*. 2010;30:795–800.
6. Tran TH, Stanescu D, Caspers-Velu L, et al. Clinical characteristics of acute HSV-2 retinal necrosis. *Am J Ophthalmol*. 2004;137:872–879.
7. McDonald HR, Lewis H, Kreiger AE, Sidikaro Y, Heckenlively J. Surgical management of retinal detachment associated with the acute retinal necrosis syndrome. *Br J Ophthalmol*. 1991;75:455–458.
8. Holland GN. Standard diagnostic criteria for the acute retinal necrosis syndrome. Executive Committee of the American Uveitis Society. *Am J Ophthalmol* 1994;117(5):663–7.
9. Mason JO 3rd, Colagross CT, Haleman T, Fuller JJ, et al. Visual outcome and risk factors for light perception and no light perception vision after vitrectomy for diabetic retinopathy. *Am J Ophthalmol* 2005;140:231–5.
10. Davis J, Chung E. Repair of retinal detachment caused by cytomegalovirus retinitis in patients with acquired immunodeficiency syndrome. *Am J Ophthalmol* 1992;113:468–70.
11. Abe T, Sato M, Tamai M. Variable R1 region in varicella zoster virus in

- fulminant type of acute retinal necrosis syndrome. *Br J Ophthalmol* 2000;84:193–8.
12. Markomichelakis NN, Zafirakis P, Karambogia-Karefillidi P, et al. Herpes simplex virus type 2: a cause of acute retinal necrosis syndrome. *Ocul Immunol Inflamm* 2001;9:103–9.
 13. Miserocchi E, Modorati G, Azzolini C, et al. Herpes simplex virus type 2 acute retinal necrosis in an immunocompetent patient. *Eur J Ophthalmol* 2003;13:99–102.
 14. Hillenkamp J, Nölle B, Bruns C, Rautenberg P, Fickenscher H, Roeder J. Acute retinal necrosis: clinical features, early vitrectomy, and outcomes. *Ophthalmology*. 2009;116:1971–1975.e2.
 15. Sims JL, Yeoh J, Stawell RJ. Acute retinal necrosis: a case series with clinical features and treatment outcomes. *Clin Exp Ophthalmol* 2009;37:473–477.
 16. Duker JS, Blumenkranz MS. Diagnosis and management of the acute retinal necrosis (ARN) syndrome. *Surv Ophthalmol* 1991;35:327–43.
 17. Blumenkranz MS, Clarkson JG, Culbertson WW, Flynn HW, Young GM. Visual results and complications after retinal reattachment in the acute retinal necrosis syndrome. *Retina* 1989;9:170–4.
 18. Aizman A, Johnson MW, Elnor SG. Treatment of acute retinal necrosis syndrome with oral antivirals. *Ophthalmology* 2007;114:307–12.
 19. Emerson GG, Smith JR, Wilson DJ, Rosenbaum JT. Primary treatment of acute retinal necrosis with oral antiviral therapy. *Ophthalmology* 2006;113:2259–61.
 20. Aslanides IM, De Souza S, Wong DT, Giavedone LR, et al. Oral valacyclovir in the treatment of acute retinal necrosis syndrome. *Retina* 2002;22:352–354.

Polypoidal choroidal vasculopathy and Central Serous Chorioretinopathy: Diseases of the same spectrum?

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Abstract

Purpose

To study the multimodal imaging features of simultaneous polypoidal choroidal vasculopathy (PCV) and central serous chorioretinopathy (CSC) in the same eye.

Methods

A retrospective observational study of cases of suspected PCV which underwent ICGA, FFA and SD-OCT from a period of August 2015 to May 2016 in a tertiary eye hospital in South India was done, to look for simultaneous features of active CSC in the same eye. The relevant history, best corrected visual acuity (BCVA), OCT, FFA and ICGA findings were analyzed.

Results

From 181 cases of PCV reviewed, 5 patients (2.8%) with features of both PCV and active CSC in the same eye were identified; 3 males and 2 females with mean age 63.2 yrs. OCT showed notched PED in 3 and irregular peaked PED in 2 cases with subretinal fluid and /or subretinal haemorrhage, over a thick choroid with a mean Subfoveal choroidal thickness of 371µm and dilated outer choroidal *pachyvessels*. FFA showed stippled hyperfluorescence at polyp area and a separate CSC leak - Inkblot in 2 and Smokestack in 3 cases. On ICGA, multiple polyps were noted suggestive of PCV and choroidal hyperpermeability was seen in late phase, separately at the site of CSC leak.

Conclusion

The coexistence of PCV, active CSC and thick choroid in the same eye at the same time provides strong evidence that these diseases have an association and perhaps originate from the predisposed thick choroid (*PACHYCHOROID SPECTRUM*).

Keywords

1. Central serous chorioretinopathy
2. Pachychoroid
3. Polypoidal choroidal vasculopathy

Introduction

Polypoidal choroidal vasculopathy (PCV) was first described by Yannuzzi et al as a condition consisting of peculiar subretinal polypoidal vascular lesions associated with serous and hemorrhagic pigment epithelial detachments (PED). Central serous chorioretinopathy (CSC) is characterized by idiopathic detachment of the neurosensory retina. Associations between these conditions are reported in literature. The history of CSC is described in eyes with PCV. In a series by Park et al, changes of previous chronic CSC have been demonstrated in eyes with PCV. PCV is also known to masquerade as persistent or recurrent CSC. Although the pathogenesis of these diseases is not clear, choroidal circulation abnormalities leading to congestion and hyperpermeability with thickened choroids, are associated with both these clinical entities.

Lately, these diseases have been grouped under the Pachychoroid Spectrum of diseases along with "Pachychoroid Pigment Epitheliopathy" and "Pachychoroid Neovascularopathy". Although the association between these diseases has been described, the simultaneous presentation has not yet been described. To this effect, we studied the multimodal imaging features in cases of suspected PCV, looking for simultaneous presence of features of CSC.

Methods

The clinical and imaging data of 181 cases of suspected PCV which underwent simultaneous fundus fluorescein angiography (FFA) and indocyanine green angiography (ICGA) from a period of August 2015 to May 2016 at Department of Vitreoretina services, Aravind Eye Hospital were reviewed, to look for features of CSC.

The relevant history, best corrected visual acuity in Snellen acuity (BCVA) and clinical features were noted. The spectral domain optical coherence tomography (OCT) and enhanced depth imaging (EDI)-OCT images (Spectralis Heidelberg Engineering and/or DRI OCT Triton plus, Topcon) as well as FFA and ICGA (Spectralis; Heidelberg Engineering) were reviewed.

PCV was suspected if serosanguinous PED or polyps were noted clinically or if tall, peaked PED with a notch or irregular PED with subretinal fluid (SRF) or subretinal haemorrhage (SRH) were seen on OCT. The diagnosis of PCV was confirmed on ICGA, if focal hyperfluorescence suggestive of a polyp was seen within the first 6 minutes on ICGA. Active CSC was identified by the presence of characteristic pattern of leak on FFA- smokestack or inkblot, along with the presence of SRF with or without serous PED on OCT. The subfoveal choroidal thickness was measured manually using callipers on Spectralis Software.

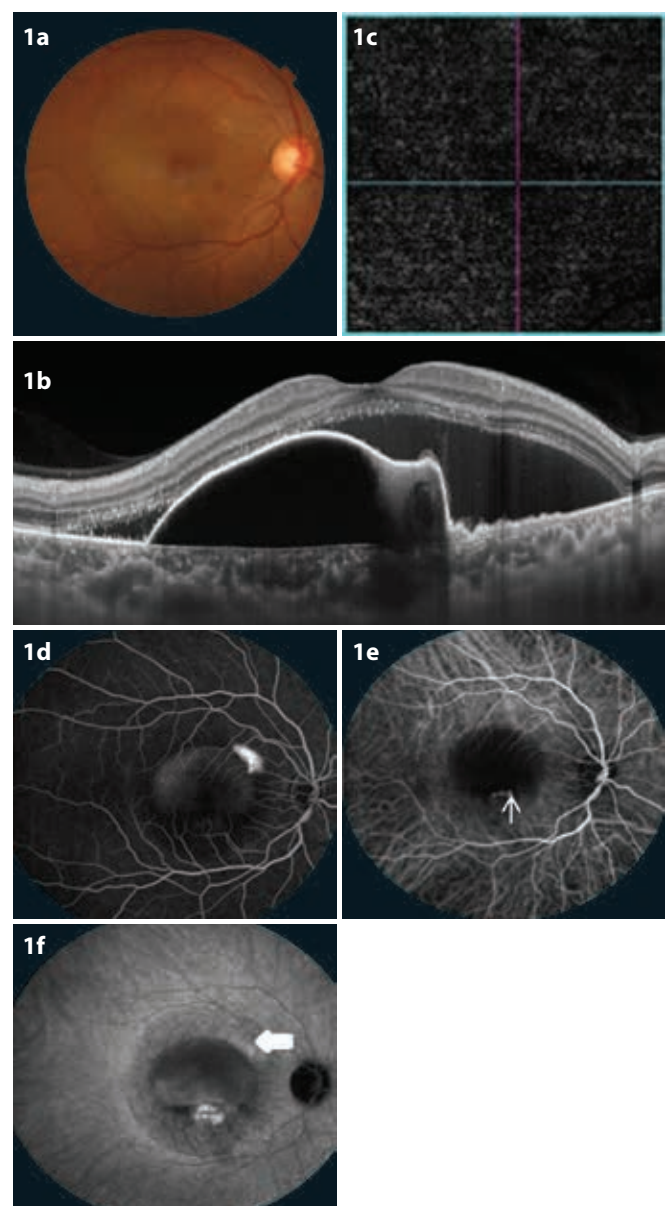
Results

Of the 181 cases reviewed, 5 eyes of 5 patients (2.8%), 3 males and 2 females, were identified with features of active PCV as well as active CSC simultaneously in the same eye. The mean age was 63.2 years (52 to 70 years). Three patients had a history of systemic hypertension. The BCVA in the affected eye was 6/18 in three cases, 6/12 in one case and 6/9 in one case. On OCT, notched PED was seen in 2 eyes and irregular peaked PEDs were seen in 4 eyes. SRF was noted in all eyes at the site of polyp or CSC. Subretinal haemorrhage was seen in 3 eyes and subretinal hard exudates in 1 eye. The mean subfoveal choroidal thickness was 371.2 μm . On FFA, the inkblot pattern of CSC leak was noted in 2 cases and 3 cases showed smokestack leak. A separate area of stippled hyperfluorescence was noted on FFA, which corresponded to the area of polyps on ICGA. Interestingly, on OCT, all eyes with the smokestack leak showed a micro retinal pigment epithelium (RPE) rip at the site of the leak. ICGA showed a cluster of polyps in all cases. The location of polyps was macular in 2 cases and extra macular in 3 cases. Case presentations of all the cases are detailed below.

