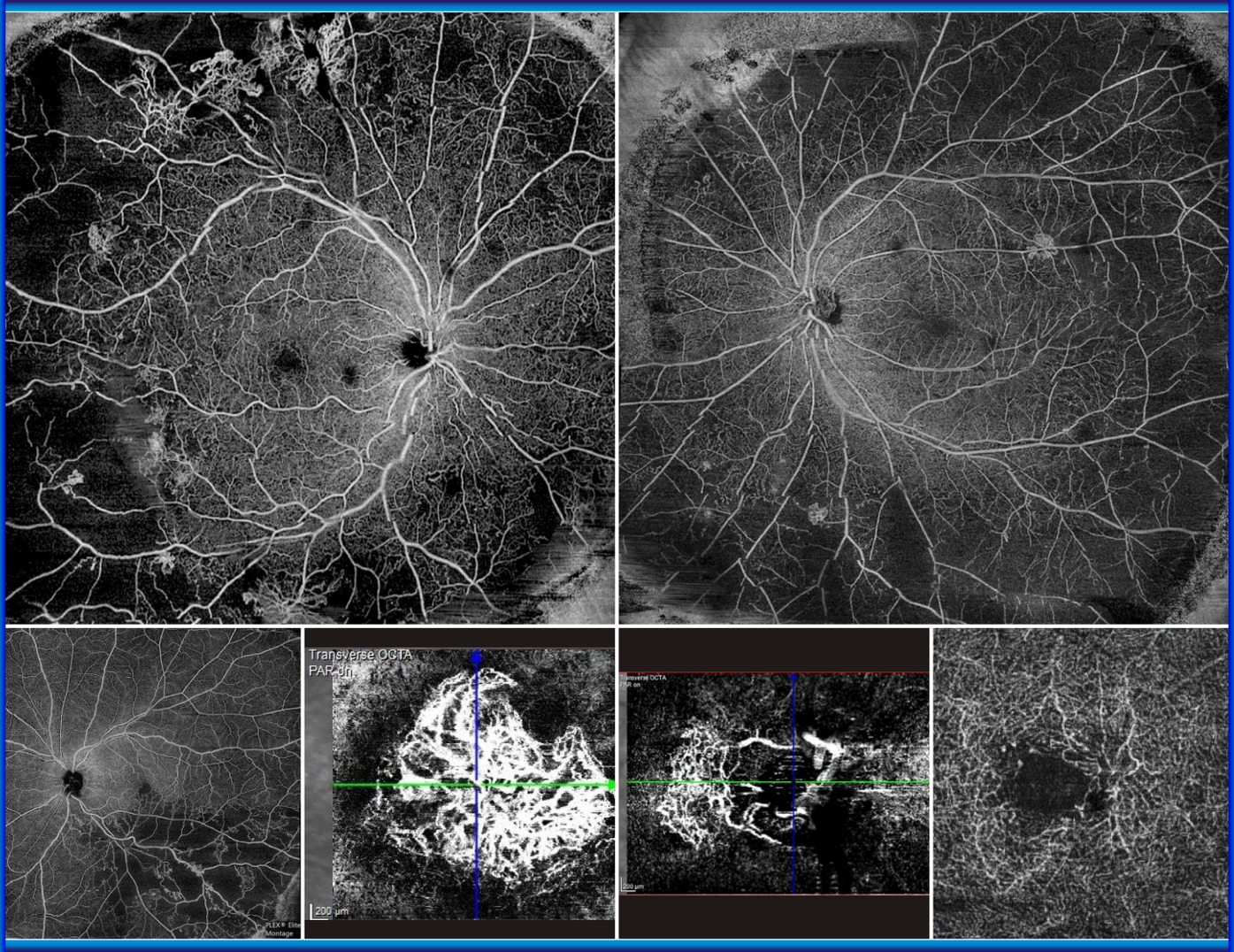
DECEMBER 2021

The Official Newsletter of the

VITREO RETINAL SOCIETY-INDIA



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Contents

From the President's Desk

Dr. Shobhit Chawla
Medical Director and Chief - Vitreo Retinal Services
Prakash Netra Kendr
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Dear friends

The year of challenges and uncertainties draws to an end . Let me wish you all a beautiful safe and peaceful festive season. We look forward to the active participation of all members in this years virtual VRSI annual meeting. The latest issue of VRSI newsletter features OCTA a technology which has now become an important part of our diagnostics. The Stalwart Speak on AMD is by none other than Dr. Philip J Rosenfeld, who is also one of the developers of the OCTA technology and also a key figure responsible for its understanding..

The Spotlight section is anchored by our energetic young colleague Darius Shroff on challenging scenarios in OCTA. The Retina Tech section focusses on insights in the new technology of Fluorescence Lifetime Imaging Ophthalmoscopy and its scope.

The last two years have defined new norms in conferences, symposiums and meetings. It has been an interesting environment of opportunities and challenges. The team of VRSI and the members have enjoyed great and unique interactions spearheaded by Dr. Anand Rajendran, our Scientific Convenor. We have had iconic Webinars on medical and surgical retina with our national faculty and international leaders in the field. I acknowledge and thank everyone's efforts. Dr Raja Narayanan our dynamic secretary has done excellent and fruitful tie ups with other societies like RSSDI, for betterment of Diabetic Retinopathy both for care and awareness. We have tried to have the best programs with involvement of both young and senior members. The Retina Image competitions every month have infused new enthusiasm and also provided interesting learning opportunity.

VRSI has been unique in its team spirit, both in cooperation and new ideas. Let us keep the lamp burning to light the way to the summit even if we are beset with dark challenges on the way.

It has been a beautiful journey in my association with VRSI which dates back to the year it was founded with twenty one members to the excellent growth it has achieved both in strength and stature on national and international front. We are all set to enjoy an excellently curated scientific feast with participation of eminent faculty, and of course, our members at our Annual meeting scheduled from 16th to 19 th December2021. At the same time, we welcome the incoming executive and wish them all success in their endeavours in steering ahead our society.

Warm regards

Shobhit Chawla
President
VRSI

From the Honorary Secretary's Desk

Dr. Raja Narayanan
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Dear Members:

Looking back, it has been a wonderful year in many aspects for VRSI under the leadership of our beloved President Dr. Shobhit Chawla. The number of memberships has soared high, along with their active participation in many activities of the Society. We have had learning opportunities from various experts through regular webinars, newsletters and roundups, spearheaded by our Convenor, Scientific Committee. We also had enthusiastic participation by members in Image Competitions, and various surveys during challenging times. We had the opportunity to participate in various state meetings and AIOS annual conference, bringing together numerous senior and young experts in the field and learning from their experience. Our collaboration with RSSDI, which is the premier Diabetes Society of India, has made strong foundations for work in controlling and eliminating blindness due to diabetic retinopathy in the near future. This has been made possible due to the relations built between the leaderships of our Societies. VRSI has been at the forefront of advocacy with various stakeholders such as National Health Authority, Insurance bodies, and the Industry to benefit patients with diabetes and diabetic retinopathy. Many patients have benefited from the approval of anti-VEGF drugs in insurance programs. We should work towards leadership in the area of research in retinal diseases, with the huge number of patients that we have in our country. Systems to develop data collection in a uniform manner, data management, analysis and publication should be developed. This would help formulate guidelines for the management of various diseases using our own data, and would be readily applicable to our population. The enthusiasm and energy that is palpable among our members to actively contribute to VRSI is heart-warming. While VRSI may look to increase the number of Executive Committee members in the future, all general members can contribute to the activities of the Society with significant impact. VRSI is aware that a lot more needs to be done in the realm of patient awareness as well as last mile care for patients, and we are optimistic that the next Governing Council will steer the Society towards reducing the burden of blindness due to retinal diseases.

I would like to thank all my seniors and colleagues who have given me the opportunity as well as supported my role at VRSI for the past many years. Personally, I have felt immense satisfaction in serving the Society and its members. I wish all members the very best in their career and health.

Best Regards,

Raja Narayanan
Hon. General Secretary
VRSI

From the Convenor, Scientific Committee's Desk

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Dear Friends and Colleagues

It has been such a pleasure bringing out this final December edition of the VRSI Newsletter 2021. In this issue, we have Dr. Philip Rosenfeld, an internationally renowned doyen in Macular Degeneration and Imaging holding forth on an enigmatic question – the role of choroidal perfusion in AMD disease progression in the'StalwartSpeak'section. The Spotlight article and highlight of the issue, anchored by Dr. Daraius Shroff, is focussed on the Challenging scenarios in OCTA, with an eminent panel of national experts offering their take on a slew ofintriguing OCTA-centred clinical cases. The Retina Tech Section has a couple of interesting articles – the first by Dr. Paul Bernstein and Dr.Lydia Sauer highlighting the role and value of Fluorescence Lifetime Imaging Ophthalmoscopyor FLIO in macular diseases and the second, by Dr.BrijeshTakkar and team introducing the novel Optogenetics Gene Therapy. In the Innovator's Isle section articles, Dr.Madanagopalan and Dr.Nivean, describe the award winning creation –the CM-T Flex IOL – an ingenious sutureless solution for aphakia. Dr.Ashish Ahuja, a young retina specialist with a passion for innovation, portrays the PVRS to aid patients with post vitrectomy positioning requirements. Dr. Sabyasachi Sengupta gives an insightful account of the current and critical status of Insurance for intravitreal injections today. An interesting Case report by Dr. Ramesh Venkatesh rounds off the issue.

It has truly been a pleasure to bring to our members a series of high end webinars in the past few months and it has been gratifying to note the participation and attendance in these. We have forged academic partnerships with numerous eminent scientific consortia like the The Yannuzzi Rounds, Retina World Congress, EVRS, APVRS, IntRIS and have co-hosted several exhilarating webinars with them.

An enthralling and invigorating Virtual VRSI Meet, from December 16th-19th 2021, is around the corner. We are delighted to note the very exuberant response from our members with a massive number of submissions. The Meet has been designed and curated with a thrust on impactful didactics from international stalwarts, Challenging Cases, with theme based sessions such as Macular Mélange, Choroidal Conundrums, Jail Breakers, Through the Looking Glass, Onco Odyssey, Dousing the Flames, Surgical Grand Prix making the programme unique. An array of international and national stalwarts are coming together to make this Meet one that should be memorable and on par with any international Meet. This Meet would mark the end of this Executive's tenure and we hope we have addressed and fulfilled, to a significant degree, the aspirations and expectations of our very vibrant and talented body of VRSI Society members. We wish the incoming executive the very best and are certain that they will take the Society to even greater heights.

We are thankful to all the members for the appreciation and incredible support these 3 years and hope to see the same enthusiastic response to VRSI activities in future. On a personal note, I would like to place on record my deep and sincere thanks to all my elders and colleagues who have been extremely encouraging and supportive in this journey. It shall always remain my greatest honour and privilege to have served a Society as venerated and esteemed as VRSI.

Dr. Anand Rajendran
Convenor
Scientific Committee
Vitreo-Retinal Society India

Guidelines - Manuscript Submission for VRSI Newsletter

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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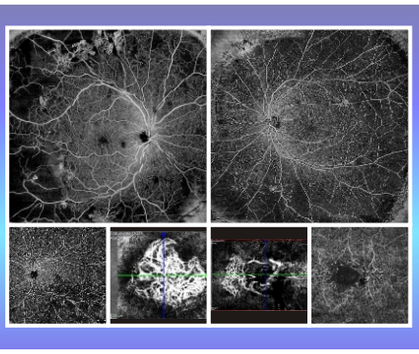

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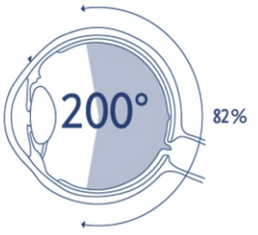

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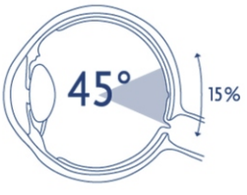

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STALWARTSPEAK

Does Choroidal Perfusion Influence Disease Progression in AMD?

Dr. Philip J. Rosenfeld, MD, PhD
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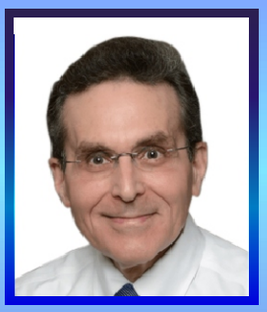
Bascom Palmer Eye Institute
Miami, USA



This article is an except from a recent Perspective that is available on-line at the American Journal of Ophthalmology.[1]

Introduction

We now know that age-related macular degeneration (AMD), a leading cause of blindness among the elderly worldwide, is a late-onset, progressive, neurodegenerative genetic disease.[2] However, in a 1997 Editorial, Ephraim Friedman proposed that AMD was caused primarily by abnormal choroidal perfusion due to scleral rigidity.[3] Was he completely wrong? We think not. He was wrong that choroidal perfusion was the primary cause of AMD since the primary cause is genetic,[4] and he was wrong that scleral rigidity played a role, but the evidence is mounting that choroidal perfusion could be an important environmental influence that explains the asymmetry of disease progression. The variability of AMD onset and progression and the relative asymmetry in severity between eyes beyond the drusen stage need to be explained.[5, 6] If AMD is a genetic disease and both eyes have the same genetics and if both eyes are exposed to the same environmental influences that are known to affect disease progression such as smoking, dietary intake, cardiovascular disease, hypertension, and obesity, then why don't both eyes progress at the same rate? When we see identical twins with variable AMD progression, we are confident in asserting that it must be due to different environmental exposures and life experiences, but how canwe explain the asymmetry in disease progression between eyes? A likely source for this underlying asymmetry could be age-dependent changes in perfusion of the choroid and choriocapillaris (CC).[7, 8]

In the past, attempts have been made to correlate ocular perfusion with disease severity with conflicting results.[9,10] However, using swept-source optical coherence tomography angiography (SS-OCTA), we can image the choroid and CC in greater detail.[7, 8, 11-13] We believe genetics plays an important role in the early stages of AMD, but choroidal perfusion may be influential in the progression from the early/intermediate stages of AMD to the later stages of dry and wet AMD.

The Role of Environmental Factors on Progression to late AMD

While genetics can predict who will get AMD, genetics does a poor job of predicting how quickly the disease will progress, predicting whether eyes with AMD will develop late stage dry or wet AMD, and predicting how rapidly the late stages will progress. If genetics were destiny, then we would expect predictable symmetry of disease progression between eyes. While extensive clinical research has characterized the fundus finding that are predictive of disease progression in AMD and these include drusen area and volume, the presence of reticular pseudodrusen, and the extent of pigmentary changes in the fundus, it is surprising that genetics offers no greater power than these fundus findings for predicting disease progression. So why

do we propose that choroidal perfusion is important in disease progression?