Case 1:

A 52 year old female presented with the complaint of defective vision in Right eye (RE) for the past 6 months. She had a history of injury in the left eye (LE) in childhood following which the eye had become phthisical. On examination, her BCVA in RE was 6/18. The anterior segment was within normal limits. Fundus examination revealed a large amount of SRF almost extending from superior to inferior arcade vessels with a speck of SRH (Figure 1 A). OCT revealed a large, tall and notched PED; with a polyp beneath the undersurface of RPE and SRF. Enhanced depth

imaging (EDI) revealed a thick choroid with subfoveal choroidal thickness (CT) of 406 μm with dilated outer choroidal vessels (Figure 1 B). On FFA, smokestack leak was noted superonasal to the fovea (Figure 1 C,D) and ICGA revealed a bunch of polyps inferior to fovea along with choroidal hyperpermeability in late phase corresponding to the site of CSC leak (Figure 1 E,F). On reviewing the OCT, a micro RPE rip was also noted in the region corresponding to the CSC leak on FFA (Figure 1 G). She was given intravitreal injection (IV) ranibizumab. Photodynamic therapy (PDT) was deferred due to the large size of PED and the attendant risk of RPE rip.



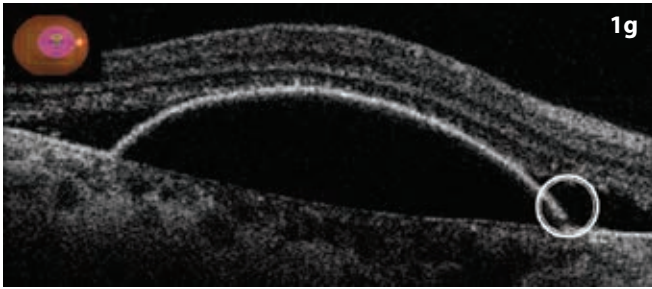


Figure 1 Case 1 A) Colour fundus photograph of RE showing subretinal fluid(SRF) with subretinal haemorrhage(SRH) B) EDI OCT image showing notched PED with SRF with subfoveal choroidal thickness(CT) of 406µm C) FFA early stage and D) FFA late stage showing a smokestack leak superonasal to fovea with gradual filling of dye in PED and a stippled hyperfluorescence inferior part of the PED E) ICGA early phase and F) ICGA late phase showing a bunch of polyps(thin arrow) in area of stippled hyperfluorescence and choroidal hyperpermeability(thick arrow) in late phase at the site of CSC leak G) Micro RPE rip(circle) in area corresponding to smokestack leak

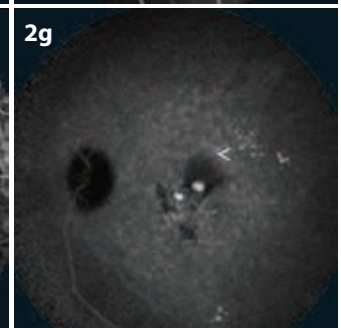
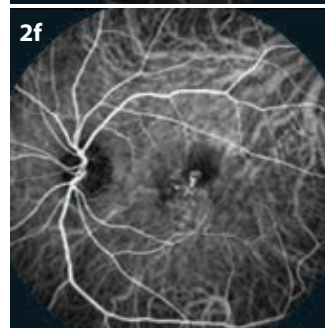
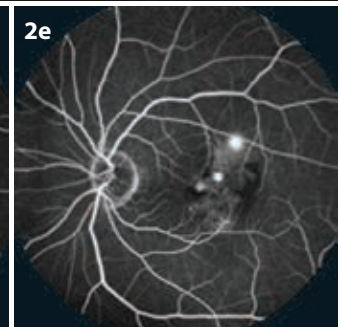
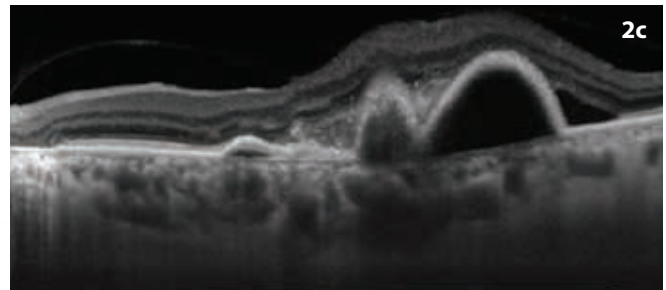
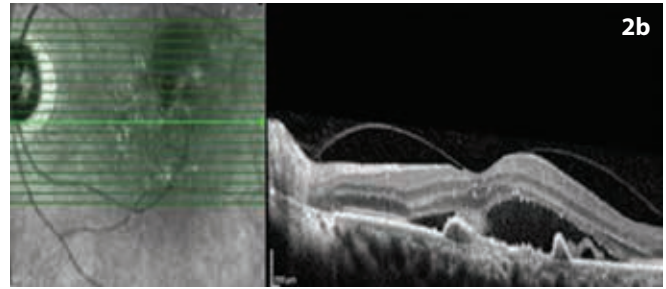
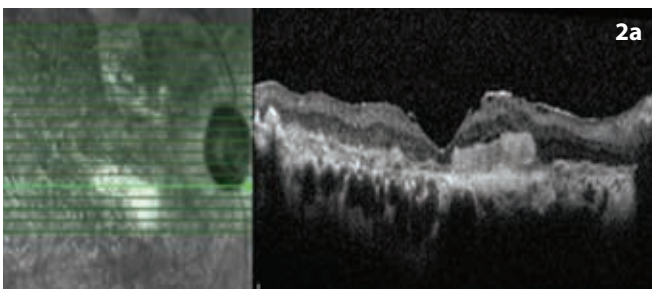


Figure 2: Case 2 A) RE OCT shows foveal thinning with subretinal scar and dilated outer choroidal vessels and subfoveal CT of 401µ B) LE OCT showing multiple irregular peaked PED and SRF with minimal SRH C) EDI OCT showing dilated outer choroidal vessels and subfoveal CT of 464µm D) FFA early phase and E) FFA late phase showing stippled hyperfluorescence with late leakage in foveal region and an extrafoveal inkblot leak superotemporal to fovea with blocked fluorescence temporal to fovea F) ICGA early phase G) ICGA late phase shows a bunch of polyps at the fovea and choroidal hyperpermeability (arrow head) at the site of inkblot leak

Case 2:

A 70 year old male presented with defective vision in the LE for past 2 months. He had been diagnosed as having occult CNVM in the LE and had received a single dose of IV Ranibizumab 1 month back. He had a history of vitreous haemorrhage in the RE and had undergone vitrectomy for the same 2 years back, but did not recover vision in that eye. He was on treatment for hypertension and ischemic heart disease. His BCVA was hand movements in RE and 6/12 in LE. Anterior segment examination showed immature cataract in both eyes. Fundus examination revealed a subfoveal scar in RE and a serous PED with SRH in the LE. OCT of RE showed foveal thinning with a subretinal scar and dilated outer choroidal vessels with subfoveal CT of 401µ (Figure 2 A) and LE showed multiple irregular PED with a tall peaked PED with SRF and minimal SRH with dilated outer choroidal vessels and subfoveal CT of 464µm (Figure 2 B,C). FFA and ICGA of RE showed staining of the scar tissue whereas in the left eye, an extrafoveal inkblot leak was noted superotemporal to the fovea on FFA (Figure 2 D,E) along with multiple polyps at the fovea with late choroidal hyperpermeability at site of inkblot leak on ICGA (Figure 2 F,G). He underwent low fluence PDT with three doses of IV ranibizumab in the left eye.



Case 3:

A 65 year old male had been diagnosed as having occult CNVM in the LE and was treated with PDT with bevacizumab in 2011. He had ischaemic heart disease. His BCVA was 6/9 in RE and 6/18 in LE. Anterior segment showed immature cataract in both eyes. On

fundus examination, RE showed a serous PED while in the LE, SRH with SRF and minimal subretinal scarring was seen (Figure 3A). OCT of RE showed a normal foveal contour with a serous PED (Figure 3C) and in LE, irregular PEDs with SRH was seen in the macular region and a large amount of SRF with a tall PED along inferior arcade was seen (Figure 3B). In both eyes, the choroid was thickened with CT being 300µm in RE and 357µm in LE. On FFA, some window defects with pooling of dye in PED were noted in RE, ICGA was normal. In the LE, a smokestack leak was noted inferotemporal to macula and a RPE rip was seen still temporal to that, with a profuse leak on FFA (Figure 3 E,F) and a cluster of polyps at the fovea on ICGA (Figure 3 G,H). OCT done through the area of smokestack leak area showed a micro RPE rip corresponding to the leakage (Figure 3D). The patient was given IV ranibizumab as he was not willing for PDT.