If we assume that the progression of AMD results from an insult to one or more of the anatomic layers directly involved in AMD progression such as the photoreceptor, retinal pigment epithelium (RPE), and CC layer, then we have to think about how we can study one layer independently from the other layers. While it's impossible to dissect out changes in photoreceptors from changes in the RPE, we can study the relationship between CC and choroidal perfusion apart from the RPE and photoreceptors.

The Hemodynamics of the Choroid and Choriocapillaris in Aging and AMD Progression

The CC is the specialized terminal capillary monolayer of the choroidal circulation that lies adjacent to the RPE. These terminal capillaries represent the only capillaries in the choroid and are essential for the metabolic health and survival of the RPE and photoceptors. One of the first clues that the CC was important in disease progression is that we know CC gives rise to choroidal neovascularization (CNV), suggesting that the choroidal circulation in general and the CC circulation in particular may be involved in disease progression.

By just studying normal aging, we learned that choroidal thickness decreases with increasing age, and this loss of choroidal thickness corresponded to a decrease in the choroidal vascular volume.[8] This loss of choroidal thickness in normal aging, which is due to a decrease in the choroidal vascular volume, corresponds to a decreased choroidal perfusion. We also showed that in normal aging, perfusion of the CC becomes increasingly impaired, with the greatest impairment found in the central macula.[7, 11] While we don't know why CC perfusion deficits accumulate preferentially within the central macula in normal aging, this age-dependent loss in CC perfusion is likely important for our understanding of why AMD preferentially affects the central macula. Moreover, this impairment may be worse in subjects with a history of cigarette smoking, poor nutritional status, elevated body mass index, and cardiovascular disease, and these conditions have been associated with overall AMD severity.

Several groups have found that CC impairment correlated with disease severity and progression on both histopathology and by SS-OCTA imaging.[12, 14-18] The most remarkable data comes from studying the growth rate of geographic atrophy, the late stage of dry AMD. The growth rate of GA has been correlated with the severity of global CC flow impairment.[12, 17, 18] These areas of CC flow impairment are referred to as flow deficits (FDs). While it's possible that features of AMD such as drusen, GA, and reticular pseudodrusen could directly cause thinning of the choroid and loss of CC perfusion, a mechanism whereby changes in the RPE and photoreceptors directly affect choroidal perfusion has not yet been identified. However, a more likely scenario is that a decrease in choroidal and CC perfusion contribute to the onset, progression, and asymmetry of AMD.

While the obvious mechanism to explain how decreased choroidal perfusion exacerbates AMD would be to assert that this decreased perfusion results in impaired nutrient exchange, macular ischemia, and oxidative stress, and these changes lead to macular damage. However, there's another effect that needs to be considered. Decreased perfusion could exacerbate the baseline over-activation of complement that occurs in eyes carrying AMD risk-alleles in the complement pathway.[19, 20] This may explain why the decreased choroidal perfusion associated with aging has a deleterious effect on those individuals carrying the at-risk genetic alleles that cause AMD. Thus, it's not the flow impairment that causes AMD, but rather, the presence of this flow impairment in an eye that is genetically susceptible to AMD that contributes to the variable onset, progression, and asymmetry of late AMD.

What's responsible for the decrease in choroidal perfusion?

In a recent paper, Hibert et al.[21] used 7 Tesla magnetic resonance imaging to show decreased flow within the ophthalmic artery (OA) in patients with AMD compared with normal age-matched controls. Although the study was limited by the small number of patients, the authors did find obstructions at the ostium of the OA that were associated with decreased blood flow within the OA in patients with AMD and the normal controls did not have these stenoses at the ostium of the OA. Interestingly, a similar obstruction at the ostium of the OA was found by Hayreh et al. when examining the ostium of the OA in cadaver specimens.[22, 23] While larger studies are needed, this observation that there is decreased blood flow in the OA is noteworthy and could be treated using the right interventional tools. This proposed model for disease progression doesn't assert that decreased choroidal perfusion causes AMD or will be found only in patients with AMD, but rather, this model suggests that decreased ocular perfusion in an eye with a genetic predisposition for AMD results in more severe and rapid disease progression.

Summary

So, the next time you see a patient with AMD, ask yourself if the disease is symmetric between the eyes. Most likely, the presence of asymmetry will be appreciated once one eye has progressed to late AMD. Remember, genetics isn't destiny, even when comparing two eyes of the same patient, and consider how the environment might influence disease progression between the eyes. While disease progression may be a stochastic process, like flipping a coin, or there may be underlying pathophysiology to explain disease progression and we might be able to intervene and slow this progression.

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OUTCOMES MAINTAINED OVER TIME[7-9]

Maintained visual gains from baseline up to 4 years [7]

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SPOTLIGHT

Challenging cases in OCT angiography







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Case 1

81-year-old Diabetic and Hypertensive female. Complained of drop in vision in both eyes. Vision in OD was CF 1M and in OS was 6/36. No history of any viral prodrome. Anterior segment –revealed cells and flare 1+. The left eye had previously undergone vitrectomy for PDR with Vitreous hemorrhage. The right eye had a Vitreous hemorrhage with no view of the retina.

Patient returned to the clinic after 4 days. Vision in OS had dropped from 6/36 to CF 1m. Ischemic area had increased on OCTA. The choroidal thickness increased from 416 to 517 microns. (Figure 2 and 3).

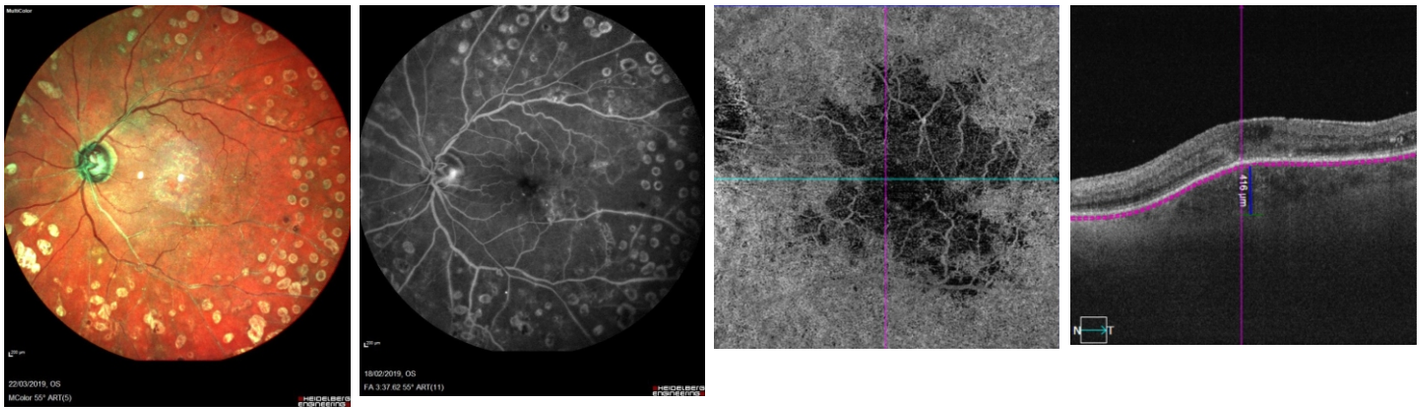


Figure 1 - OS- Multicolour fundus, FA, OCT and OCTA

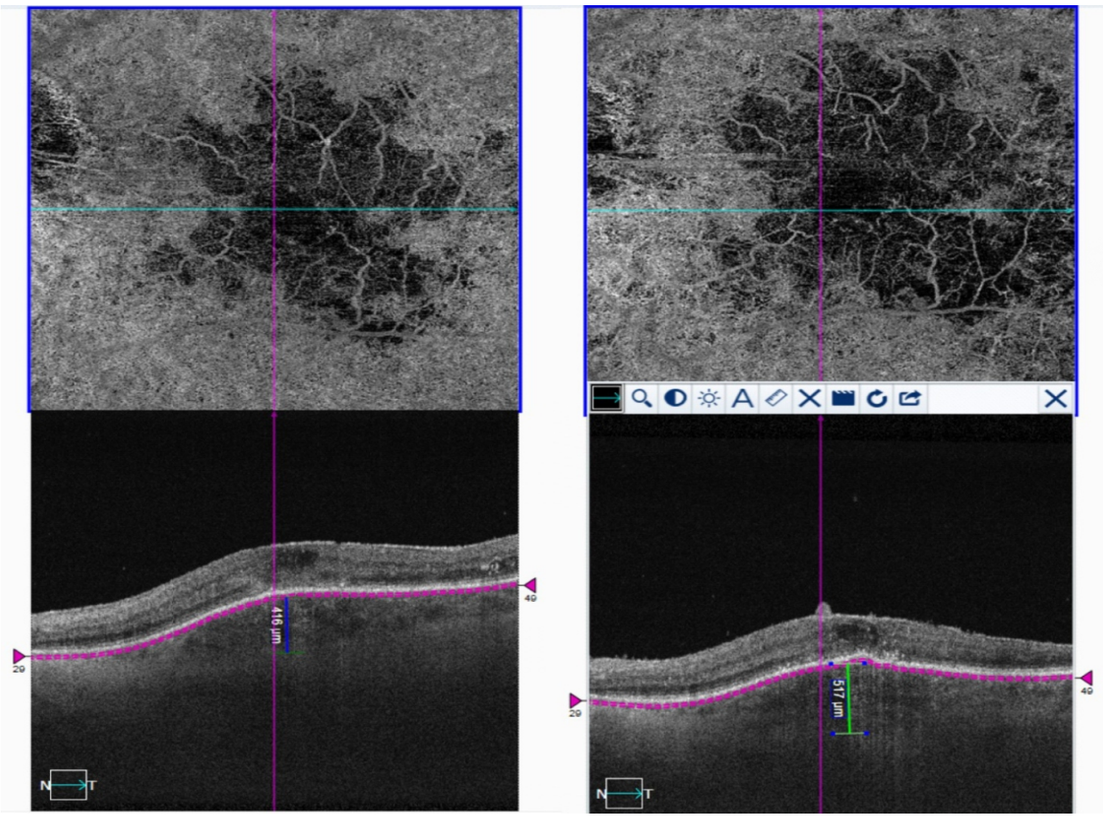


Figure 2 - Ischemic area shows an increase on OCTA

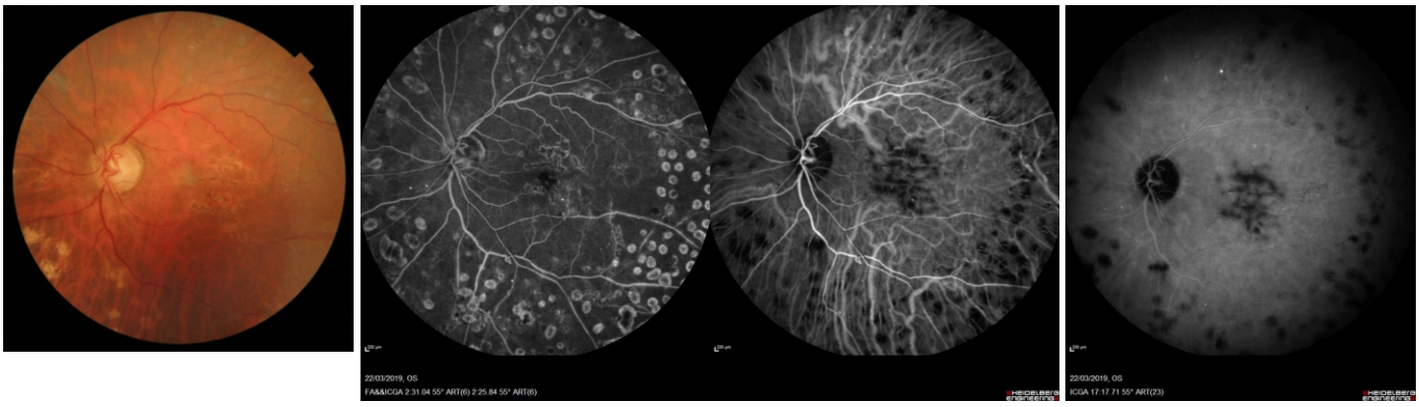


Figure 3 - Colour photograph, FFA and ICG after drop in vision

Questions :

1. **What is your diagnosis ?**
2. **How would you manage this case ?**
3. **What does the OCTA show ?**
4. **What would be the prognosis ?**

1. What is your diagnosis ?

AA : This elderly woman with presumed unilateral maculopathy (other fundus not being able to be examined due to vitreous hemorrhage) that is made up multiple small curvy oval isolated lesions with a distinct border measuring from 200-800 microns in size. Similar cases or case series have been described in the literature as atypical APMPPE in the elderly. Gass in his 4th edition of the Stereoscopic Atlas of Macular Diseases (1997, page 672-673) described 3 such patients at the end of the section on APMPPE. All of them had either unilateral or bilateral profound central visual loss, shows persistent hypofluorescence on fluorescein angiography, with mild late staining of the borders of the lesion. Visual recovery was poor or limited. Mark Johnson and Taich wrote a series of 6 similar cases up as – APMPPE in older adults in 2008. This condition is definitely distinct from the classic APMPPE that is seen as bilateral sudden onset of creamy placoid lesions that are much larger and more widely distributed in the posterior pole, that have a typical fluorescein appearance of early hypo fluorescence and late hyperfluorescence. Recent multimodal imaging features include opacification of the outer nuclear area, the ellipsoid line and the adjacent underlying choriocapillaris corresponding to the placoid patches on OCT and central hypo AF surrounded by a ring of hyper AF on autofluorescence imaging.

If one went by just the fluorescein features of persistent hypofluorescence in the central macula, one should consider Persistent placoid pigment epitheliopathy in the differential diagnosis. Persistent placoid is bilateral, usually a single large placoid affecting the central macula with or without evidence of CNVM at the onset. It is characterized by development of multiple CNVM and the response to steroids or immunomodulatory drugs is variable. Visual prognosis is variable with some patients continuing on to progressive outer macular atrophy, while others may recover. The spectrum of variable severity has evolved over time, though the initial case series had a uniformly poor and progressive course.

Other conditions to consider in the differential diagnosis are – Placoid syphilis, Retinal pigment epitheliitis (Krills' disease), acute macular choroidal infarct.

MB : APMPPE, serpiginous choroiditis, relentless placoid chorioretinitis, syphilitic posterior placoid chorioretinitis, persistent placoid maculopathy. Though the rapid progression suggests otherwise, in an elderly person I would want to rule out malignancy, especially lymphoma.

MPS : Initial pseudocolor photograph shows grossly attenuated / arterioles (silver wiring like pseudo appearance), yellow patch at

the macula and scattered laser photocoagulation marks. The single frame of FA provided shows areas of focal venular compression by the arterioles, focal disc leak, capillary non perfusion involving the macula and temporally, some perivenular leakage, distorted foveal avascular zone, irregular caliber and filling of the overlying retinal arteriole. There is an area of focal leakage along the superotemporal venule. OCT shows epiretinal membrane, one cystic space with loss of outer retinal structures. Focal elevation of the RPE Choroid complex below the fovea with a few hi reflective foci close to the RPE. No vitreous cells. OCTA shows irregular large flow void areas in choriocapillaries.

Considering the presence of anterior segment cells and sudden onset of vision loss and infective or inflammatory pathology involving the choroid is a possibility. Infiltrative pathology such as a lymphoma is also to be considered.

Rapid progression in 4 days with the ICG showing choroidal hypoperfusion. True Color photo now – shows pigment alteration at the fovea – cannot comment if these occurred within 4 days as the earlier photograph was pseudocolor. FA shows patches of hypofluorescence with surrounding hyperfluorescence and the disc leak is not seen.

OCT shows increased hypereflective spot at the outer retina and RPE and within the retina, focal breach at the RPE and a nodular elevation above ILM nasal to fovea. No vitreous cells. Focal choroidal elevation has increased but no hypereflective spots are seen within. Choroidal vascular structures within the elevation and adjacent area are indistinct now. The area of choroidal flow void to have increased significantly.

AT : Differential is that of choriocapillaris flow impairment in the macula – placoid like. Clinically yellow lesion with defined borders in macula – OCTA – no detectable flow in OCTA.

- Inflammatory – idiopathic Persistent placoid, macula serpiginous, AMPPE
- Infective- syphilis, TB, sarcoid.

VG : Keeping in view the age of patient i.e., 81 years presenting with choroidal lesion, my first concern will be to look for masquerades and metastasis. Though it can be granuloma due to other causes, but my primary concern will be to rule out masquerades in this age group before I proceed.

UN : The diagnosis is Macular Choriocapillariopathy. It could be a primary disease or secondary choriocapillariopathy. The differentials could be APMPPE, macular serpiginous choroidopathy or serpiginous like choroidopathy, persistant placoid maculopathy, AMN and granulomas in view of the inflammation recorded. Considering the age APMPPE, AMN may be a rare event while others are more likely. However the presence of outer retinal disease on structural OCT, and rapidity of progression points more in favour of APMPPE. A detailed FFA analysis with hypo early and late hyper would confirm the diagnosis of APMPPE. Here the FFA provided is not sufficient. Serpiginous choroidopathy would have bordering staining of the lesion on FFA. Choroidal thickening is seen in acute APMPPE and is known to regress with resolution. Curiously there is a dilated choroidal vessel abruptly ending at the central hypocyanescent area on ICGA which is a variation in this case. Persistant placoid maculopathy is unlikely as most of these entities have good vision unless they develop CNVM which is rampant in these cases.

2. How would you manage this case ?

AA : Imaging with FA, OCTA, OCT to establish the diagnosis and rule out persistent placoid pigment epitheliopathy, where recurrent and multiple CNVM are common, where anti VEGF injections may help. Rule out thrombotic causes, acute hypertensive crisis, choroidal infarcts etc. No treatment is known to help, the most one could try is an intravitreal Triesence (preservative free triamcinolone) injection to see if this may limit the inflammatory component of the disease.

MB : Systemic workup for infectious and non infectious inflammatory etiologies especially TB , syphilis and toxoplasmosis, a systemic evaluation for possible malignancy. Possibly even a vitreous biopsy if in doubt.

APMPPE is known to be self limiting, though steroids form a part of the management though there is no definite proof that they help in the long run.

VG : I would get a detailed history from the patient regarding her systemic profile including any alterations in the bowel habits, loss of appetite, weight etc that may give a clue towards any underlying malignancy. Then I will pay attention and characterize the cell type in anterior chamber. If I find that cells that are bigger than leucocytes and are not producing any fibrin or synchaeia, I would simply do anterior chamber paracentesis and do cytology as well as IL6/10 ratio. This ratio is very crucial as IL 10 is elevated in malignancies and IL 6 in inflammations. In the meantime I will
also get whole body PET scan.

Paying attention to right eye is important to me. Though it has been mentioned that patient has diabetic vitreous

haemorrhage, but again I would look at the character of cells. If the haemorrhage seems grey with non pigmented cells, I would again suspect masquerades rather than diabetes and plan vitrectomy for right eye. However, it is important to take undiluted sample of vitreous under air to begin with using low cut rate of 800 cuts/min and characterize the cell types. These cells are fragile and have to be transported to laboratory immediately in ice box under the supervision of expert cytologist who should be ready to receive sample and process it immediately. Again, IL 6-IL 10 ratio, MYD 88 and flow cytometer of vitreous sample from right eye will be very useful.

AT : Exclude infective causes, as patient elderly diabetic hypertensive systemic steroids problematic – discus unclear treatment options including local steroid

UN : Careful assessment of FFA/ICGA, AF, followed by a trial of oral steroids in view of the drop in vision and being one eyed after a work-up for tuberculosis and other infectious / inflammatory etiologies (rule out TB serpiginous like choroiditis).

3. What does the OCTA show ?

AA : OCTA shows poor flow in the choriocapillaris – whether this is all vascular insufficiency or partly infiltrative and secondary vascular insufficiency is debatable. The OCT B scan shows involvement with opacification of the outer nuclear layer, outer plexiform layer, EZ and IZ and localized increase in choroidal thickness.

MB : There is only 1 slab available of the OCTA, showing flow /signal void areas which are confluent, have an amoeboid pattern and have increased in area on the subsequent visit. The OCT shows intraretinal cystoid spaces, outer layer hyperreflectivity and a localized thickening of the choroid.

AT : The OCTA shows no detectable flow in choriocapillaris defined boundaries

VG : The enface OCTA provided shows area of capillary non perfusion that could be due to overlying ischaemia of the choriocapillaris causing secondary ischemic choriocapillaropathy.

UN : OCTA shows choriocapillary filling voids with decorrelation artifacts of the overlying retinal vessels. The choriocapillary void area appears geographic and seems to be more than the outer retinal changes on structural OCT but seems to correlate well with focal thickening of the choroid. OCTA also demonstrates the increase in voids with follow up.

4. What would be the prognosis in this case of presumed APMPPE of the elderly ?

AA : Extremely poor, often progressive initially, and limited to no visual recovery.

MB : I would first like to rule out a more serious pathology such as lymphoma or an infection before coming to a diagnosis . In case of APMPPE in the elderly, the prognosis for vision is guarded, with gradual progression to geographic atrophy, development of CNV and a final picture similar to advanced AMD.

AT : Chance of visual recovery worse than younger patients – increased risk of CNV, also co-existing DR also likely to impair choroidal/choriocapillaris flow and be a risk factor for poor recovery.

VG : APMPPE is a disease of young, bilateral showing multifocal placoid lesions in the posterior pole and primary site of inflammation is inflammatory involvement of the choriocapillaris that is primary choriocapillaritis resulting in ischaemia with overlying RPE alterations. In this patient, there are no placoid, yellowish lesions and also the primary site is choroidal stroma with secondary involvement of choriocapillaris. Thus the phenotypic expression of disease is not suggestive of APMPPE.

UN : APMPPE presenting with the following characteristics ; Age older than 60 years, unilaterality, interval before involvement of the second eye of at least 6 months, recurrence of disease, and leakage from choroidal veins are all risk factors for poor visual outcome, progression to geographic atrophy and choroidal neovascular membrane.

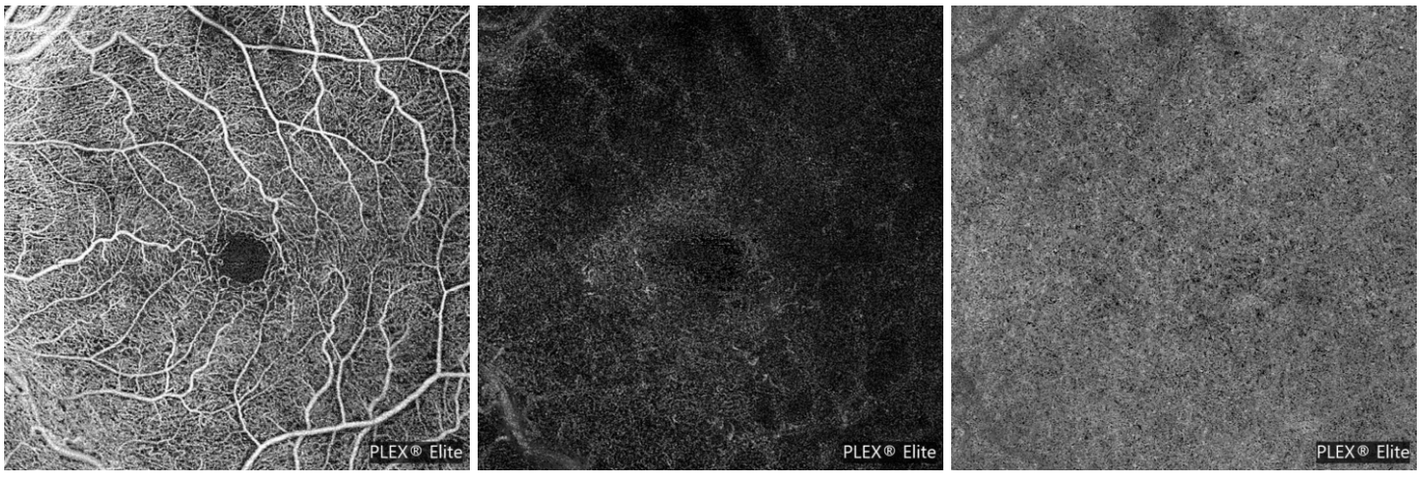
- This case highlights the importance of considering Acute multifocal placoid pigment epitheliopathy even in elderly cases. Alexander Taich and Mark Johnson wrote a series of 6 similar cases up as – APMPPE in older adults in 2009 in Retina Journal.
- Multimodal imaging has an important role as the OCTA documents the choriocapillaris flow impairment well and this corresponds accurately to the ICGA.
- Follow up using OCTA is easy as it is non-invasive.
- The visual prognosis in these cases is generally very poor.

Reference: Taich A, Johnson M. A syndrome resembling Acute posterior multifocal placoid pigment epitheliopathy in older adults. Retina 2009;29:149.

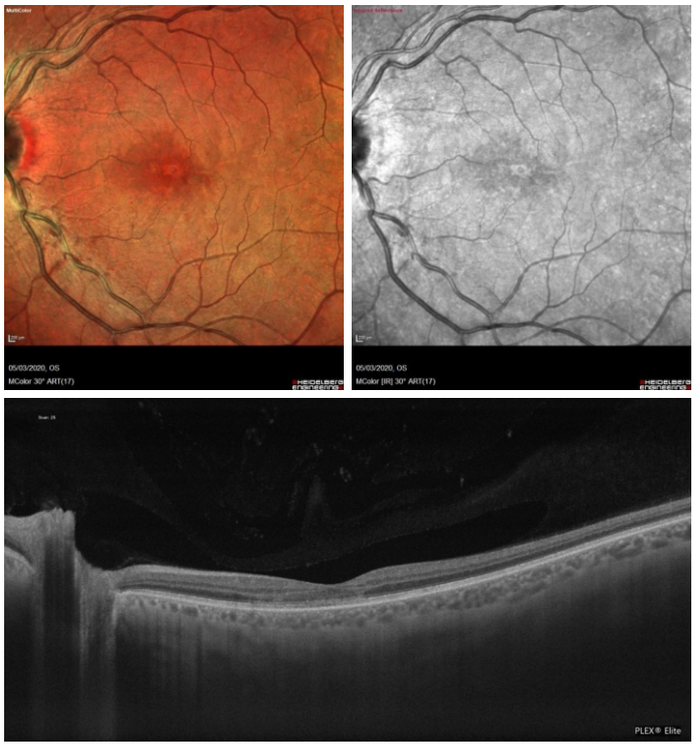
Case 2

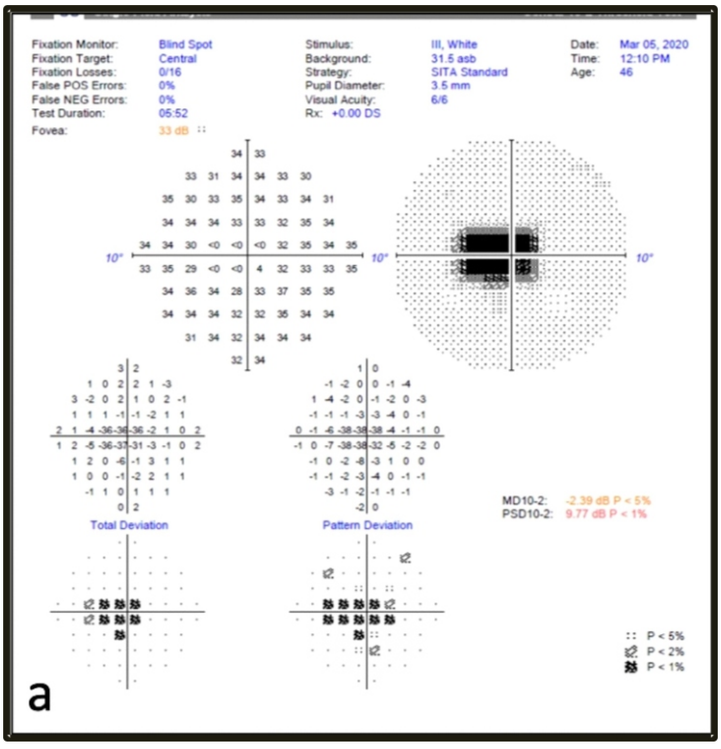
A 45-year-old one eyed lady presented with blurred vision and sudden onset scotoma in the left eye for a week. She was a known case of systemic lupus erythromatosus (SLE) on weekly methotrexate 20 mg, and daily prednisolone 5 mg and hydroxychloroquine 200mg therapy. Her right eye had CRVO related neovascular glaucoma with no perception of light for several years.The best corrected visual acuity (BCVA) in the left eye was 6/6P, N6.

Figure 1 - OCTA of the left eye



SUPERFICIAL DEEP CHORIOCAPILLARIS





QUESTIONS:

1. What is the diagnosis ?
2. What changes seen on the OCTA help to clinch your diagnosis ?
3. Is there any change expected in the choriocapillaris layer ?
4. Management options for AMN in patients with systemic inflammatory conditions. Any role of IVMP/ oral steroids ?