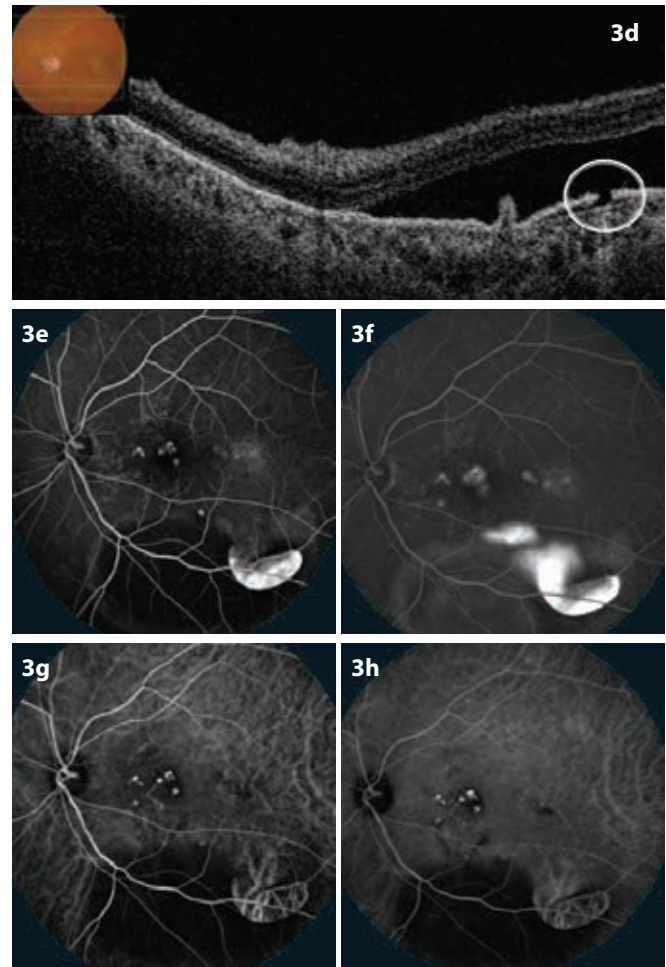
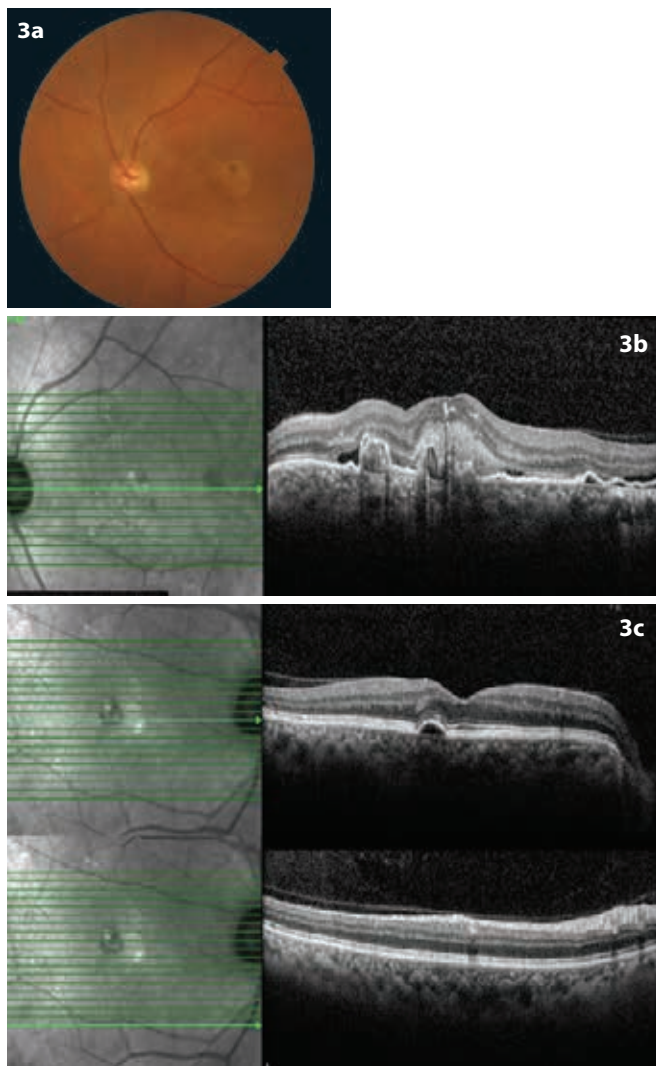


Figure 3: A) Colour fundus image shows SRH with SRF and minimal subretinal scarring B) LE OCT shows irregular PEDs with SRH under fovea with SRF. Subfoveal CT was 357µm C) RE OCT shows serous PED. Choroid is thickened with dilated outer choroidal vessels D) LE OCT through the smokestack leak shows micro RPE rip (circle) E) FFA early phase and F) FFA late phase showing stippled hyperfluorescence with late leakage in the foveal region with smokestack leak inferotemporal to the macula and a large RPE rip G) ICGA early phase and H) ICGA late phase showing a bunch of polyps at the foveal region.

Case 4:

A 67 year old male presented with the complaint of defective vision in the LE since past 14 days. He was on treatment for diabetes mellitus and hypertension. His BCVA was 6/6 in RE and 6/18 in LE. Anterior segment examination was within normal limits in both eyes. Fundus examination revealed RPE changes at the fovea in the RE and PED with subretinal hard exudates in LE. OCT of RE showed RPE irregularity (Figure 4C), while in LE showed SRF with hard exudates and a PED inferonasal to fovea along with fibrin (Figure 4 A,B). Double layer sign was present on OCT. The subfoveal CT in LE was 360µm. FFA and ICGA of RE were within normal limits. In LE, FFA showed an inkblot leak inferonasal to the fovea (Figure 4 D,E) and multiple polyps were noted superior to

fovea on ICGA (Figure 4 F,G). The patient underwent focal laser to the ink blot leak followed by IV Ranibizumab.

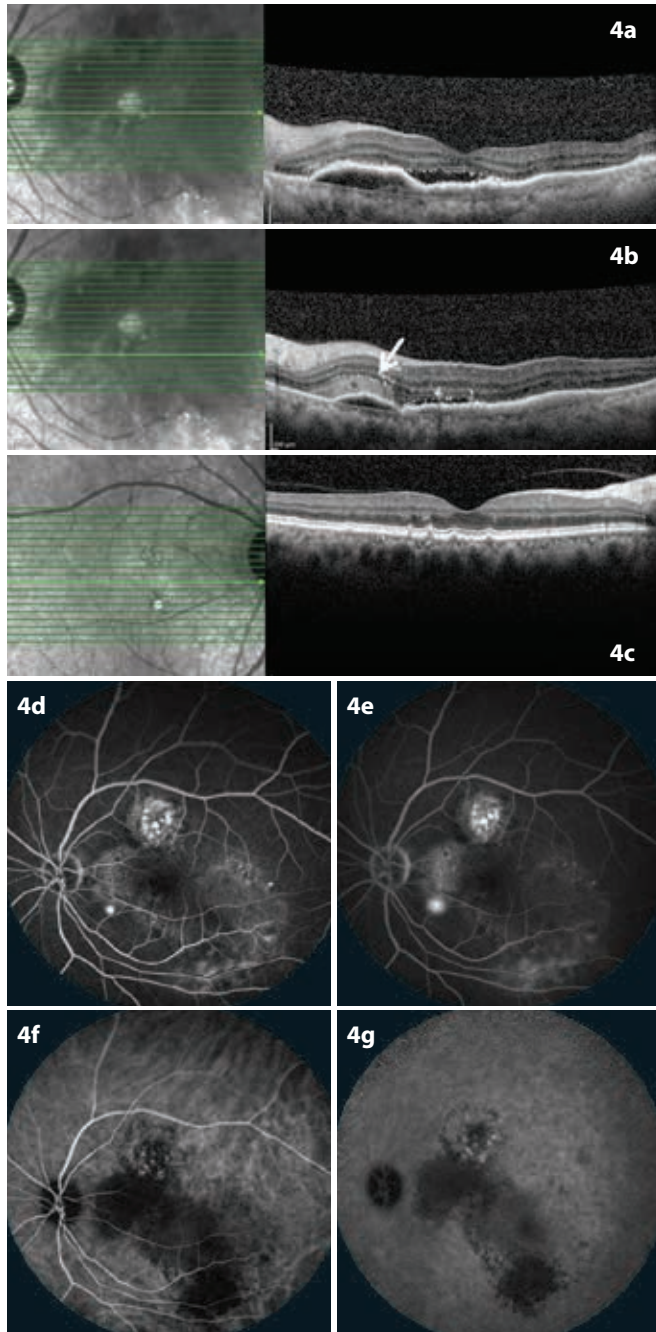
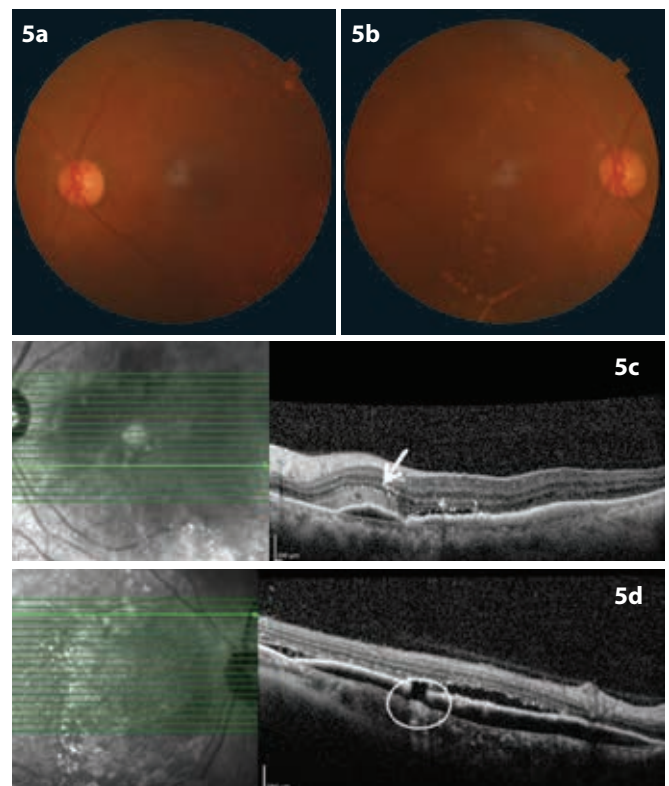


Figure 4: A) LE OCT through fovea shows subretinal fluid with hard exudates B) LE OCT inferior to fovea shows a PED with fibrin (arrow) C) RE OCT shows RPE irregularity D) FFA early phase and E) FFA late phase shows stippled hyperfluorescence superior to fovea with late leakage and a separate inkblot leak inferonasal to fovea F) ICGA early phase and G) ICGA late phase shows multiple polyps superior to the fovea and blocked fluorescence due to serous PED

Case 5:

A 62 year old female presented with the complaint of defective vision in both eyes since 6 months. She was on treatment for systemic hypertension. On examination, her BCVA was 6/9 in both the eyes. She had immature cataracts in both the eyes. The retinal evaluation of RE showed a very large serous PED extending between the arcade vessels with subretinal deposits at the edge of PED with SRF. LE showed some subretinal deposits temporal to the macula and a large PED with subretinal deposits nasal to disc (Figure 5 A,B). OCT of RE showed a large PED with SRF with vitelliform deposits at the posterior pole and a large irregular PED with SRF superior to the disc with double layer sign. LE OCT showed RPE changes at fovea with irregular PEDs (Figure 5C). OCT taken nasal to disc showed a micro RPE rip (Figure 5D). In the left eye, although the subfoveal CT was 269µm, the sublesional CT was 423µm. FFA and ICGA of RE showed branched vascular network with polyps superior to disc whereas in LE, FFA showed a smokestack leak nasal to disc corresponding to the microrip on OCT (Figure 5 E,F) and ICGA showed branched vascular network and polyps superior to disc (Figure 5 G,H). Also, a pachyvessel was noted in the subfoveal region. She was given IV ranibizumab and focal laser photocoagulation to the polyps for the RE. LE was kept under close observation.