1. What is the diagnosis ?

AA : The history of sudden scotoma but with 6/6 p vision in a 45 year old woman with a reddish brown appearance to the central macula that has a hypo reflective appearance on the near infrared image with reduced flow in the deep capillary plexus and preserved flow in the superficial capillary plexus is consistent with Acute Macular neuroretinopathy (AMN). The OCT shows involvement of the outer retina, with the outer nuclear layer and the IZ-EZ lines

MB : Acute macular neuroretinopathy involving the fovea**.**

MPS : Presence of petaloid red brown lesions around the fovea, the OCT changes are suggestive of Acute macular neuroretinitis. OCT and color photo are representative of AMN. OCTA: DCP shows significant reduction in vascularity. (But this would not be a feature which clinches the diagnosis as PAMM which presents with similar clinical features also shows reduction in DCP. OCT is a better tool)

AT : Findings -loss of definition of EZ corresponding to hyporeflectivity on infra-red reflectance image. In addition, altered reflectivity of ONL.

VG : I would also keep in mind the possibility of AMN. In the current scenario, I would get a history of receiving any COVID vaccination as AMN following COVID vaccination is being seen recently.

Another differential diagnosis I would suspect is MEWDS in this patient, given the enlarged blind spot seen on visual field and foveal granularity. Though it is difficult to comment on the fundus photographs that have been provided, but there seem to be few white dots temporal to fovea seen on multicolour as well as NIR.

UN : The diagnosis is AMN because it is the outer retina that is affected on structural OCT compared to middle layer reflectivity seen in PAMM.

2. What changes seen on the OCTA help to clinch your diagnosis ?

AA : OCTA shows reduced flow in the deep capillary plexus and preserved flow in the superficial capillary plexus, demonstrating the occlusion is at the deep capillary plexus.

MB : The OCT is more characteristic in this case. There is hyper reflectivity of the outer plexiform and outer nuclear layers with irregularity of the ellipsoid zone. The multicolor image and infra red image also show the well defined dark area that suggests AMN. The OCTA shows flow deficit in the deep plexus. There is possibly a subtle deficit in the CC layer but I would be hesitant to commit to this as it is probably too early in the course of the disease to be very obvious .

MPS : Though the role of microvascular occlusion at level of DCP in AMN is not conclusively established as in PAMM, the decrease in vascularity at DCP is reported and may be responsible.

AT : No flow void clearly discernible in DCP or CC corresponding to hyporeflectivity change on IRF, seems to be a flow void in the superior peripheral macula. However structural OCT suggests AMD, IRF pattern atypical for AMN

VG : SCP is normal. It is difficult to comment on DCP because of the quality of image but I suspect there are areas of flow void.

UN : Choriocapillary voids help in differentiating AMN from PAMM (in PAMM the choriocapillaries are usually normal).

3. Is there any change expected in the choriocapillaris layer ?

AA : When the original description of this entity was made by Bos and Deutman, they postulated that relative choroidal ischemia was the likely mechanism, as the FA showed normal retinal vascular flow in these eyes. His theory was the watershed zone between the deep retina supplied by retinal circulation and the area perfused by the choriocapillaris was affected. They were correct in localizing the vascular deficit to be in the deep retina, however the postulation that the etiology was in the choroidal circulation has been shown by OCTA and OCT to be unlikely. One would not expect the choriocapillaris to show changes. It is still possible that some eyes may have this occur from transient choroidal insufficiency.

MB : CC layer flow deficits have recently been described on OCTA , suggesting that AMN results from a choroidal vascular insult as opposed to PAMM which is an insult to the DCP

MPS : Few authors have reported decrease in choriocapillaries in AMN.

AT : Controversial even in the acute phase – unclear whether choriocapillaris change due to projection abnormality from outer retina.

VG : In AMN, the zones of CC flow deficit colocalize with the areas of ONL and EZ abnormality. Thus I would like to see en face OCT and confirm that CC flow deficits areas were not because of signal attenuation. Once that is done, and I am sure that perfusion of the CC is compromised, I would like to see the correlate between areas of flow void in CC with ONL and EZ abnormalities seen in AMN.

For MEWDS, I would like to pass OCT scan through hyper-reflective dots seen temporal to fovea and see the structural alterations.

4. Management options for AMN in patients with systemic inflammatory conditions. Any role of IVMP/ oral steroids ?

AA : Since this patient is one eyed and has an underlying autoimmune disease – Lupus, the patient should be evaluated for activity of the lupus and treated accordingly. The AMN lesion itself is unlikely to be influenced by steroids. However, all attempts to prevent another episode should be undertaken. (Other associations such as being on SSRIs etc. need the dose of SSRIs to be adjusted, patients on oral contraceptives, should be encouraged to come off the contraceptives etc.)

MB : AMN is known to be self limiting, but in case of an associated systemic disorder as in this case, the rheumatologist could be involved in deciding whether to modify the existing treatment the patient is on**.**

AT : No clear role, discus on individual level

MPS : While AMN resolves spontaneously and no treatment is suggested,
considering that the patient is one-eyed and has history of SLE, I would consider temporarily increasing the systemic steroids, particularly if associated with SLE flare up. The retinal veins appear dilated and tortuous – there is a possibility of early central retinal vein occlusion in this eye. Considering that the other eye was lost to CRVO, and underlying inflammatory systemic disease, systemic steroids would be a reasonable option.

VG : AMN per se is not an indication for me to start IVMP. However, I will evaluate this patient more extensively with wide-field FFA

UN : She is already on Wysolone and Methotrexate and has good vision. Needs no change in treatment presently.

Features that should alert us to a diagnosis of Acute Macular neuroretinopathy (AMN) include

- Presence of a sudden scotoma with good vision vision.(6/6p in our case)
- Younger to middle age group.
- Reddish brown appearance to the central macula that has a hypo reflective appearance on the near infrared image.
- Reduced flow in the deep capillary plexus.
- Preserved flow in the superficial capillary plexus.
- The choriocapillaris may appear normal in several of these cases.
- This case of AMN reflects the importance of multimodal imaging especially the near infra red image which can help to clinch the diagnosis.

Case 3

A 44 year old lady complained of drop in vision in the right eye for the past 1 week. Visual acuity was 6/24P N36 in OD, 6/9 N8 in OS.

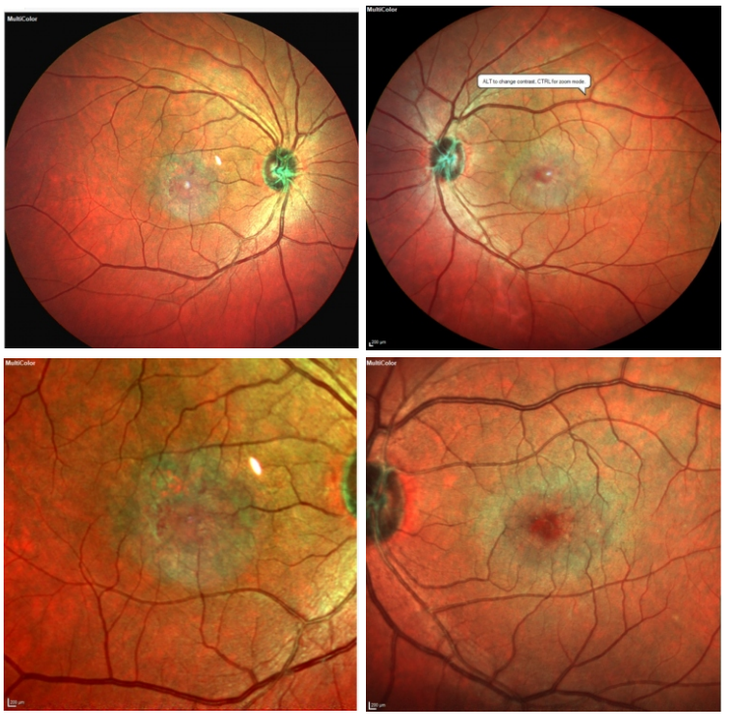


Figure 1 - Multicolour photo of both eyes.

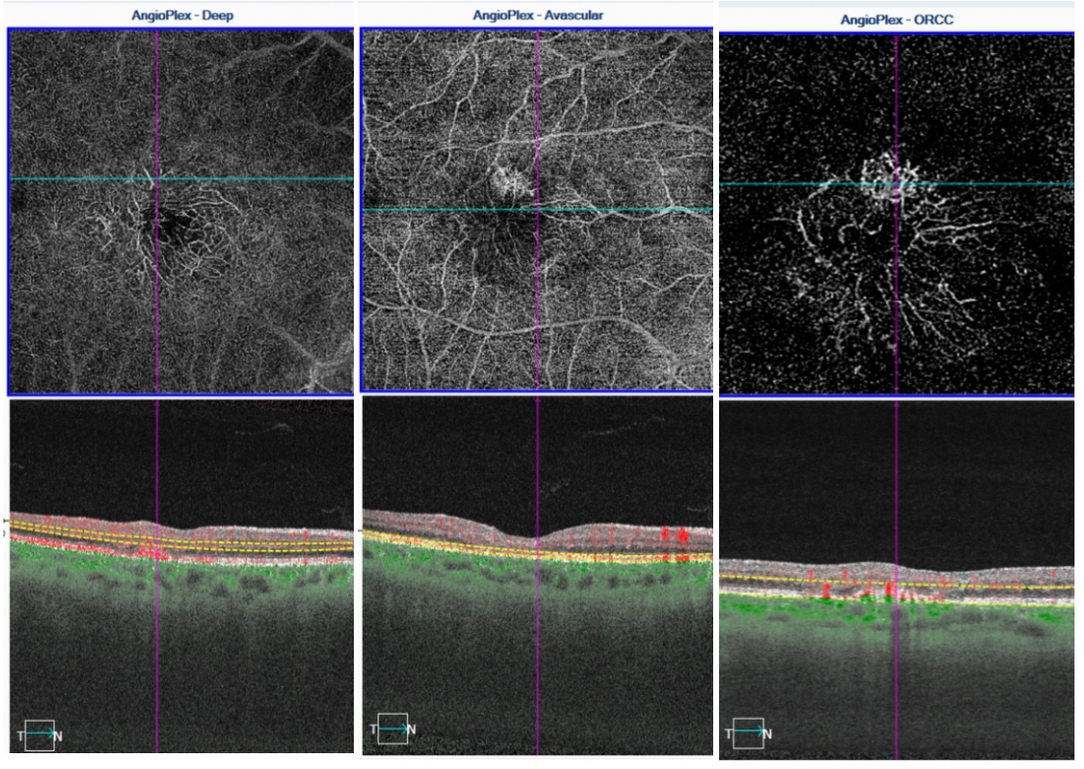


Figure 2 - OCTA image with corresponding b scan.

Questions

1. How useful do you find OCTA in Mac Tel ?
2. Any tips of distinguishing / delineating CNV in these cases
3. What treatment regimen do you folllow- monthy, tr and ext/ prn
4. Post anti VEGF the vision was 6/12p n12 and patient still complains of missing letters and distortion. How do you titrate end point of therapy in these challenging cases?

1. How useful do you find OCTA in Mac Tel ?

AA : OCTA is not necessary to make the diagnosis of type 2 Juxtafoveolar telangiectasia (Mactel 2) in this patient given the clinical appearance of bilateral gray ring, right angled venules dipping into the retina temporally, small pigment figures etc. However, in eyes with early changes clinically, the OCTA showing vascular telangiectasis in the deep network temporally is very useful in considering the diagnosis. OCTA is also likely to be useful in understanding the pathogenesis of the condition.

MB : OCTA in Mactel has definitely increased our understanding of the disease. OCTA has demonstrated a well-preserved GCLP in the earliest stages in the presence of dilated DVC vessels, loss of capillaries and characteristic dilation and dendritic appearance of the DVC vessels and invasion of the abnormal vessels into the normally avascular outer retina PR-OCTA is further able to clarify the vertical course of the right angle venules , retinoretinal anastomosis and formation of chorioretinal anastomosis in some cases of subretinal neovascularization**.**

MPS : OCTA is a useful tool in MacTel- it can identify MacTel early in cases where clinical signs are not apparent. Deep capillary plexus shows changes early in MacTel. Subretinal neovascularization can appear as a closely knit network of smaller vessels, distinctly separate from the MacTel changes of rarefaction of the intervening capillary network, dilation and telangiectasia of the larger vessels.

AT : Helpful in confirming CNV**.**

VG : Fluorescein angiography shows changes in superficial plexus that may remain unaffected and remain remarkably well preserved, even in advanced disease in MacTel. Mac Tel tends to affect deep vascular network even in early disease stages where OCT may be normal and FFA too may fail to detect these changes. Moreover, leakage seen on FFA in these patients may simulate choroidal neovascularization resulting in un-necessary injections of Anti VEGF. OCTA clearly demonstrates vascular changes in deep network including decreased vascular density and telangiectasia and CNV can be seen clearly**.**

UN : OCTA is useful in making a quick diagnosis of MACTEL in eyes with explained visual loss and perifoveal pigmentary alterations. The earliest change is often seen temporally and at DCP level before the abnormality involves the SCP and goes all around the fovea. The characteristic widening of FAZ, widening of the intercapillary spaces and spidery abnormal capillaries help in diagnosis. OCTA is also useful in identifying early proliferative MACTEL as identified by invasion of the capillaries in avascular layers.

2. Any tips of distinguishing / delineating CNV in these cases. Which OCTA slabs do you examine most carefully in such cases ?

AA : In theory, the new vessels in this condition are not CNVMs, but subretinal neovascular membranes (SRNVM) since the new vessels originate in the photoreceptor layers growing out of the deep capillary plexus, and grow downwards towards the RPE and possibly may make connections to the choriocapillaris in some eyes late in the disease. The outer retina/photoreceptor slab is the place to look for the new vessels, once they have reached the RPE and grow horizontally and have secondary RPE envelopment of the vessels, one may be able to see increased reflectivity on the enface image at the RPE/ choriocapillaris level depending on the thickness of the proliferating fibrovascular tissue.

MB : CNV or SRNV which is probably a more appropriate term , is identified in the avascular slabs, and the ORCC slab. It is important to distinguish between capillary proliferation in the avascular layers from neovascularization. In the presence of a right angled vessel, a careful examination of all the layers from superficial to avascular layers may help trace the SRNVM.

MPS : All slabs of OCTA are to be examined as neovascularization in MacTel can be intraretinal, extending to the subretinal space and rarely can extend as epiretinal neovascularization.

AT : Outer retina -CC slab also a more superficial one to help interpretation of the OR-CC slab where the CNV is most easily detected

VG : Since these patients can have RAP too, it is important to identify the area of network with flow on B scan and slab can be placed on this area of interest besides the usual ORCC.

UN : Studying the avascular and DCP layer consequently helps to identify SRNVM from artifacts. Also looking at vascular signals on structural OCT , Outer retinal reflective humps corresponding to invasion and or pigment migration are clues that confirm SRNVM. Often one may have to resort to FFA in case of doubt. Also one needs to remember that these NV complexes have often less IRF or SRF compared to other CNVMs.

3. What treatment regimen do you follow- monthly, treat and extend or PRN ?

AA : These SRNVMs are generally small and respond very well to anti VEGF agents. Only a few injections are needed, and then can be observed. Occasionally, one sees a small deep retinal haemorrhage but no leakage on FA. These can just be watched as they are just a bleed from the vessels and not a full blown neovascular membrane.

MB : I would start anticipating a monthly loading regimen followed by PRN. However, patients with Mactel and CNV do not always have significant exudation and hge especially if there is no RCA, and these require fewer injections, often PRN is adequate.

MPS : While OCTA may help identify neovascularization, need to treat and endpoint of treatment is guided by OCT signs of intraretinal and subretinal fluid. I follow PRN. Difficult to judge end point. Will consider: Symptoms, Vision, any hemorrhage, enlargement of network.

AT : TREX- then Prn when stable at the 3-month extension.

VG : PRN.

UN : I would adopt a Loading dose with PRN.

4. Post anti VEGF the vision was 6/12p N12 and patient still complained of missing letters and distortion. How do you titrate end point of therapy in these cases ?

AA : The residual missing letters and distortion is due to patchy loss of the outer retina and overall thinning of the retina and not from leaking fluid. Once the OCT shows resolution of the SRF and flattening of the outer retina, I observe these eyes and only retreat if the fluid reappears.

MB : In Mactel, there are two components, the angiogenic and the neurodegenerative. The latter would cause impairment of vision that does not respond to anti VEGF therapy and it is important to recognise this and also educate the patient about the same. I would use an OCTA to confirm CNV regression and OCT B scan to distinguish between the exudation caused by the CNV and hypo reflective spaces caused by the neurodegenerative component.

AT : OCTA shows transient undetectability on OCTA a few weeks post anti-VEGF. Best is tracking structural OCT looking at retinal thickness in area of neovascularisation

VG : In these particular situations, I would look at the flow signal within CNV, including a reduction in size, complete flow resolution, and persistence of flow compared to previous OCTA and OCT and development of new fine vessels, loops or increase in area of CNV compared to previous visit in a symptomatic patient will
favour re-injection.

UN : Vision can be used as a guide, only in some cases. Quantifying the EZ loss on OCT or enface imaging helps to understand visual deficit in these eyes. Adjustment of the dose would depend on OCT findings and or FFA.. Often patients complain of increasing metamorphopsia when there is an active neovascularisation.

- OCTA is not essential to make the diagnosis of type 2 Juxtafoveolar telangiectasia (Mactel) but is useful in making a quick diagnosis of Mactel in eyes with explained visual loss and perifoveal pigmentary alterations.
- In eyes with early changes clinically, the OCTA showing vascular telangiectasis in the deep capillary plexus temporally is very useful in confirming the diagnosis.
- Leakage seen on FFA in these patients may simulate choroidal neovascularization resulting in un-necessary injections of Anti VEGF. Hence OCTA confirmation of the network can help in decision making regarding treatment.
- In theory, the new vessels in this condition are not CNVMs, but subretinal neovascular membranes (SRNVM) since the new vessels originate in the photoreceptor layers growing out of the deep capillary plexus, and grow downwards towards the RPE.
- The ORCC/avascular slabs need to be studied to look for the new vessels.Generally, a PRN regimen is followed in these cases.

Case 4

A 26 year lady, complained of drop in vision in right eye since the past 10 days. Her refractive error was -13 D OU. Best corrected vision was 6/36, N18 in the right eye and 6/6 N6 in the left eye.

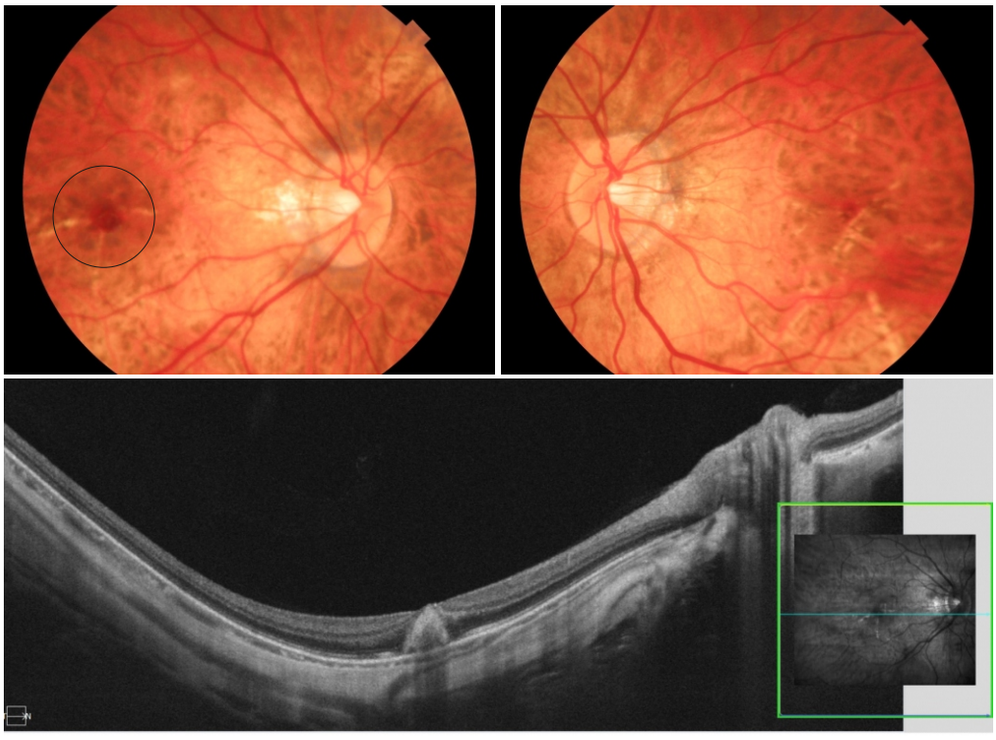


Figure 1 - Colour photograph of both eyes and OCT scan of the right eye through the heme spot.

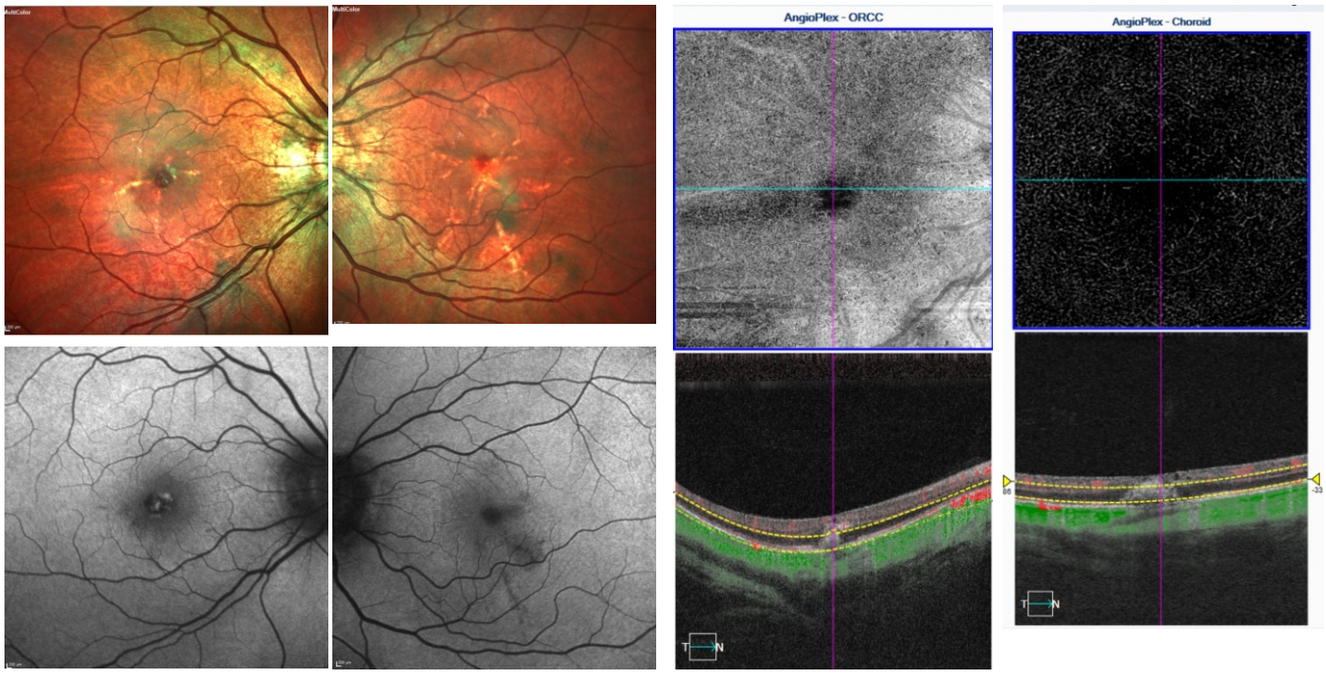


Figure 2 - Multicolour image, Fundus autofluorescense and OCTA through the right eye hemorrhage.

Questions

1. In high myopia how useful is OCTA for determining CNV ?
2. In this case is there a CNV or is it only hemorrhage with lacquer cracks ?
3. As no network on OCTA would you still treat this case with antiVEGF ?
4. What is your treatment regimen- loading dose/ treat and extend or PRN in myopic CNV ?

1. In high myopia how useful is OCTA for determining CNV ?

AA : The CNVMs in high myopes are quite small and OCTA may not always be able to detect these vessels. The hyperplasia of the RPE enveloping the CNVM may also contribute in preventing visualization of distinct vessels on OCTA.

MB : OCTA is useful for detection of CNV in eyes without significant atrophy at the posterior pole . The presence of a staphyloma and extensive atrophy may necessitate more careful manual segmentation to pick up subtle pathology. In the latter situation, where there are a lot of artifacts an FFA may be better.

MPS : OCTA can be a screening tool, but the contour of the eye can affect
segmentation and presence of myopic atrophy can cause unmasking of the underlying choriocapillaries can erroneously appear as CNVM.

AT : OCTA has good sensitivity, studies are conflicting about sensitivity, good but not 100%. There are also segmentation/acquisition issues in highly myopic dome/staphylomatous eyes

VG : It is quite useful in in detecting CNVs in high myopia as these new vessels characteristically appear as 'interlacing' and 'tangles' vascular networks on OCTA. However, literature reports that it does not appear to be sufficient when used alone can miss CNV sometimes should be interpreted alongwith SD-OCT and fluorescein angiography.

UN : OCTA is a very useful investigation in diagnosing CNVM in myopia. One caveat is that getting a good image is sometimes difficult due to underlying contour changes of the retina (like DSM) leading to segmentation errors.

2. In this case is there a CNV or is it only hemorrhage with lacquer cracks ?

AA : Generally, if it is only a hemorrhage at a lacquer crack the OCT B scan will not have a thick lesion that extends into the full thickness of the retina as this one has. Another clue is to check the area of distortion on the Amsler grid. If due to a small hemorrhage the size of the distorted area is likely to be small, however if the distortion extends to an area larger than one would expect from the size of the hemorrhage, it is likely to be a CNVM.

MB : The CNV is not obvious either clinically or on OCT/OCTA. Is there a history of manevers similar to those related to Valsalva retinopathy? There is definitely a hemorrhage over the lacquer crack that could later on lead to CNV formation. Underlying the hemorrhage , one is also able to see a perforating scleral vessel . It is important to also note that hemorrhage could be a precursor for a new lacquer crack as well.

MPS : The OCTA image does not suggest presence of CNVM. However, only one image is presented. OCT image does not show presence of IRF or SRF but the OCT image of the OCTA shows a few inner retinal hyporeflective areas that may indicate presence of IRF and one hyporeflective elevation close to the RPE layer (does not show increased flow though).

It is preferable to perform a fluorescein angiogram to confirm the absence of a CNVM in myopia when OCTA is inconclusive, though a myopic CNVM may not be evident even on FA if the overlying hemorrhage is thick.

VG : I do not see increased flow in the area of SHRM on OCT B scan or any
neovascular network on OCTA through the slab provided. So, I do not think this patient has CNV.

UN : In this case it appears like a Bruchs rupture bleed as there is no typical vascular signals on OCTA corresponding to the hyperreflective foci as would be expected in CNVM.

3. As no network on OCTA would you still treat this case with anti VEGF ?

AA : I would treat this eye given the thickness of the lesion and will pay much attention to the patient's symptoms. If the patient tells you that he or she has a sudden central scotoma in an eye with significant myopic atrophy and FA, OCT and OCTA do not clearly demonstrate evidence of new vessels, I will treat the patient with 1-2 anti VEGF injections as often the patients become symptomatic even of imaging does not demonstrate the very small vessels. It is gratifying to see the patient return with

improvement of their vision.

MB : I would watch, review the patient after 3 -4 weeks, repeat imaging and then take a call.

AT : Possibly yes – may consider other imaging modalities – but if lesion sub/juxtafoveal with acute drop in vision then risk benefit may be in favour of treating.

MPS : I would not treat if the FA also does not show CNVM but reexamine the patient in 2 weeks and repeat non-invasive imaging to ensure that it is only hemorrhage secondary to a lacquer crack and also to rule out occurrence of a new neovascular complex at the location of the lacquer crack.

VG : No.

UN : No, I would not use antiVEGF agents in this case. However I would like to confirm the absence of CNVM by doing angiography, preferably a combined FFA/ICGA before I make a final call.

4. What is your treatment regimen in myopic CNV- loading dose/ treat and extend or PRN in myopic CNV ?

AA : It depends on the size of the lesion and the symptoms and presence of PIC/MFC scars. Generally, in those eyes where the CNVM is from a scar the number of injections needed are higher than if from a lacquer crack lone. I do treat with every 5 weekly injections for 2 or more and extend or hold off further injections based on the OCT appearance. Sometimes the lesion completely vanishes on OCT, then I hold injections.

MB : Plan and counselling is for loading dose followed by PRN, but I would decide based on the response. Small CNVs may show an excellent response to even a single anti VEGF. If I were to treat this patient who does not show a definite CNV, I would re evaluate after the first injection and then decide whether to proceed.

AT : PRN

MPS : Most myopic CNVM can be treated on a PRN basis but there are patients who require more frequent anti-VEGF injections. A monthly review initially can identify such patients who can then be treated with a treat and extend regimen.

VG : I use PRN as many a times patients just respond to one or two injections only.

UN : Myopic CNVM are treated on a PRN basis with antiVEGF agents either ranibizumab or aflibercept. This is supported by data from RADIANCE, REPAIR and MYRROR trials. After the initial anti-VEGF injection, monitoring monthly for the first 3-4 months for stability of disease activity, with clinical evaluation and appropriate imaging (OCT/OCTA and/or FA) is essential

5. How useful is fundus autofluorescence in these cases ?

AA : If the reactive RPE is stimulated by the new vessels, one may be able to see increased AF, however this is not a consistent finding and is often not present when the retinal hemorrhage obscures the RPE or the blood is only from a lacquer crack.