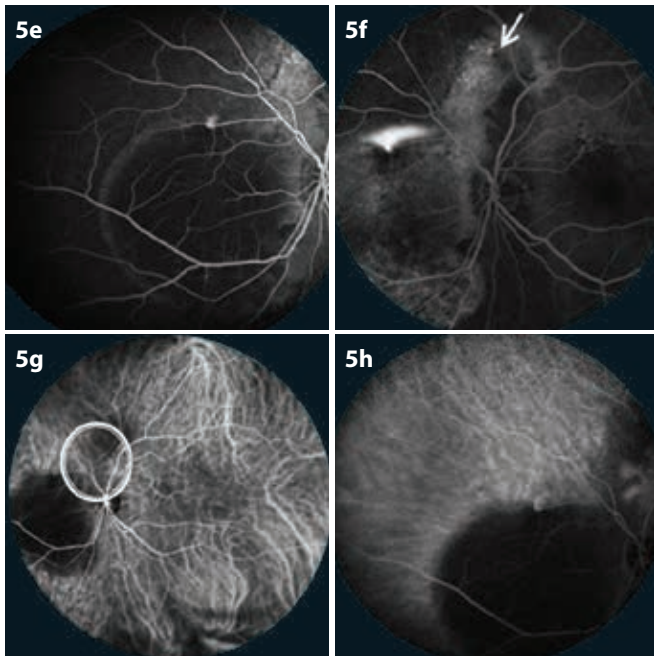


Figure 5 : A) Colour fundus image showing few subretinal deposits temporal to fovea B) Colour fundus image showing large PED with subretinal deposits nasal to disc C) OCT shows RPE irregularity with shallow irregular PED D) OCT nasal to disc showing micro RPE rip(circle) E) FFA early phase and F) FFA late phase showing stippled hyperfluorescence superior to disc(arrow) and smokestack leak nasal to disc G) ICGA early phase and H) ICGA late phase shows polyps superior to disc(thick circle) and a pachyvessel in foveal region with choroidal hyperpermeability at site of smokestack leak

DISCUSSION

Pachychoroid is a newly described entity defined as focal or diffuse abnormal and permanent increase in choroidal thickness, which is generally associated with dilated outer choroidal vessels. The absolute choroidal thickness may be less in case the choriocapillaries and Sattler layer vessels are attenuated. Pachychoroid is associated with choroidal hyperpermeability on ICGA. Warrow et al described “Pachychoroid Pigment Epitheliopathy”(PPE) as retinal pigment epithelium (RPE) changes with reduced fundus tessellation, overlying a thick choroid but without any history of subretinal fluid. C. Pang and K. Freund have described a type I choroidal neovascularization developing over focal areas of choroidal thickening and termed it as “Pachychoroid Neovascularopathy”(PNV).

Pachychoroid features have been noted in PCV as well as CSC. The pathophysiology of both these diseases is poorly understood. In PCV, arteriosclerotic changes along with engorged vortex veins due to chronic choroidal venous congestion have been noted. Choroidal hyperpermeability along with the loss of RPE function secondary to choroidal hydrostatic pressure has been observed in CSC.

Here, we describe 5 cases with features of active PCV along with active CSC in the same eye simultaneously along with a thickened choroid and dilated outer choroidal vessels. Findings suggestive of PPE associated with a pachyvessel on ICGA were also noted in one eye. Also, these findings are seen over multiple areas on the fundus and not just confined to the macula, indicating an abnormality involving the entire choroid.

Hence, the varied clinical entities of pachychoroid spectrum of diseases may be linked in a more simplistic manner. In eyes with a pachychoroid, if the RPE is able to overcome the fluid overload, there might just be subtle pigmentary changes or small PED due to the stress on the RPE- called as Pachychoroid pigment epitheliopathy. If RPE is unable to overcome the fluid overload, a serous macular detachment results, in which case we see a CSC. In chronic stages due to the excess stress on RPE, micro rips may occur in the Bruch’s membrane. If these eyes develop a Type 1 choroidal neovascular membrane, a Pachychoroid neovascularopathy can be seen. And a long-standing type1 CNVM can develop polyps or the dilated choroidal vessels may themselves develop polyps at the terminal ends to result in Polypoidal choroidal Vasculopathy.(Figure 6)

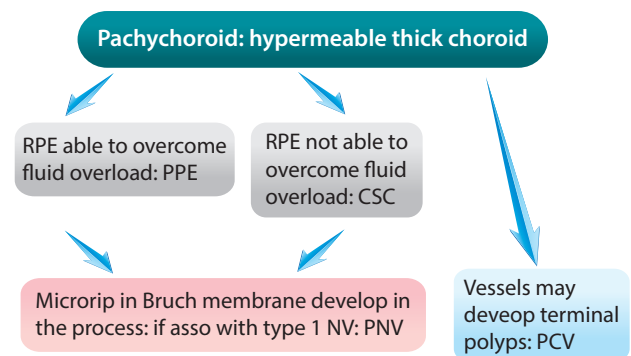


Figure 6: Schematic description of the Pachychoroid Spectrum of Diseases

CONCLUSION

To the best of our knowledge, the simultaneous coexistence of PCV, CSC and pachychoroid features has been unreported till now. This study provides further evidence to the hypothesis that these diseases are associated and form a part of the same spectrum. However, larger longitudinal studies with longer follow-up are required to shed further light on the pathogenesis as well as the progression of the entities belonging to this spectrum of diseases and may, therefore, help in planning better treatment protocols in the future.

References

1. Yannuzzi L a, Sorenson J, Spaide RF, Lipson B. Idiopathic polypoidal choroidal vasculopathy (IPCV). *Retina*. 1990;10(1):1-8.
2. Gemenetzi M, De Salvo G, Lotery a J. Central serous chorioretinopathy: an update on pathogenesis and treatment. *Eye (Lond)*. 2010;24(12):1743-1756.
3. Toyama T, Ohtomo K, Noda Y, Ueta T. Polypoidal choroidal vasculopathy and history of central serous chorioretinopathy. *Eye (Lond)*. 2014;28(8):992-997.
4. Park HS, Kim IT. Clinical characteristics of polypoidal choroidal vasculopathy associated with chronic central serous chorioretinopathy. *Korean J Ophthalmol*. 2012;26(1):15-20.
5. Yannuzzi LA, Freund KB, Goldbaum M, et al. Polypoidal choroidal vasculopathy masquerading as central serous chorioretinopathy. *Ophthalmology*. 2000;107(4):767-777.
6. Okushiba U, Takeda M. [Study of choroidal vascular lesions in central serous chorioretinopathy using indocyanine green angiography]. *Nihon Ganka Gakkai Zasshi*. 1997;101(1):74-82.
<http://www.ncbi.nlm.nih.gov/pubmed/9028111>. Accessed July 10, 2016.
7. Spaide RF, Hall L, Haas A, et al. Indocyanine green videoangiography of older patients with central serous chorioretinopathy. *Retina*. 1996;16(3):203-213.
8. Sasahara M, Tsujikawa A, Musashi K, et al. Polypoidal Choroidal Vasculopathy with Choroidal Vascular Hyperpermeability. *Am J Ophthalmol*. 2006;142(4):601-607
9. Balaratnasingam C, Lee W-K, Koizumi H, Dansingani K, Inoue M, Freund KB. Polypoidal Choroidal Vasculopathy: A Distinct Disease or Manifestation of Many? *Retina*. 2016;36(1):1-8.
10. Warrow DJ, Hoang Q V, Freund KB. Pachychoroid Pigment Epitheliopathy. *Retina*. 2013;33(8):1659-1672.
11. Pang CE, Freund KB. Pachychoroid neovascularopathy. *Retina*. 2015;35(1):1-9.
12. Nakashizuka H, Mitsumata M, Okisaka S, et al. Clinicopathologic findings in polypoidal choroidal vasculopathy. *Investig Ophthalmol Vis Sci*. 2008;49(11):4729-4737.
13. Nicholson B, Noble J, Forooghian F, Meyerle C. Central Serous Chorioretinopathy: Update on Pathophysiology and Treatment. *Surv Ophthalmol*. 2013;58(2):103-126.

Macular Buckle with Morin-Devin T implant for pathological Myopia with Macular hole- A case report

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Purpose

To investigate the efficacy of primary buckling with Morin-Devin T implant for Macular detachment with macular hole and posterior staphyloma.

Methods

52 yr, Female with right eye posterior staphyloma, localized neurosensory detachment and macular hole underwent primary Macular Buckling with Morin Devin T implant. During the immediate postoperative day the wedge indentation was found misaligned to fovea. A revision surgery was done at 2 weeks with repositioning of the macular wedge.

Results

SD-OCT confirmed the indentation at the macular hole with resolution of SRF. BCVA at 2 weeks was 1/60 which improved to 2/60 at 3 months follow up.

Conclusion

Primary Macular Buckling can be an effective procedure in eyes with Myopic foveoschisis and associated pathologies. Devin – Morin T implant is a relatively simple procedure with short surgical time.

Introduction

Pathological Myopia with associated Myopic traction Maculopathy (MTM) is a relatively common disease entity in Posterior segment eye disease in Asian Population¹. Myopic traction maculopathy includes foveoschisis, foveal retinal detachment, lamellar or full-thickness macular hole, and/or macular detachment² and is generally associated with a posterior staphyloma³. OCT studies have shown frequent association of Myopic Foveoschisis with Macular hole with or without Retinal detachment and the pathogenesis and management of the same

has inspired much debate in literature⁴.

Release of epiretinal traction by Pars Plana Vitrectomy with or without ILM peeling with gas or Silicon oil tamponade has enjoyed a reasonable success. However, PPV with ILM peeling in high myopic eyes is surgically challenging associated with low rate of macular hole closure, frequent complications like extrafoveal hole formation and redetachment post tamponade removal.^{5,7}

Scleral wall modulation by scleral shortening or episcleral buckling have been reported with good anatomical and functional results.^{6,7}

We report a case of a 52-year-old woman who had Posterior staphyloma with Macular hole and Macular Detachment limited to Vascular arcade in right eye. Patient underwent Primary Macular Buckling with Morin Devin T implant. Postoperatively, however the indentation of macular buckle was infero-temporal to the fovea. Patient underwent a revision Buckling surgery 2 weeks postoperatively. Satisfactory results were obtained intraoperatively and postoperatively in and after the revision surgery. Patients BCVA improved from light perception (PL) to 2/60 on Snellens acuity testing at 3 months.

Morin-Devin T implant {France Chirurgie Instrumentation (FCI), Paris, France}: Morin Devin T implant has two components a 4mm wide silicone band and a 7mm solid macular wedge (Fig. 1A). The T-shaped macular buckle is created by threading the band through the solid silicone macular wedge's biconvex end (Morin–Devin 'T'-shaped macular wedge).⁸

Surgical Technique⁸ : 180° temporal limbal peritomy was performed. Superior (SR), inferior (IR), and lateral recti (LR) muscles were carefully isolated and secured. The Inferior oblique (IO) muscle belly was hooked and secured taking care not to miss any IO fibers.

The 4 mm solid silicon band was passed under the IR, IO and LR. In the plane between the LR and the SR the 4mm band was threaded through the macular wedge creating the T (Fig. 1B).