MB : Autofluoresence has no particular benefit in eyes with extensive atrophy, though in this case, the lacquer cracks are well seen on the multicolor image.

AT : Not useful in treating per se, but may be helpful in delineating lacquer cracks that have RPE loss and myopic maculopathy that has prognostic utility

MPS : Fundus autofluorescence changes can aid in predicting visual gain after anti-VEGF therapy in myopic CNVM, eyes with hyperfluorescent CNV gaining better vision. However, autofluorescence alone cannot be relied upon to aid in diagnosis of myopic CNVM.

VG : Fundus AF pattern may be used alongwith other imaging modalities especially in predicting final visual outcome but does not help me as standalone modality for detecting CNVs.

UN : Autofluorescence is an important investigation in these cases. Intense hyperautofluorescence CNVMS have better prognosis and response to therapy than patchy hyperautofluorescence. Autoflorescence is also useful to differentiate Bruch's rupture bleed from myopic cnvm bleeds, the former being hypoautofluorescent and latter often showing hyperautofluorescence. Also during follow up demonstration of ensuing atrophy can be detected well on autofluorescence follow up imaging. A decreased autofluorescent growing patch denotes increasing atrophy. A new patch of patchy or intense hyperfluorescence in an area of preceding iso/hypoautofluorescence is probably an indication of recurrent CNVM.

- Myopic CNV are generally small with minimal SRF and exudation. OCTA is a useful tool for detection of CNV in highly myopic eyes.
- The presence of a staphyloma and extensive atrophy may necessitate more careful manual segmentation in OCTA to pick up subtle pathology.
- In cases with a staphyloma where there are a lot of artifacts on OCTA performing a fluorescein angiography is important.
- Generally, these eyes do well with pro re nata (PRN) therapy of antiVEGF agents.

Case 5

Case Courtesy : **Dr. Ritesh Narula**

50-year-old lady. Not a Diabetic or Hypertensive. Complained of drop in vision in the right eye since last 1 year Visual acuity OD-6/24, OS - 6/6. No old Records available (History of some injection in eye 1 year back, no improvement) No treatment taken for last 1 year due to Covid 19 Lockdown, vision slightly worse than before OU: Phakic (clear lens); Rest Anterior segment OU: NAD.

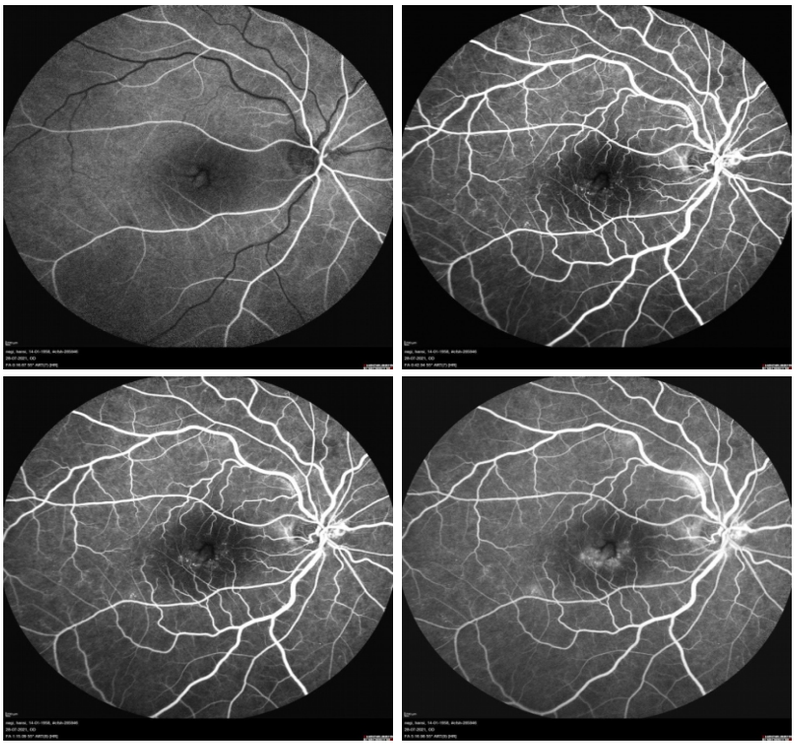


Figure 1 - Fundus Fluorescein Angiography OD Multiple leaking micro aneurysms at post pole No Vascular block or CNP area near macula seen FFA OS: WNL

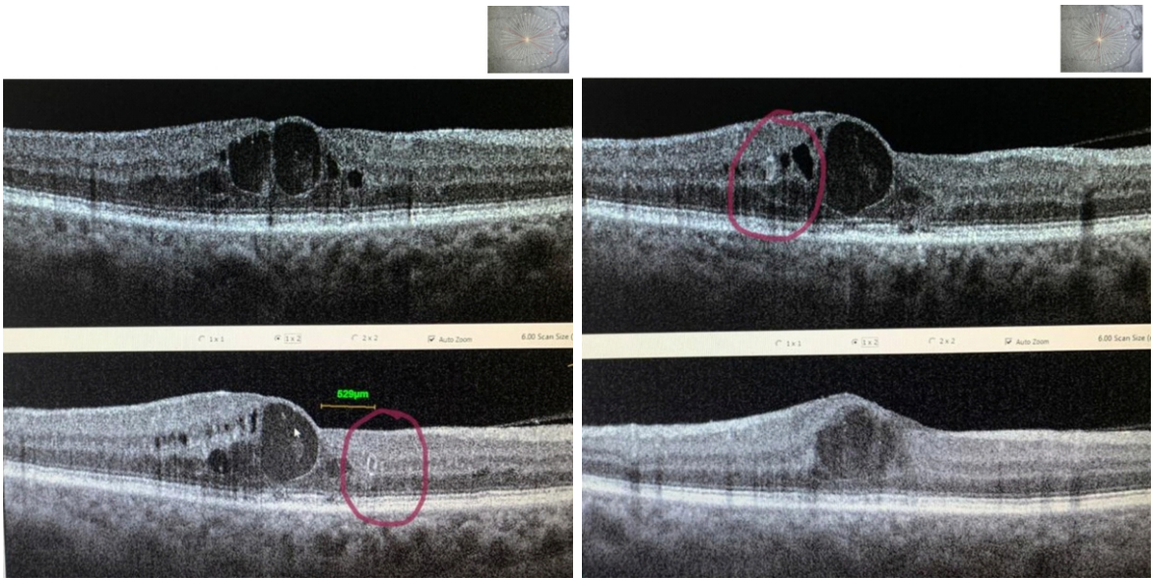


Figure 2 - OCT OD

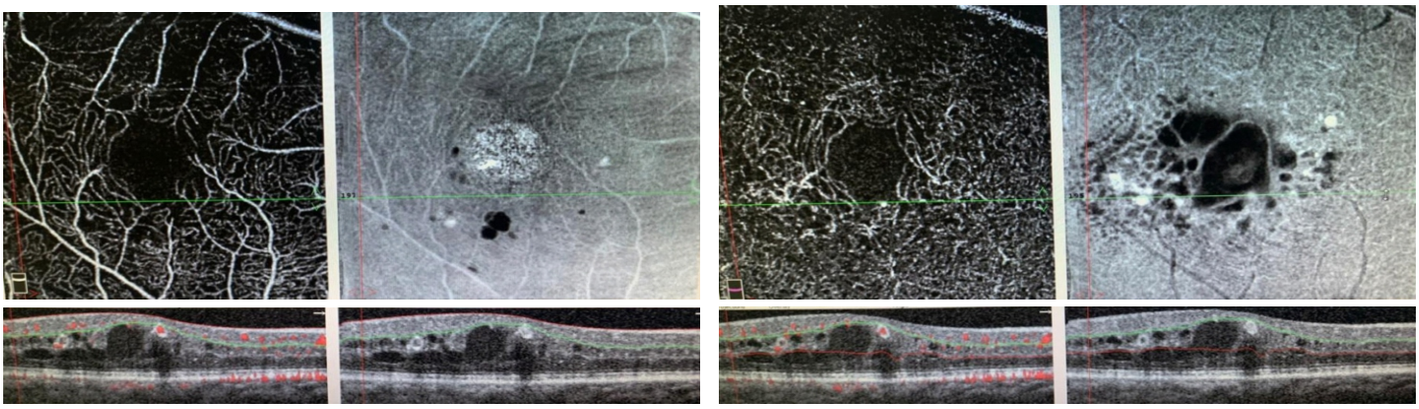


Figure 3 - OCT-A with En Face Image OD

Questions

1. What is the diagnosis ?
2. What are the changes seen on the OCT and OCTA (the high flow aneurysmal walled lesions) ?
3. What helps to clinch your diagnosis ?
4. Management options for such a patients and prognosis ?

1. What is the diagnosis ?

AA : Presuming this is unilateral, one has to consider Type 1 Juxtafoveal telangiectasia or radiation retinopathy in this patient (even though she is a female, Type 1 JFT is more common in men). The lack of systemic vascular risk factors such as diabetes and hypertension, the presence of microaneurysms ad vascular permeability changes both above and below the horizontal raphe (rules out macular BRVO). Macular BRVO can look like this, but often one can see collaterals in the vicinity and the changes are generally limited to the superior or inferior macula.

MB : I would have been happy to see a color photograph before trying to interpret the investigations. Assuming this is a unilateral pathology in a diabetic I would have a differential diagnosis of Idiopathic Macular telangiectasia type 1 or DME. I would also like to carefully examine the periphery for similar telangiectatic lesions that can occur in IMT, as well as images of the fellow eye. There are no features of RVO that could have accounted for the unilateral presentation.

MPS : This 50 year old lady with no contributory systemic history has had an intravitreal injection a year back. No color photographs are available. Flourescein angiogram shows some dilation of the retinal veins, patchy areas of capillary non perfusion and few telangiectatic vessels along the arcades and temporally and multiple microaneurysm at the macula. These could indicate a compensated central retinal vein occlusion as a diagnosis.

VG : I think this patient most likely had Macular Branch vein occlusion one year ago.

UN : The diagnosis is PEVAC right eye.

2. What are the changes seen on the OCT and OCTA (the high flow aneurysmal walled lesions) ?

AA : The vertical B scan OCT images show the distinct microaneurysms in the deep capillary plexus. The enface structural image shows cross sections of the cysts.

MB: The size of the mentioned lesions are larger than typical microaneurysms, There is cystoid macular edema as well. On OCTA , the lesions are less in number than FFA, one lesion is seen on the deep plexus slab at the lower border of the FAZ.

AT : PEVAC-resembling lesion – needs exclude DM/HT/RVO.

MPS : OCT shows intraretinal cystoid spaces and thick walled intraretinal aneurysms; OCTA shows distorted foveal avascular

zone, rarefaction of deep capillary plexus and aneurysmal dilations.

VG : The changes show cystoid macular edema, irregular FAZ both in SCP and DCP and reduced capillary density especially in DCP

UN : On the OCT cystoid spaces with some turbidity within and hyperreflective foci. Also seen is aneurysmal lesion representing the PEVAC lesion. On OCTA the PEVAC lesions are seen lighting up in SCP layer and seen clearly in the DCP layer. Also seen in the DCP layer are abnormal capillaries suggestive of microvascular abnormalities.

3. What helps to clinch your diagnosis ?

AA : The presence of leaking MAs on FA, cysts on OCT and enface image, presence of MAs on OCT & OCTA all suggest type 1 JFT. One cannot completely rule out a macular BRVO, the treatment is the same anyway with focal laser to the aneurysms with or without prior 1-2 anti VEGF injections.

MB : In the absence of definite saccular dilatation of the perifoveal vessels, though there is dilatation of the temporal perifoveal vessels,I would stick to a differential diagnosis, probably have a careful look at the macula of the fellow eye before deciding for sure.

MPS : The thick-walled aneurysms can be seen in some cases of resistant diabetic retinopathy and have been named as TelCaps (telangiectatic capillaries) by some authors.

VG : The presence of Irregular FAZ indicates an ischaemic insult. The secondary aneurysmal dilations are known to ocular in long standing vascular occlusions are to me they are secondary manifestations of occlusion rather than primary cause of macular edema.

UN : The fact that the patient has no systemic diseases like HT or DM and the unilateral presentation of this lesion with exudation is suggestive of PEVAC. Also OCTA and FFA are contributory to the diagnosis.

4. Management options for such a patients and prognosis ?

AA : The First step is to rule out all causes of the vascular changes and arrive at a reasonable cause for the findings. Diabetes, hypertension, history of radiation, wide field imaging to look for peripheral Coats' type changes, fellow eye angiogram, rare causes of background retinopathy such as amyloidosis, anemia, etc. are ruled out, I would do 2-3 monthly anti VEGF injections and reassess the vision and OCT appearance to see if the cysts have decreased. I would treat the visible microaneurysms with careful focal laser. Sometimes repeat focal laser may be necessary depending on the appearance of new aneurysms due to remodeling of the
vasculature or progression of the telangiectasia.

MB : Treatment would include anti VEGF agents for the CME, consider focal laser to the larger lesions if there is no response.

AT : Exclude risk factors – reduce risk of further events. Anti-VEGF and laser if no response.

MPS : TelCaps (telangiectatic capillaries) are seen them in resistant DME and they respond better to focal laser photocoagulation better than anti-VEGF agents. Steroids seem to work better than anti-VEGF's as well in eyes with these larger, thick walled aneurysms.

VG : Anti VEGF injections followed by intravitreal Dexa implant. I don't see any DRIL, hyper-reflective dots and its difficult to comment whether EZ is disrupted just under the fovea or not. So I think the patient does have a chance for some visual recovery.

UN : Commonly, PEVAC is unresponsive to intravitreal anti-VEGF therapy, but it could display a spontaneous resolution of intraretinal cystic spaces without any treatment. However the aneurysmal lesions may persist for a long time. Focal laser photocoagulation is shown to be a better way to treat the pathology**.**

Differential diagnosis for high flow aneurysmal walled lesions with cystoid macular edema include macular BRVO, type 1 macular telangiectasis and perifoveal exudative vascular anomalous complex (PEVAC).

PEVAC typically presents as a perifoveal isolated aneurysm, similar to a large microaneurysm, associated with small retinal hemorrhages, intraretinal exudation & in some cases, hard exudates.

It is important to be aware of this entity as it is generally seen in

- Non-diabetic patients
- Typically, the condition was associated with visual decline caused by CME
- Poor Prognostication-Response to treatment being sub optimal.