The macular Wedge was than negotiated under the Lateral rectus bisecting the plane between the insertion of the IO and the Superior Oblique (SO). A long curved forceps holding the macular wedge tip was used to negotiate the Macular wedge and to place the indentation of biconvex wedge under the Macular Detachment and hole. Care was taken not to be forceful during Macular wedge navigation in view of thin staphylomatous sclera, risk of inadvertent scleral perforation, avoid trauma to Optic Nerve Head and prevent short ciliary vessels avulsion.

Simultaneous Indirect ophthalmoscopy with a +20 Diopter lens was used to confirm the desired indentation. Multiple reflexes of indentation due to the instrumentation, the solid silicon wedge and relative inexperience created lot of doubts, which were put to rest once, desired indentation was achieved.

The anterior end of the Macular wedge was secured underneath the Lateral rectus by anchoring its superior and inferior borders with the sclera. 5-0 Ethibond suture was passed through the borders and anchored directly to the sclera. 3 anchoring sutures were passed at the superior border and 2 anchoring sutures were passed at the inferior border of the 7 mm silicon macular wedge to prevent future displacement of the indenting wedge (Fig.1C).

discarded and the cut end was secured nasal to the insertion of SR with 5-0 ethibond sutures. The inferior end of the 4 mm band was similarly fashioned and anchored nasal to the insertion of IR. Tenon and Conjunctiva were secured with 8-0 Vicryl in usual fashion.

Post operatively however the indentation of macular wedge was infero temporal to the macular hole. A revision surgery was done 2 weeks post-operatively in the above described procedure and satisfactory results were obtained intraoperatively and post operatively.

Postoperatively BCVA improved to 2/60 at 3month. SD-OCT showed significant buckle effect and resolution of macular detachment. At 3 months follow up the macular hole had closed. A persistent restriction of eye movement on Lateral Gaze was noted at last follow up (Fig.2).

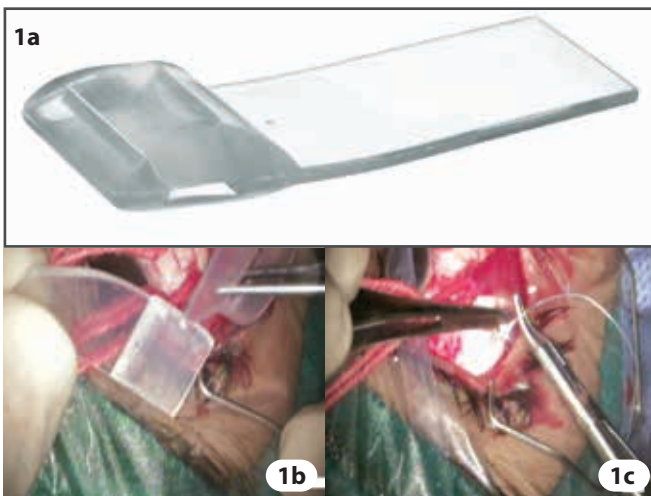


Fig. 1. Morin- Devin T Implant. A. 7mm solid macular wedge with biconvex end. B. Creation of T-shaped macular buckle by threading the 4mm silicone band through the solid silicone macular wedge's biconvex end. C. Anchoring of superior border of Macular wedge with 5-0 ethibond sutures to the sclera

The 4mm band was passed underneath the SR. Macular buckling height and minimal lateral adjustment can at this point be regulated by simultaneous traction on the superior and Inferior end of the 4 mm band. Extra long band of the superior end was

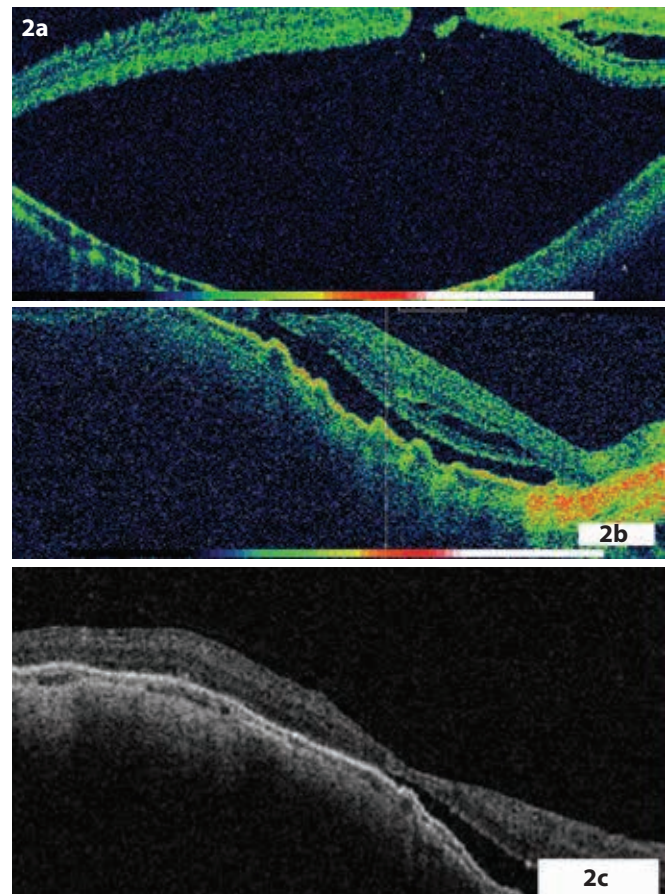


Fig. 2 SD-OCT showing reattachment after macular buckling with Morin-Devin T implant. A. Pre-operative OCT showing macular hole with posterior ectasia of scleral wall. B. 1 month post-op OCT showing persisting Macular hole with significant indentation at the Fovea. C. 3 month follow-up showing closure of macular hole with persisting of detachment nasal to fovea.

Discussion

Myopic Traction Maculopathy (MTM) in varying severity invariably coexist with posterior staphyloma and are much more closely related than previously thought. Progressive axial elongation along with antero posterior vitreous traction and taut Internal Limiting membrane creates shearing forces responsible for foveoschisis with or without Macular hole with or without retinal detachment.^{2,9}

Pars Plana Vitrectomy with ILM peeling and tamponade has shown significant success rate in Various small pilot study.^{5,10} for eyes with Macular Foveoschisis and associated Macular Hole and Posterior staphyloma. Significant surgical expertise is required while working in an eye with abnormal scleral rigidity, a phenomenally longer axial length, mismatched instruments to axial length size and visibly reduced contrast at the posterior pole due to myopic degeneration. Low Macular hole closure rates⁵, development of extrafoveal holes⁷, progression of foveoschisis post ILM peeling¹¹ and redetachment post tamponade removal⁷ mars the eventual success rate of surgery and leaves a question whether the real pathology i.e progressive axial elongation and posterior staphyloma had been addressed.

Scleral wall modulation by means of macular buckling changes the configuration of the posterior pole from concave to a plano-convex relieving anteroposterior traction, tangential traction, sclero retinal mismatch and also reinforces the RPE and neurosensory retina adherence by bringing them together in a chorioretinal atrophied area.¹²

Although eclipsed by PPV for a long time macular buckling has shown resurgence in recent times with reports coming from various centres emphasizing high success rates of Macular Buckling with or without vitrectomy.^{6,7,8,12}

Different Macular Buckles have been described in literature like Ando plombe , T-shaped macular buckle , AJL macular buckle, L-shaped macular buckle ,Adjustable macular buckle and Wire-strengthened sponge explant.¹²

However complexity of different procedures and unfamiliarity have dissuaded Macular Buckling becoming popular especially in Indian Subcontinent.

Two relatively simple methods one with Ando plombe implant and other with Morin Devin T implant have come into vogue.

Morin Devin T implant scores a huge economic advantage over Ando Plombe Implant in a country like India. Unlike other procedures the T implant doesn't requires Muscle disinsertion, does not require posterior suture and any access to posterior pole

making the procedure relatively simple. Inherent disadvantages of macular buckle like intraoperative risk of scleral perforation, compromise of short posterior ciliary circulation, damage to ONH, abduction deficit, misalignment under the fovea and late development of chorioretinal atrophy exist in T implant too.^{8,12}

In our case we achieved satisfactory chorioretinal apposition, resolution of sub retinal fluid and closure of Macular hole at 3 month follow up on SD-OCT. We believe that MTM with co-existing pathology can be addressed with scleral wall reshaping using a relatively simple technique of macular Buckling with Morin –Devin T implant.

Key-words

High myopia, myopic foveoschisis, posterior staphyloma, macular buckling, Morin –Devin T Implant.

References

1. Wong YL, Saw SM. Epidemiology of Pathologic Myopia in Asia and Worldwide Asia Pac J Ophthalmol (Phila). 2016 Nov/Dec;5(6):394-402.
2. Johnson MW. Myopic traction maculopathy: pathogenic mechanisms and surgical treatment. Retina. 2012;32(Suppl 2):S205–S210.
3. Gaucher D, Haochine B, Tadayoni R, et al. Long-term follow-up of high myopic foveoschisis: natural course and surgical outcome. Am J Ophthalmol 2007;143:455–462.
4. Shimada N, Ohno-Matsui K, Baba T, et al. Natural course of macular retinoschisis in highly myopic eyes without macular hole or retinal detachment. Am J Ophthalmol 2006;142: 497–500.
5. Ikuno Y, Sayanagi K, Oshima T, et al Optical coherence tomographic findings in macular holes and retinal detachment after vitrectomy in highly myopic eyes. Am J Ophthalmol. 2003;136:477–81
6. Baba T, Tanaka S, Maesawa A, et al. Scleral buckling with macular plombe for eyes with myopic macular retinoschisis and retinal detachment without macular hole. Am J Ophthalmol 2006;142:483–487.
7. Mateo C, Burés-Jelstrup A, Navarro R, Corcóstegui B. Macular buckling for eyes with myopic foveoschisis secondary to posterior staphyloma. Retina. 2012 Jun;32(6):1121-8
8. Devin F, Tsui I, Morin B, et al T-shaped scleral buckle for macular detachments in high myopes. Retina. 2011;31 (1):177–80
9. Takano M, Kishi S. Foveal retinoschisis and retinal detachment in severely myopic eyes with posterior staphyloma. Am J Ophthalmol 1999;128:472–476.
10. Kanda S, Uemura A, Sakamoto Y, Kita H. Vitrectomy with internal limiting membrane peeling for macular retinoschisis and retinal detachment without macular hole in highly myopic eyes. Am J Ophthalmol 2003;136:177–180.
11. Shukla D, Dhawan A. Foveoschisis after vitrectomy for myopic macular hole with secondary retinal detachment. Eye 2009; 23:2124–2125.
12. Pradeep S, Vinay Kumar S. Macular Buckle in Myopia, Sci J Med & Vis Res Foun 2015; XXXIII:71–74

Rare case of Autosomal Recessive Bestrophinopathy associated with a large full thickness macular hole with posterior pole neurosensory detachment

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Case Report

A 14-year-old girl presented with complaint of noticing progressive loss of right eye vision over 1 month. She had best-corrected visual acuity (BCVA) of 20/600 in right eye and 20/30 in left eye. Right eye had a large full-thickness macular hole (MH) with posterior pole retinal detachment (RD) (Figure-1). Left eye had multifocal yellowish subretinal lesions spread over posterior pole along with diffuse subtle RPE atrophic changes (Figure-2). Left eye fundus fluorescein angiogram (FFA) showed diffuse multifocal mixed hyper and hypo fluorescent lesions in early phase that persisted in late phase without change in fluorescence (Figure-3). The hypofluorescence corresponded with yellowish lesions and hyperfluorescence corresponded with subtle RPE atrophic lesions (Figure-4).