RETINA TECH

Macular Pigment Investigated with Fluorescence Lifetime Imaging Ophthalmoscopy (FLIO)

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Macular pigment consists of three xanthophyll carotenoids that can be found within the fovea of human eyes. These three carotenoids are dietary lutein and zeaxanthin (from colorful fruits and vegetables) and meso-zeaxanthin (a metabolite of lutein).[1, 2] They give the central macula, the so-called macula lutea, its characteristic yellow appearance.[3] Macular pigment protects the fovea from toxic light damage by absorbing light within the blue wavelength range. Clinical imaging of macular pigment is important, as abnormalities in macular pigment occur in different retinal diseases, and supplementation with macular pigment carotenoids can be helpful in certain cases.[4, 5] In other diseases, the appearance of macular pigment is helpful in making a diagnosis. Evaluation of macular pigment therefore has a high yield in clinical practice. A fluorescence-based imaging modality called fluorescence lifetime imaging ophthalmoscopy (FLIO) has demonstrated additional benefit in the evaluation of macular pigment in recent years, which will be further highlighted in this article.[6, 7]

Conventional autofluorescence imaging investigates the brightness of the fluorescence by creating a gray-scale image representing the amount of fluorescence photons detected. Areas with greater amounts of photons detected appear bright (hyperfluorescent), and areas with fewer photons appear dark (hypofluorescent). Due to its blue light absorptive properties, macular pigment is hypofluorescent and appears dark in conventional fundus autofluorescence images. This led to the assumption that macular pigment does not fluoresce at all. However, studies have found that there is fluorescence from macular pigment.[6, 8]It can sometimes be difficult to determine whether hypofluorescence originates from healthy areas with macular pigment or whether the hypofluorescent signals stem from atrophy within the diseased retina, which can also show hypofluorescent characteristics.[9, 10]

Based on the absorption spectrum of macular pigment within the blue light range, the amount of pigment can be calculated in comparison with green-light autofluorescence because macular pigment does not absorb green light. This method is called dual-wavelength autofluorescence imaging.[11]Figure 1 A shows macular pigment measured with dual-wavelength autofluorescence imaging in a healthy 24-year-old female. It is a helpful tool in clinical practice to evaluate amounts and distributions of macular pigment. However, it is critical to have a reliable reference area without macular pigment in order to obtain correct calculations. In eyes with advanced diseases, accurate calculation of macular pigment can be challenging.[7]

FLIO is another fluorescence-based imaging modality but instead of investigating the fluorescence intensity, FLIO analyzes the fluorescence lifetimes of the human retina in vivo.[6, 12-20] A confocal scanning laser ophthalmoscope raster-scans the retina, and utilizing highly accurate infrared-reflectance based eye-tracking, fluorescence photons are detected in their correct spatial location by two hybrid photon detectors. Not only do these detectors recognize how many photons are recorded, but

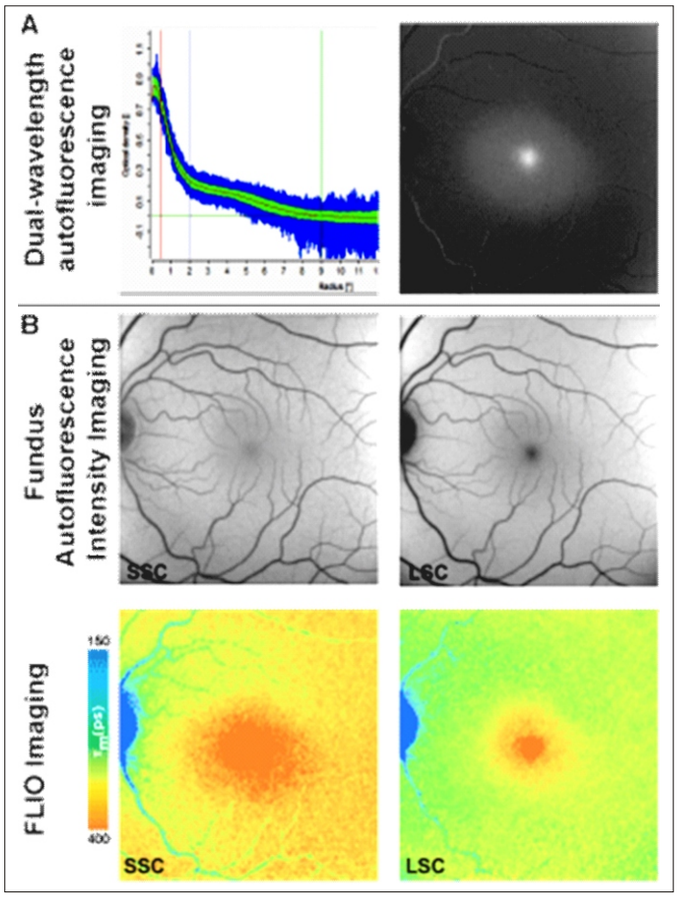

Figure 1: A Dual wavelength autofluorescence imaging and B Fundus autofluorescence intensity and lifetime (FLIO) imaging in a healthy 24-year-old female. SSC: Short spectral wavelength channel, 498-560 nm, LSC: Long spectral wavelength channel, 560 – 720 nm.

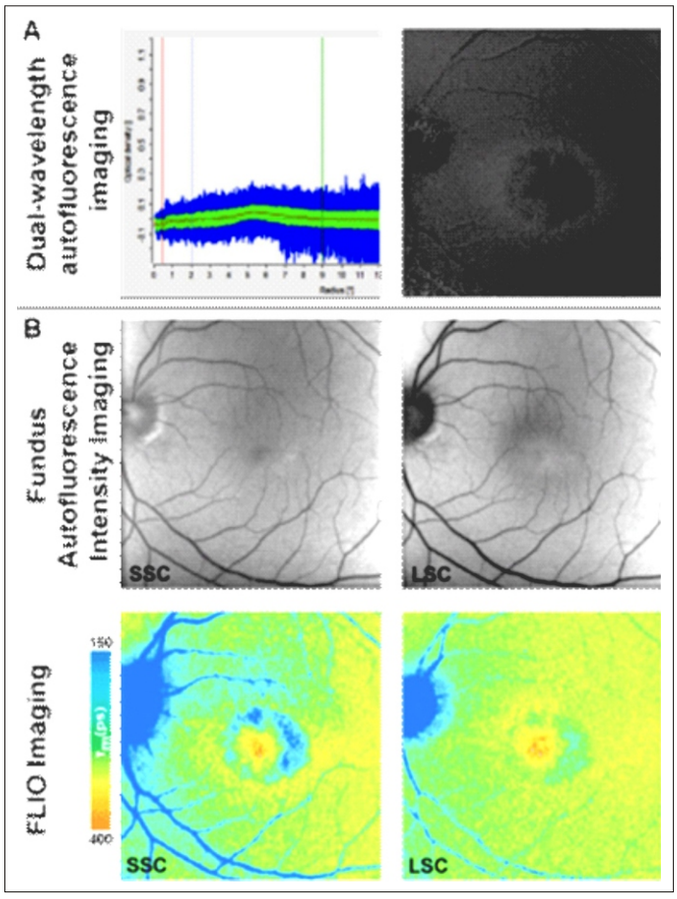

Figure 2: A Dual wavelength autofluorescence imaging and B Fundus autofluorescence intensity and lifetime (FLIO) imaging in a 51-year-old female with macular telangiectasia type 2 (MacTel). SSC: Short spectral wavelength channel, 498-560 nm, LSC: Long spectral wavelength channel, 560 – 720 nm.

furthermore a time-statistic is obtained where photons are recorded in 1024 time-channels, based on the time that has elapsed since fluorescence excitation. A photon-arrival statistic is obtained, representing the number of photons over time for each investigated spot. In total, 65,536 spots representing a 30-degree field of the retina are investigated. A sophisticated algorithm is utilized to fit a multi-exponential curve onto the decay curve of fluorescence photons. The amplitude-weighted mean decay of fluorescence is calculated as the main parameter analyzed with FLIO, and a false-color coded image is created to represent the spatial distribution of individual autofluorescence lifetimes. By investigating the shape of the decay curve, this modality is believed to be independent of the fluorescence intensity. Fluorophores that largely absorb and have only small amounts of fluorescence can therefore be investigated. This property is specifically helpful when investigating macular pigment.

By utilizing FLIO it was found that macular pigment has short autofluorescence lifetimes.[6, 7, 15, 17, 18]FLIO lifetimes are depicted in false-color coded images; short FLIO lifetimes are depicted in red color, and long FLIO lifetimes are depicted in blue color. Figure 1 B shows the distribution of FLIO lifetimes in a healthy eye. Macular pigment contributes to the short lifetimes in the fovea depicted in red. The first study that highlighted a correlation of macular pigment with FLIO lifetimes was published in 2015. [6]In that study, one-wavelength reflectance was used to investigate macular pigment in a cohort of healthy individuals. These values were correlated with FLIO lifetimes, and a strong and highly significant correlation was reported between short fluorescence lifetimes in the fovea and macular pigment. In addition, the spatial distribution of macular pigment was identical to the spatial distribution of short FLIO lifetimes. Further studies repeated the correlation using dual-wavelength

autofluorescence imaging and reported similar results.[7] In addition, retinal carotenoids were investigated ex vivo, and short fluorescence lifetimes were reported. These studies challenged previous assumptions that macular pigment does not fluoresce, as, in fact, a small fluorescence signal can be obtained from macular pigment. Fluorescence lifetimes from carotenoids were found to be 50 to 60 picoseconds.[7]Patients with albinism lack the foveal depression, and these individuals have little to no macular pigment. Short foveal FLIO lifetimes are absent in patients without macular pigment.[7]

Utilizing FLIO imaging might be helpful in determining the state of the fovea in age-related macular degeneration, especially in the presence of geographic atrophy.[5, 9, 10, 21-24] Both macular pigment as well as geographic atrophy show hypofluorescent characteristics, so it may be difficult to determine if the fovea is spared from atrophy and if macular pigment is present in individual eyes. Using FLIO imaging, areas of atrophy have prolonged FLIO lifetimes relative to short FLIO lifetimes in areas with macular pigment. Determining the presence of a spared fovea by macular pigment imaging with FLIO may influence a clinician's decision to start a patient on oral carotenoid supplementation to protect a spared fovea. A different study investigated FLIO lifetimes in patients with macular holes.[25]In macular holes, vitreo-macular adherence causes traction to the fovea as the vitreous liquefies with age, resulting in a small hole in the center of the macula. This defect occurs in the region with highest macular pigment density. Investigated with FLIO, these eyes show displaced short FLIO lifetimes adjacent to the macular hole, where retinal layers with macular pigment have relocated. In some cases, an operculum can be seen, representing a small part of the fovea that adheres to the posterior vitreous. These opercula can contain macular pigment, and if they do, short FLIO lifetimes will be detected in these structures. Some patients were followed after macular hole repair, and re-distribution of macular pigment to a more normal configurations was associated with better visual outcomes. Another disease where macular pigment shows abnormal distributions is called macular telangiectasia type 2 (MacTel).[26, 27] In contrast to the normal central peak of macular pigment, the macular pigment in MacTel eyes is distributed in a ring surrounding the so-called MacTel zone, an oval region with diameters six degrees horizontally and five degrees vertically.[27-29] FLIO imaging also shows the ring of short lifetimes surrounding the MacTel zone, as well as prolonged FLIO lifetimes within this zone.[30, 31]Figure 2 shows macular pigment and FLIO lifetimes in a 51-year-old female with MacTel. However, the prolongation of macular FLIO lifetimes in MacTel seems to be unrelated to macular pigment.[32]This highlights how FLIO has the ability to image not only macular pigment but also other minor fluorophores in the retina that may be helpful to accurately distinguish MacTel from other retinal diseases.

Overall, FLIO presents an additional modality to investigate the human retina in vivo that is independent of fluorescence intensity and therefore facilitates investigation of minor fluorophores in the retina. Analyzing the fluorescence of macular pigment by using FLIO is helpful, as distinct retinal conditions may be determined based on these findings. FLIO imaging goes beyond simply analyzing macular pigment and can provide important additional information about various retinal diseases. Although access to FLIO devices is still limited to a few research centers at the current time, this technique has a large potential to provide benefitsto clinical practice in the future.

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RETINA TECH

Optogenetics Gene Therapy in Retinal Dystrophy

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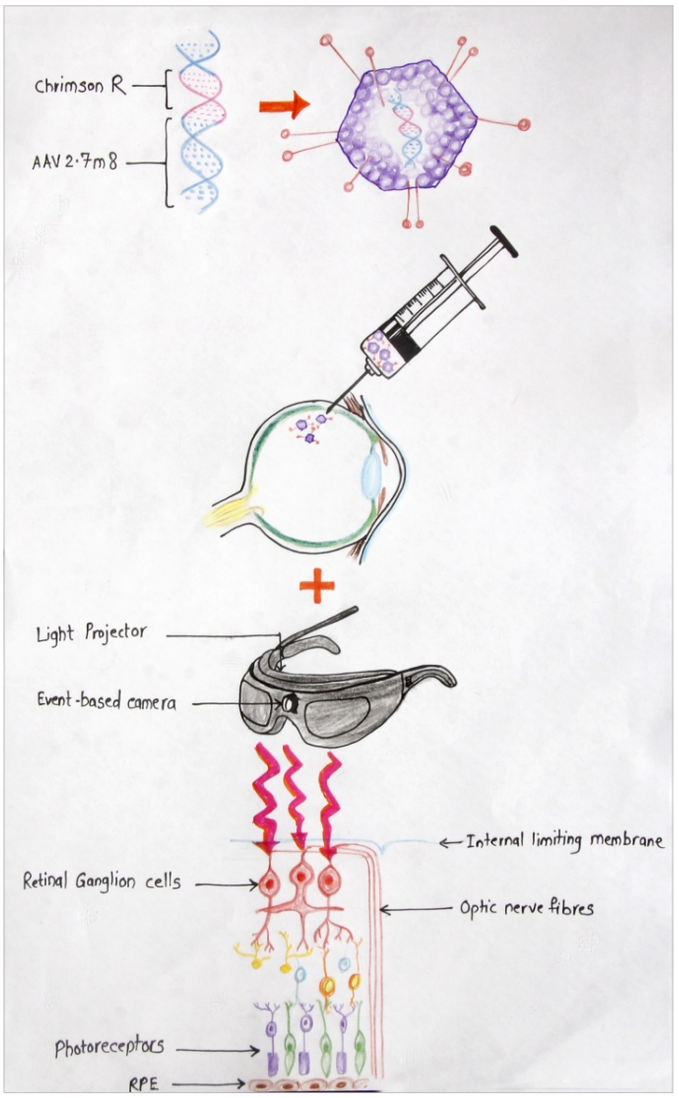
The management of inherited retinal dystrophy (IRD) has been challenging since centuries, and multiple therapies have had dismal outcomes following initial promise. Halting IRD and its relentless progress to intense visual disability has been elusive, and functional visual gain is a very distant goal. In recent times there have been promising advancements in surgically implantable low vision aids and injectable gene therapy.[1,2] These newer advancements have surfaced renewing hopes for a better answer, for both patients and physicians. Optogenetic therapy potentially is a combination of these two modalities. We discuss relevant details of partial recovery of vision by optogenetic therapy reported in a case by Dr Jose-Alain Sahel and his group.[3]

The Science:

The term Optogenetics can be split into two parts; “Opto” and “Genetics”. The optical device comprises of goggles (wearable optical device) that has a camera upfront to capture images, a projector at the patient ocular interface and a processing unit that runs the software. It has the ability to project the captured image on to the patient's retina at specific wavelengths (595nm) within the 10



Schematic explanation of functioning of Optogenetics

degree visual angle.[4,5] The genetics aspect involves injection of an AAV (Adeno associated viral) vector carrying the transgene coding for the protein ChrimsonR fused with tdTomato fluorescent protein. ChrimsonR is a channelorhodopsin found in algae. It is sensitive to amber-red light (595nm) and allows for light sensitive motion of the organism naturally.[7] The hypothesis of optogenetics involves transformation of "viable retinal cells (ganglion cells in the reported case)" into "artificial photoreceptors" that can respond to specific wavelength of light projected by the optical device worn by the patient and fire electric signals (Figure). This system is able to stimulate the central retina.