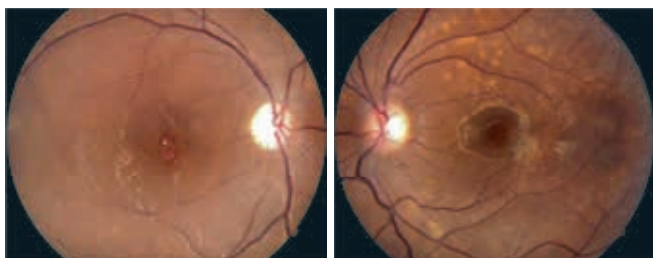


Figure-1: Right eye preoperative fundus photo showing a large full-thickness macular hole with posterior pole retinal detachment

Figure-2: Left eye fundus photo showing multifocal yellowish subretinal lesions spread over posterior pole along with diffuse subtle retinal pigment epithelial atrophic changes

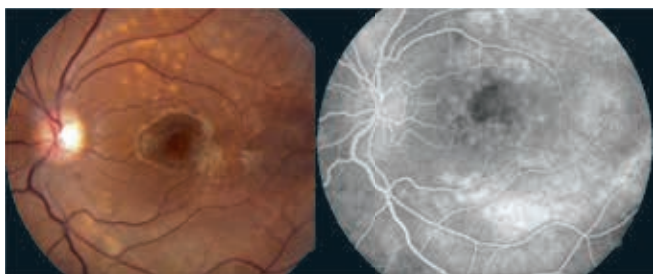


Figure-3: Left eye fundus fluorescein angiogram showing diffuse multifocal mixed hyper and hypo fluorescent lesions in early phase persisting in late phase without change in fluorescence

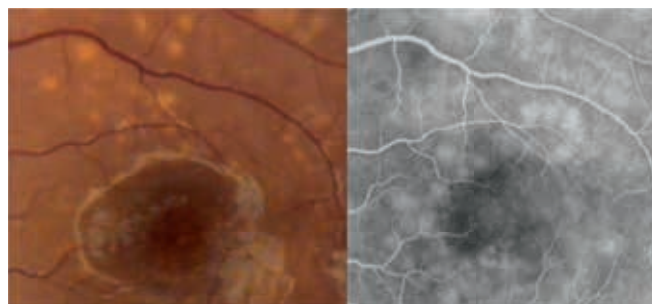


Figure-4: The hypofluorescence on left eye angiogram corresponded with yellowish lesions and hyperfluorescence corresponded with subtle retinal pigment epithelial atrophic lesions

OCT showed intraretinal cystic spaces and subfoveal fluid in OS (Figure-5). Right eye OCT showed MH with Post Pole RD with intraretinal cystic spaces (Figure-6).

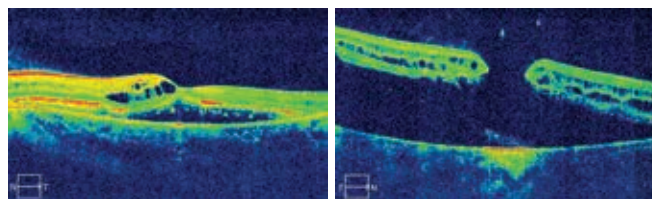


Figure-5: Left eye optical coherence tomography shows intraretinal cystic spaces and subfoveal fluid

Figure-6: Right eye optical coherence tomography shows macular hole with posterior pole retinal detachment with intraretinal cystic spaces

Patient was started on oral prednisolone 1 mg/kg and sustained release oral acetazolamide 250 mg daily and right eye 25G MH surgery with 14% C3F8 injection was performed. Intraoperatively, the posterior hyaloid was strongly adherent to retina and attempts to induce hyaloid separation lead to extension of posterior pole RD up to ora. Fluid-air exchange (FAX) was done through the MH. ILM removal was not very challenging and a large ILM peel from entire posterior pole was easily accomplished.

Two months postoperatively, right eye retina was attached and

macular hole closed with BCVA of 20/100 (Figure-7). But intraretinal cystoid changes reappeared. Left eye had no significant change in fundus lesions, CME and BCVA (Figure-8). The final cycloplegic refraction was 1.25D OU.

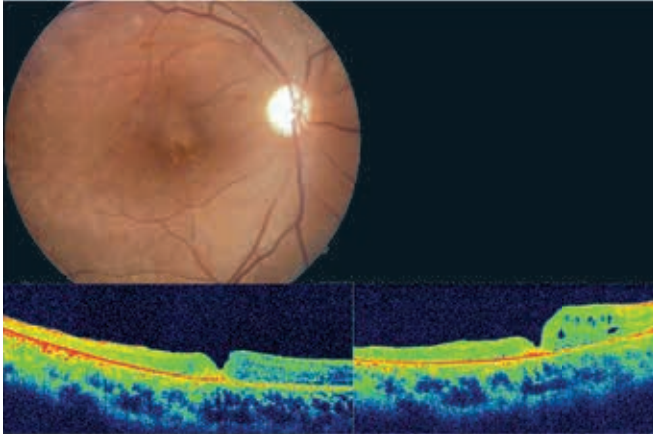


Figure-7: 3 weeks postoperatively the right eye retina was attached and macular hole closed (a and b). But intraretinal cystoid changes reappeared at 2 months (c)

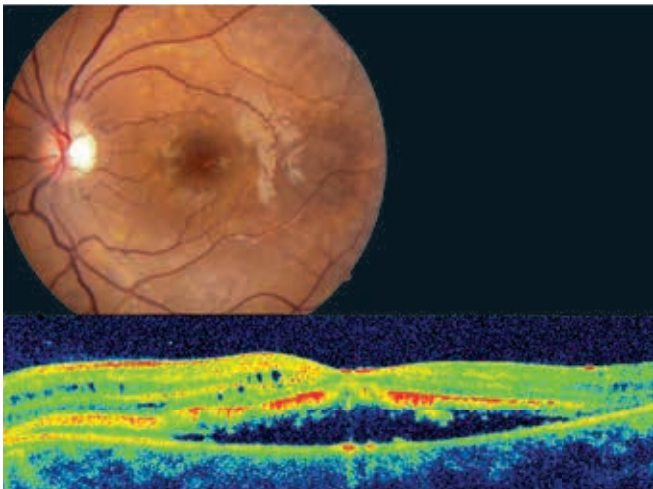


Figure-8: Left eye had no significant change in fundus lesions until 2 months of follow-up

Electro-oculogram (EOG) done postoperatively showed reduced Arden's ratios of 1.07 OD and 1.08 OS.

Discussion

The presence of intraretinal cystic lesions and subfoveal fluid suggests diseases causing CME and foveoschisis as differential diagnoses. Of them X-Linked Congenital Foveoschisis doesn't manifest in females. Autosomal Dominant or inflammatory/vascular CMEs are ruled out by absence of classic petaloid appearance on FFA. Familial Hyaloidoretinopathies like Goldmann-Favre Syndrome (GFS) and Autosomal Dominant Vitreoretinopathopathy (ADVIRC) may have foveoschisis and

CME but are ruled out by absence of fibrillar liquefied vitreous and annular band of pigmentation normally seen in both diseases besides absence of many other features like night blindness in GFS or punctate white retinal opacities in ADVIRC.

The clinical features especially the non foveal distribution of subretinal yellow deposits, absence of any inflammation, typical FFA findings, intraretinal cystic spaces and subfoveal fluid with hyper reflective deposits on OCT, and abnormal EOG, all point to the diagnosis of the rare disease **Autosomal Recessive Bestrophinopathy** (ARB). ARB is thought to be a variant of Best's disease caused by bi-allelic compound heterozygous or homozygous mutations in the Best-1 gene on chromosome 11q12 (the same gene whose mutations cause Best's disease and ADVIRC) which encodes bestrophin-1, a calcium activated chloride channel expressed specifically in RPE. Bestrophin-1 dysfunction has been associated with defective regulation of subretinal fluid reabsorption and aberrant phagocytosis of the photoreceptor discs leading to accumulation of lipofuscin in RPE and subretinally.¹

While Best's disease is characterized by vitelliform lesions that typically occur at macula because of abnormal deposition of lipofuscin in the RPE, ARB is associated with subretinal deposits predominantly outside macula, mainly at the posterior pole and along vascular arcades²⁻⁶. These are often small and fleck-like or punctate in shape, white or yellow in colour, and hyperfluorescent on fundus autofluorescence imaging. OCT shows subretinal and intraretinal fluid accumulation at macula^{2,5-8} and ultrahigh resolution OCT may show elongated outer segments.⁴

Unlike Best's disease, ARB is associated with diminished rod- and cone-driven ERG responses (although ERG changes may appear late), but it shares the presence of a severely reduced or absent EOG light rise with Best's disease as well as ADVIRC.²⁻⁸

No histopathological data are available due to the novel description of the ARB phenotype.⁹

We are unaware of any reports in literature describing development of MH and RD in a case of ARB but there are 4 case reports describing MH leading to RD in Best's disease that is genetically and pathologically similar to ARB¹⁰⁻¹³. Out of them 3 eyes underwent surgery. One with MH and RD in a 41-year-old male with preexisting PVD underwent vitrectomy with FAX. Fluid reappeared after ambulation but disappeared rapidly with prone positioning. Margins of MH were lasered and BCVA recovered to 20/200¹⁰. Another with MH and RD in a 15-year-old boy with attached posterior hyaloid underwent vitrectomy with FAX. Again fluid reappeared after ambulation but disappeared rapidly with

prone positioning. Margins of MH were lasered and BCVA recovered to 20/200¹². Third patient underwent pneumatic retinopexy followed by postoperative laser of margins of MH with successful reattachment¹³.

Soliman et al¹³ postulated that the rupture of cyst in the vitelliform stage may lead to MH formation. Failure of RPE pump to keep the subretinal space dry owing to widespread dysfunction of the RPE may predispose the MHs progression to RD. They compared it with the RPE dysfunction in high myopes and postulated that same mechanism of RPE dysfunction leads to progression of MH to RD in both the situations. But incomplete/anomalous PVD and contraction of cortical vitreous, and the failure of inner retinal layers especially ILM to conform to the shape of posterior staphyloma are considered to be more important pathomechanisms in Myopic Foveoschisis and myopic MH leading to posterior pole RD¹⁴. Besides that the rapid reabsorption of fluid after face down positioning in both the case reports suggest that RPE pump may not be poor in at least the Best's disease. Moreover in our case of ARB, despite significant intra-retinal and sub-retinal fluid we didn't find any prominent and well-defined foveolar cyst that could have ruptured and caused MH formation and the cortical vitreous had such a strong adhesion with retina that during PVD induction RD extended beyond the equator.

We also report that PVD induction upto vitreous base along with a large ILM peel with gas with facedown positioning could achieve successful hole closure and retinal attachment without need for any laser (unlike in previous case reports).

The eye achieved a final BCVA of 20/100 without any reappearance of subfoveal fluid. We hypothesize that anomalous vitreoretinal adhesion may possibly have had a role in the development of MH and posterior pole RD in our case. This hypothesis needs to be tested by future studies.

References

1. Xiao Q, et al. Bestrophins and retinopathies. *Pflugers Arch*. 2010;460:559–569
2. Burgess R, et al. Biallelic mutation of BEST1 causes a distinct retinopathy in humans. *Am J Hum Genet*. 2008;1:19–31
3. Kinnick TR, et al. Autosomal recessive vitelliform macular dystrophy in a large cohort of vitelliform macular dystrophy patients. *Retina*. 2011;3:581–595
4. Gerth C, et al. Detailed analysis of retinal function and morphology in a patient with autosomal recessive bestrophinopathy (ARB) *Doc Ophthalmol*. 2009;3:239–246
5. Boon CJ, et al. Autosomal recessive bestrophinopathy. Differential diagnosis and treatment options. *Ophthalmology*. 2013;120:809–820
6. Borman AD, et al. Childhood-onset autosomal recessive bestrophinopathy. *Arch Ophthalmol*. 2011;129(8):1088–1093
7. Davidson AE, et al. A synonymous codon variant in two patients with autosomal recessive bestrophinopathy alters in vitro splicing of BEST1. *Mol Vis*. 2010;16:2916–2922
8. Iannacone A, et al. Autosomal recessive best vitelliform macular dystrophy: report of a family and management of early-onset neovascular complications. *Arch Ophthalmol*. 2011;2:211–217
9. C Crowlay et al. Autosomal recessive bestrophinopathy associated with angle-closure glaucoma. *Doc Ophthalmol*. 2014; 129(1): 57–63
10. Schachat AP, et al. Macular hole and retinal detachment in Best's disease. *Retina*. 1985 Winter-Spring; 5(1):22-5.
11. Mehta M, Katsumi O, et al. Best's macular dystrophy with a macular hole. *Acta Ophthalmol (Copenh)*. 1991 Feb; 69(1):131-4.
12. Glacet-Bernard A, et al. Full-thickness macular hole and retinal detachment complicating Best's disease. *Eur J Ophthalmol*. 1993 Jan-Mar;3(1):53-4
13. Soliman MM, et al. Vitelliform macular dystrophy: a cause of macular holes with retinal detachments. *Eye (Lond)*. 1994;8 (Pt 4):484-7.
14. From 'Myopic Foveoschisis: a clinical review', R Gohil et al, *Eye* (2015) 29, 593–601

Do it Yourself retinal camera adapter for smartphones – the DIYretCAM

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ABSTRACT

This article describes the utility of a smartphone based fundus camera adapter in various clinical scenarios. The DIYretCAM is a cost-effective device especially in documenting the far periphery up to the pars plana, in bedridden patients and in neonatal and paediatric retinal imaging. Its role in teleophthalmology needs to be explored because of its low cost, high quality image acquisition coupled with the versatile connectivity of the smartphone.

Introduction

Documenting fundus changes plays an important role in the follow up of various retinal diseases. Conventional and hand held fundus cameras have been in use for the past several decades, enabling clinicians to capture high quality retinal photographs for monitoring and follow of patients. Recently smartphones, along with a condensing lens, have been used to document fundus changes.^[1,2] Devices are now available to support the condensing lens at a fixed distance from the camera of the smartphone, making the procedure easy for the clinician. We designed such a device, called the DIYretCAM, based on the Do It Yourself (DIY) concept, using commonly available materials. In this article, we present our initial experience with this cost-effective fundus documentation technique.^[3]

The device consists of a smartphone back cover, an optical tube onto which the 20 D lens is fixed, and an optional slit lamp mount [Figure 1]. The device can be slit lamp mounted to give more control, and thus better focus of the retina while imaging the disc and posterior pole [Figure 2].



Figure 1: DIYretCAM on the slit lamp mount.

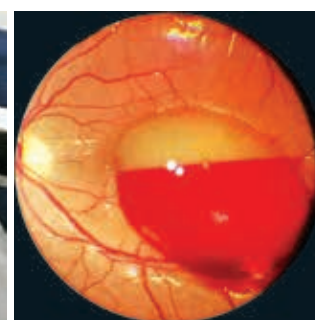


Figure 2: Fundus photograph taken with the DIYretCAM showing subhyaloid haemorrhage in Valsalva retinopathy.

DIYretCAM imaging in routine clinical practice

DIYretCAM or smartphone based retinal imaging technique supplements the fundus camera in the clinical setting. DIYretCAM helps to document the central as well as peripheral fundus changes in a bedridden patient. DIYretCAM scores over the conventional fundus camera with its ability to take high quality images of the far periphery up to the pars plana [Figure 3]. This is possible with simultaneous scleral depression, wherein the clinician holds the DIYretCAM in one hand and does scleral depression with the other hand [Figure 4] as in routine indirect ophthalmoscopy.



Figure 3: Documenting peripheral retina up to the pars plana with simultaneous scleral depression.

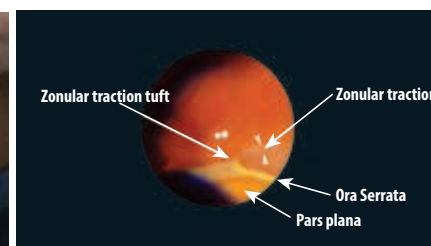


Figure 4: Zonular traction tuft

DIYretCAM's role in documenting changes in Retinopathy of Prematurity (ROP) and other neonatal retinal diseases

DIYretCAM is the most cost effective imaging technique currently available for documenting changes in neonatal retina [Figure 5a and 5b]. In ROP, it captures high quality images of the posterior [Figure 6a and 6b] as well as peripheral retina [Figure 7]. To our knowledge, capturing such high-quality images in neonates is not possible with any other technique. This is useful not only in monitoring the disease, but also in educating the parents about the condition.

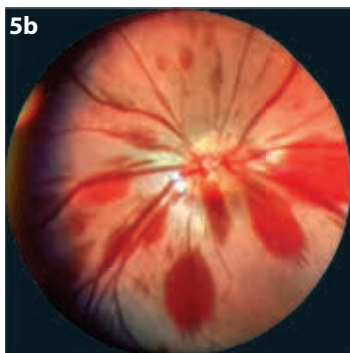


Figure 5a: "Abnormal foveal changes" in a neonate with Stage 2 ROP; probably representing the clinically evident changes similar to the "foveal disruptive" changes on SD OCT as described by Vinekar et al^[5]

Figure 5b: Retinal haemorrhages in a neonate with thrombocytopenia.

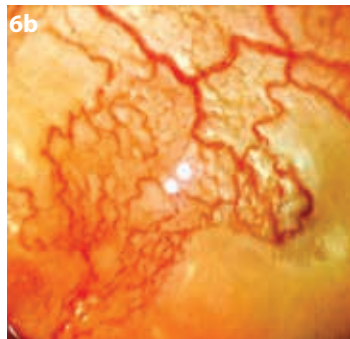
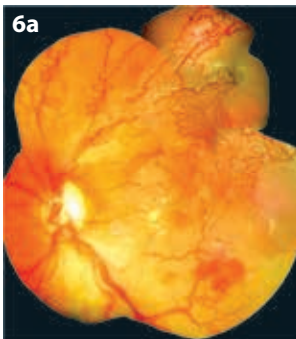


Figure 6a: Montage showing aggressive posterior ROP (APROP).

Figure 6b: The vascular loops in APROP.

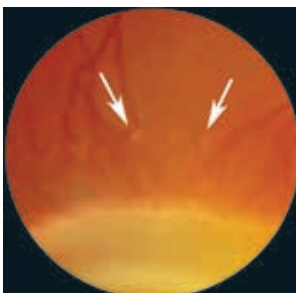


Figure 7: Popcorn lesions (arrows) in ROP

DIYretCAM's role in documentation

The advantages of this device are its low cost, portability and multimodal setup (slit lamp mounted as well as hand held). In addition, there are advantages that are specific to the mobile technology that smartphone based fundus devices have, especially connectivity options like Wi-Fi and 4G, that allow transmission of images for tele-ophthalmological consultation. Smartphone cameras have also improved over the years and they can capture high resolution pictures even under low light conditions. The image can be edited on the phone itself using the Adobe Photoshop Express App [Figure 8]. Montage of multiple fundus photographs can also be created on the phone using PicsArt app, thus negating the need for a computer for image editing and transmission [Figure 9].^[4]

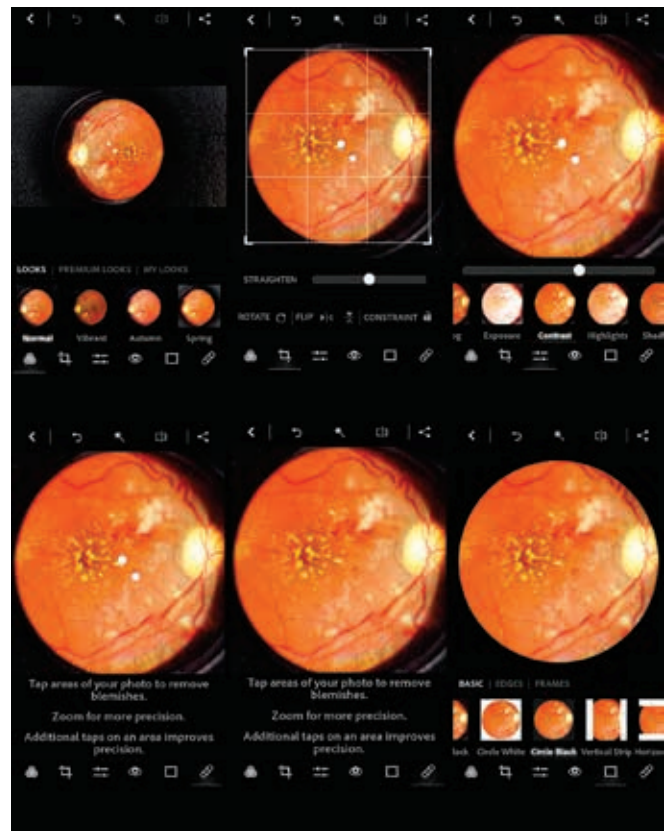


Figure 8: The images can be edited using Photoshop express app on the smartphone.

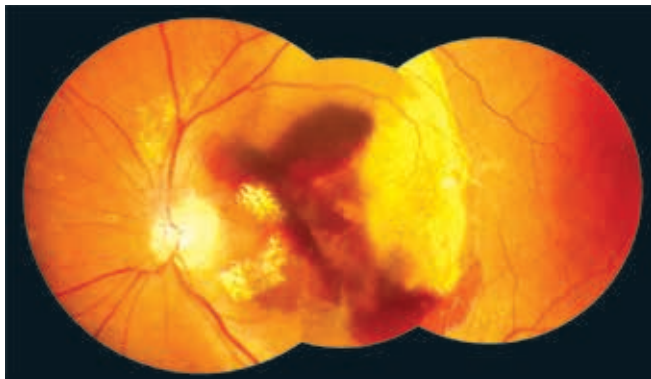


Figure 9: A montage of 3 fundus photos taken with DIYretCAM showing AMD with partially dehemoglobinized submacular haemorrhage. The pictures were edited and the montage was created on the smartphone using the PixArt app. The image was then sent from the phone by email, as a cover picture for the Kerala Journal of Ophthalmology's first online issue. No other device or computer was used either to edit or transmit the image, highlighting the role of smartphone technology in tele-ophthalmology.

Conclusion

The technique has a learning curve. Having a specific camera app which supports a database to store the images and patient information helps to improve the archiving of the images on the phone. Camera FV-5 for android and Camera Pro for the iPhone are good camera apps with multiple features which are useful for fundus photography.^[4]

In our experience, the DIYretCAM [Figure 10] was found to be a useful and cost-effective tool in several clinical situations. Its role in tele-ophthalmology needs to be explored.

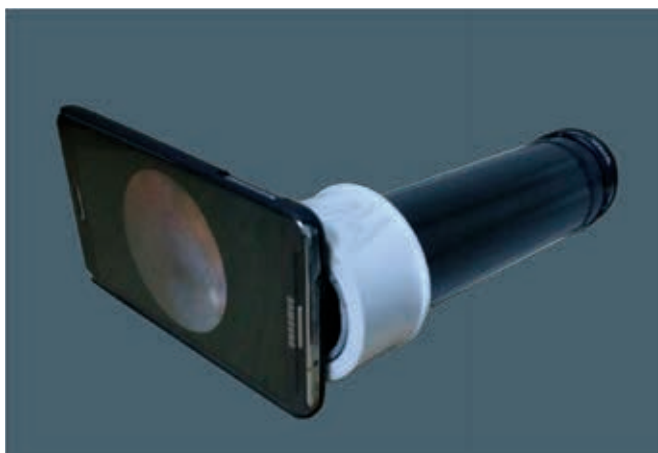


Figure 10: DIYretCAM

References

1. Shanmugam MP, Mishra DK, Madhukumar R, Ramanjulu R, Reddy SY, Rodrigues G. Fundus imaging with a mobile phone: A review of techniques. *Indian J Ophthalmol* 2014;62:960-2
2. Raju B, Raju N. Regarding fundus imaging with a mobile phone: A review of techniques. *Indian J Ophthalmol* 2015;63:170-1
3. Raju B, Raju N, Akkara JD, Pathengay A. Do it yourself smartphone fundus camera – DIYretCAM. *Indian J Ophthalmol* 2016;64:663-7
4. Raju B, Raju N. Initial experience with DIYretCAM – A do it yourself retinal camera. *Kerala J Ophthalmol* 2016;28:53-5
5. A. Vinekar, K. Avadhani, M. Sivakumar et al., "Understanding clinically undetected macular changes in early retinopathy of prematurity on spectral domain optical coherence tomography," *Investigative Ophthalmology and Visual Science*, vol. 52, no. 8, pp. 5183–5188, 2011.

ROP: Pearls & Paradigms!

Dr. Vasumathy Vedantham MS, DNB, FRCS, FIAMS

- We are facing the third epidemic of ROP in the world today!
- The incidence of ROP in various NICUs in India ranges from 20 to as high as 45%!
- Western screening guidelines are not suitable in the Indian scenario!
- ROP occurs in bigger and larger birth weight babies in India compared to the west!
- ROP occurs 1 to 2 weeks earlier in India compared to the west!
- NNF guidelines suggest screening of all preterm infants below 1750 gms birth weight and upto 34 weeks of gestational age!
- Dilated Indirect ophthalmoscopy with diluted tropicamide eye drops is the recommended ROP screening technique!
- Teleophthalmology with a mobile retinal camera is fast gaining popularity as a screening tool in rural areas!
- ROP is of two types: Conventional and Aggressive Posterior ROP (AP-ROP)!
- Conventional ROP is described according to Zones, Stages and presence or absence of Plus disease!
- Zone I is an imaginary circle centered on the optic disc with the radius twice the distance between the centre of the optic disc and the macula!
- Zone II is an imaginary circle peripheral to Zone I straddling the nasal ora serrata!
- Hence any ROP nasally is either in Zone I or II and never III!
- Zone III is the remaining temporal crescent!
- Stage 0 ROP is immature retina!
- Stage I ROP is a white demarcation line at the junction between vascular and avascular retina!
- Stage II is characterised by a ridge which develops when the demarcation line gets thicker and raised!
- There may be small white spots (early new vessels) referred to as popcorns or hotdogs in Stage II ROP!
- Stage III ROP is extraretinal fibrovascular proliferation into the vitreous from the ridge!
- Stage IV is subtotal RD, IV A not involving the macula and IV B involving the macula!
- Stage V ROP is total RD!
- Dilatation and tortuosity of arterioles and venules in the posterior pole is referred to as plus disease!
- Threshold ROP is Stage III ROP in Zones I and II, with 5 contiguous or 8 non-contiguous clock hours of neovascularisation!
- High Risk prethreshold ROP is Stage III ROP in Zones I and II, without 5 contiguous or 8 non-contiguous clock hours of neovascularisation with or without plus disease, Zone II Stage II ROP with plus, Zone I any stage ROP with Plus, all these are referred to as type I ROP!
- AP-ROP has abnormal collaterals, shunts, nodes and hemorrhages in the posterior pole, often with very severe plus disease and is seen in very tiny babies!
- AP-ROP with NVE and Type I ROP need to be treated within 48-72 hours of diagnosis (Golden period)!
- Gold standard of treatment is laser photocoagulation with LIO (Laser indirect ophthalmoscope) wherein all the avascular retina is treated!
- Anti-VEGF injections (0.03ml) of Bevacizumab, Ranibizumab and Aflibercept are being tried with increasing success when laser is not possible due to small pupils, vitreous haemorrhage or Zone I ROP!
- Follow up has to be longer and more rigorous after anti-VEGF injections than laser due to delayed vascularisation and late recurrences!
- All ROP babies even after resolution need lifelong follow-up to rule out refractive errors, squint, amblyopia, Glaucoma, and RD!

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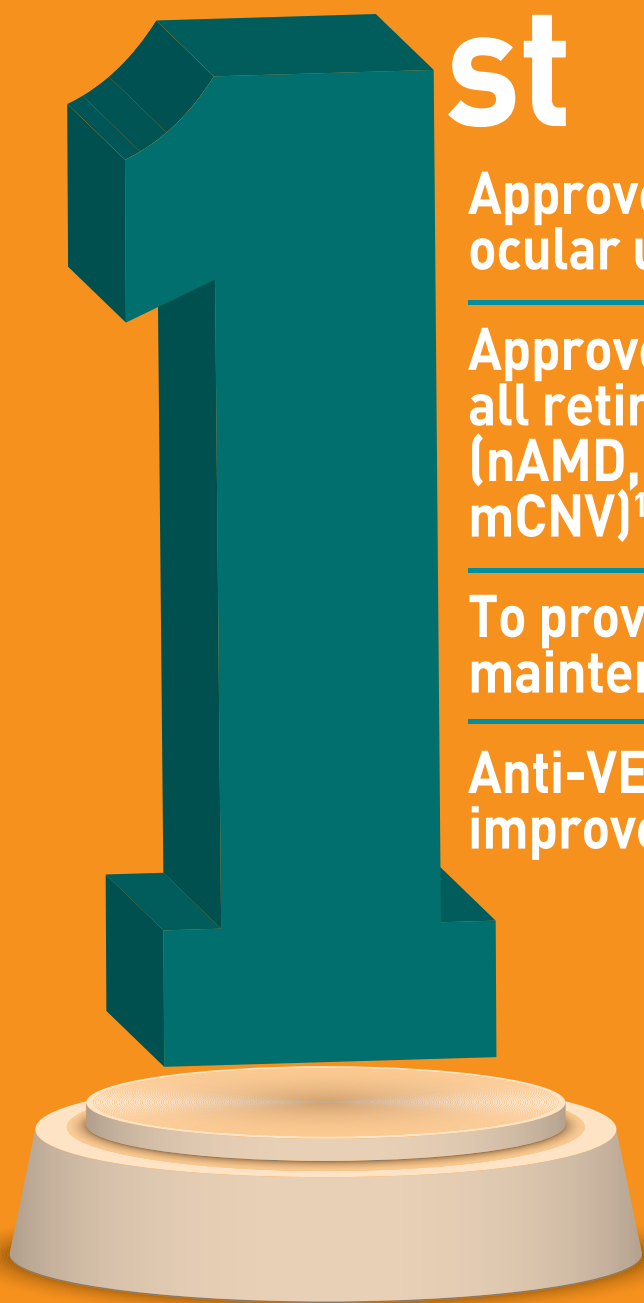
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1. Leo a Kim & Patricia A D'Amore. A brief history of Anti- Vefg for the treatment of ocular angiogenesis, The American journal of pathology, Vol.181, No.2, August 2012
2. Accentrix® Summary of Product Characteristics, Novartis AG; September 2015.
3. Accentrix® DSUR 5 (Oct 2014– Oct 2015), Drug safety and epidemiology, Novartis; November 2015.
4. Novartis data on file, Emerging Market Brand Launch Meeting, November 2014.



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