The Study:

The successful report emanates from the PIONEER study which is evaluating safety and tolerability of optogenetic therapy in non-syndromic retinitis pigmentosa (RP) in a multicentric dose escalation trial (USA, England, France).[4,5] The study is a Phase 1/2a intervention trial that initiated in 2018, and aims for completion of results in 15 patients by 2025. Participants are adults (≥18 years to ≤75 years) with full field electroretinogram (ERG) proven non syndromic RP having viable ganglion cells and retinal nerve fibre layer with severe vision loss (no light perception to light perception), and the ability to wear the optical device.

Methods and outcome measures:

The participants are emphatically trained to use the device. The training involves oculomotor training without the goggles, simple coordination exercises with goggle on and daily life chores related exercises spanned over a year after giving the AAV vector injection intravitreally. The 3 doses of injections being given to the patients include $5X10^{10}$ vector genomes (vg), $1.5X10^{11}$ vg and $5X10^{11}$ vg in 0.1 ml. Maximal tolerable dose is being identified on the basis of predefined toxic responses. Three visual tests are performed at weeks 38, 52 and 72 following the injection at different contrast thresholds. All the visual tests are done in 3 modes; a) Natural Binocular, b) Natural monocular and c) Monocular stimulated by goggles.

The evidence and the case report:

Till now only one case report is available from the study. This involves a 58-year-old gentleman with non-syndromic RP for 40 years due to biallelic USH2A gene mutation, having visual acuity amounting to perception of light only. In the first visual test at 18 weeks post injection, the subject was able to identify, perceive and locate a single object with 92% success rate in the monocular stimulated mode, whereas there was no success in other modes. The second visual test was done at 52 weeks and here the subject was able to perform the test on multiple objects with a success rate of 63% in monocular stimulated mode vs. none in other modes. At 72 weeks electroencephalogram (EEG) was recorded for cortical

excitability in the occipital lobes. The EEG was decoded by a binary decoder with 78% accuracy that was higher than the chance level. Significantly, this patient reported subjective visual benefits 7 months after the injection.

The outlook:

As per the authors amber light was chosen as it is considered safe in terms of heat generation in the retina which is well below the prescribed standards. Functional magnetic resonance imaging could not be employed for cortical changes as the subject had to wear metallic goggles. The authors suggest waiting for the visual tests till more than 4 months as some time is required for episomal integration and transduction process followed by visual integration. However, the maintenance of visual results beyond a year was reported as an indicator of a good long-term outcome by the authors though 5- year results of this patient as well as the whole study cohort are awaited. Promisingly, the results were consistent across various contrast levels and the authors supplemented the case report with video content showing all the 3 tests. The subject did report vertical white vibrations while performing the tests, which have largely gone unexplained. The optogenetic expression may be limited only to 8.2 degrees or central 2.5 mm of the retina.

The comparison:

Optogenetics with ChrimsonR is very different from Luxturna based gene therapy.[7] Table 1 summarizes the major differences between these two modalities of therapy. While the former is largely mutation independent, Luxturna can be used only for RPE65 deficient cases. Optogenetics targets eyes with poor vision in older patents, whereas Luxturna targets the better eye in younger patients. Optogenetics depends on EEG for visual tests, whereas the latter depends on ERG. Macular thickness is a big concern with Luxturna because it uses subretinal injections, intravitreal injections with optogenetics seem to be easier and safer in these respects. Trials of Luxturna used mobility tests to report outcomes, whereas optogenetics group is using indoor tests based on perception of objects. Retinal ganglion cells are the target of optogenetics, whereas RPE cells are the target for Luxturna.

	Optogenetic therapy	Luxturna based gene therapy
1. Patient selection	Older age group	Younger age group
2. Visual acuity	Targets the eye with poor visual acuity	Targets the eye with better visual acuity
3. Gene mutation	Independent	Limited for RPE 65 gene mutation
4. Target cells for therapy	Retinal ganglion cells and not dependent on residual macular thickness	RPE cells and dependent on residual macular thickness
5. Mode of delivery of the vector genome	Intravitreal, safer and easier	Subretinal and requires training
6. External medical device	Light stimulation googles	None
7. Post therapy assessment	• Indoor perception of objects • Electroencephalogram	• Mobility tests • Electroretinogram

The challenges:

It should be remembered that optogenetics requires a device to be worn by the patient, and the early stages the vibrations or "noise" reported by the patient needs to be observed carefully as the transduction of the protein has not been mapped yet for its location in the retina. Further, the trial has not yet evaluated goggle on the untreated eye. Yet the partial recovery noted in the patient is very encouraging given the lack of therapy for IRDs.

The promise:

Optogenetics has thus shown a promising result in cases where severe visual loss has occurred due to IRDs. It can potentially be offered to many patients independent of their mutations, provided there are viable retinal cells that can be transduced. Generally, ganglion cells have been shown to be spared till very late in disease in mouse models, and thus can be possible cellular targets for optogenetics therapy in IRDs.[8] The long-term results of the POINEER study and phase 3 randomized trials will answer many questions for the community.

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INNOVATOR'S ISLE

Scleral fixated IOL surgery simplified: The CM-T Flex IOL

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Abstract

The CM-T Flex intraocular lens (IOL) is a novel IOL with unique design that simplifies complex scleral fixated intraocular lens (SFIOL) surgery. A "T" shaped haptic at both ends of the lens helps anchor it to the sclera with minimal manipulation of the IOL. Unlike existing techniques for SFIOL surgery that uses sutures or complex maneuvers to anchor the haptics to sclera, the CM-T Flex uses a simple grasp and pull technique to achieve the same result. This report presents the use of CM-T Flex IOL to provide refractive rehabilitation in a 62-year-old patient with surgical aphakia and its follow-up for 24 months.

Introduction

Cataract surgery is a commonly performed surgery with exceptional success rates. However, occasional complications do occur and the capsular support is lost. Placing an intraocular lens (IOL) in this eyes is a challenge.[1] Among the specialized options available in these situations is the Scleral fixated IOL (SFIOL). These lenses are designed so that the haptics can be anchored to the sclera to provide additional stability.[2] Almost all existing IOLs and techniques for scleral fixation employ either sutures threaded through specialized eyelets or tucking of prolene haptics of a three piece IOL into the sclera to fix the IOL in place behind the pupil. With an aim of eliminating these complex maneuvers, the innovative CM-T Flex IOL was developed.[3, 4] Using a simple grasp, pull and release technique, this IOL is anchored to the sclera.

CM-T Flex IOL Design

The IOL is a hydrophilic foldable lens with an end-to-end length of 13.50 mm. The lens has an A constant of 118. The refractive index of the material is 1.460. The unique haptic design has T shaped ends that are connected to the 6 mm circular optic by means of semi-circular connecting arms. The semicircular arms are flexible and can help when the IOL is used in eyes of differing axial lengths and white-to-white diameters. IOL-iris touch is avoided by a 10° angulation that is incorporated in the IOL design between the optic and semicircular arms of the haptic.

Case report

A 62-year old woman was referred from a peripheral center after complicated cataract surgery in the right eye. She had posterior capsular rent during temporal clear corneal phacoemulsification three days ago. On examination, minimal corneal edema, cortex remnants in the anterior chamber, aphakia and nuclear remnants in the vitreous was noted in the right eye. After explanation of the condition, discussing the plan of refractive rehabilitation with a CM-T Flex IOL and obtaining an informed written consent, SFIOL surgery with CM-T Flex IOL was planned.

The IOL power was calculated using an A constant of 118. A power of 19.50 was obtained. Local anesthesia was

administered with lignocaine and bupivacaine as peribulbar injection. Localised peritomies were made 180 degree apart at the limbus at 3 and 9 'o' clock meridia. Using crescent knife, partial thickness scleral flaps attached at the limbus of dimensions 3.5 mm x 3.5 mm were made. Under the scleral flaps, a 23-gauge needle was used to create full thickness openings into the vitreous cavity. Thereafter, regular 3-port vitrectomy was performed after creation of standard ports with 23-gauge trocar cannula system in the inferotemporal, superotemporal and superonasal quadrants. During vitrectomy, nuclear and cortical remnants were removed using the vitreous cutter. Retinal periphery was checked with scleral depression to ensure the absence of breaks.

The CM-T Flex SFIOL was loaded onto the cartridge and injector using adequate amount of viscoelastic material. Using the right hand, the lens was injected into the eye through the pre-existing temporal corneal incision that was used for phacoemulsification (Figure 1). In the meantime, the left hand introduced a PraNiv T Flex intraocular forceps (Appasamy Associates, Pondicherry, India) into the eye from the left sclerotomy below the partial thickness scleral flap. As the IOL entered the eye, it was guided

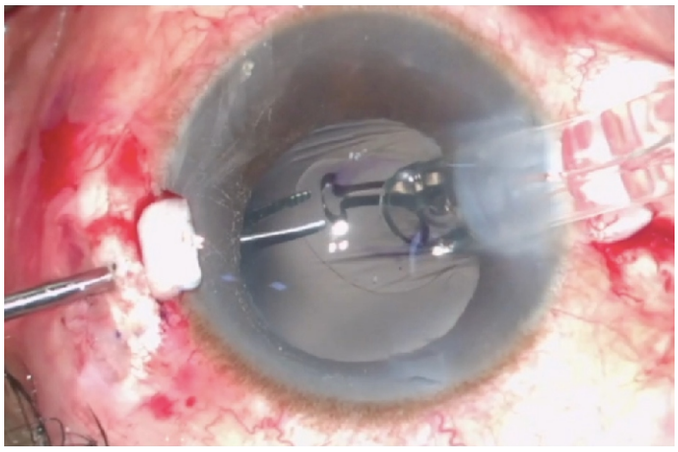

Figure 1. Insertion of CM T-Flex IOL through clear corneal incision. The PraNiv forceps is introduced into the eye from the left through a sclerotomy under a partial thickness scleral flap.

below the iris so that the leading T shaped haptic approached the waiting open forceps behind the pupillary plane. The PraNiv forceps is specially designed with short teeth that prevent the soft hydrophilic material of the T haptic from being damaged. This forceps was thus used to grasp the T shaped haptic at its center. Once grasped, the PraNiv forceps was brought out of the eye carrying the leading T shaped haptic along with it. As the T shaped haptic deforms and exits the sclerotomy, owing to its pliable hydrophilic material, it quickly reforms to take its original shape. The horizontal limbs of the T rest on either side of the sclerotomy and prevent the IOL from slipping back into the eye. In the meantime, the trailing haptic was made to rest on the temporal corneal wound after being pushed out of the cartridge (Figure 2).

To exteriorize the trailing haptic, the handshake maneuver was employed by using the Nishi grasping forceps (Appasamy

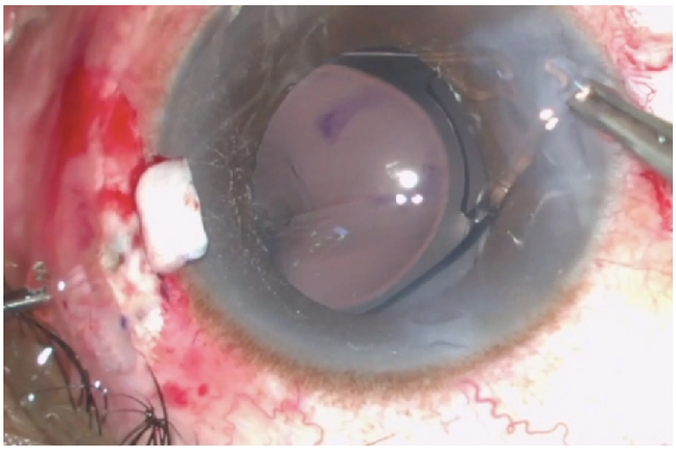

Figure 2. On the left, the PraNiv forceps has brought the “T” shaped leading haptic out of the eye. On the right, the trailing haptic rests on the corneal wound.

Associates, Pondicherry, India), which was introduced into the eye through a stab incision at the limbus (Figure 3). As with the leading haptic, once exteriorized, the T haptic sprang back to its original shape and secured the IOL to the sclera. The posterior

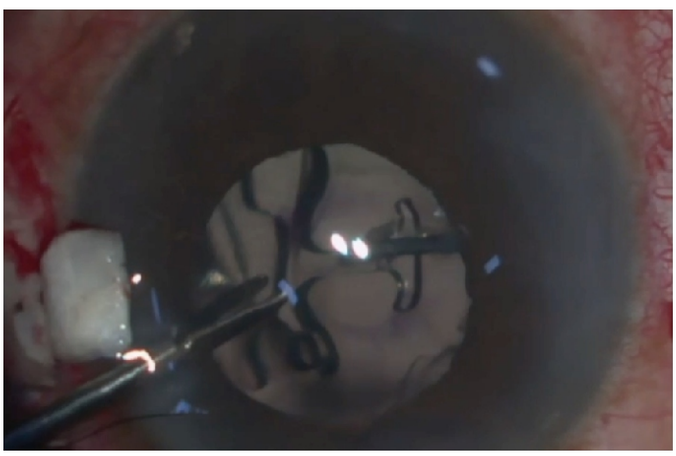

Figure 3. The handshake maneuver is performed with the Nishi forceps to exteriorize the trailing haptic of CM T-Flex IOL

segment was rechecked to make sure that there were no treatable lesions on the retina. The IOL was well centered (Figure 4). The partial thickness scleral flaps and peritomies were closed with a interrupted 8-0 polyglycolic acid sutures.

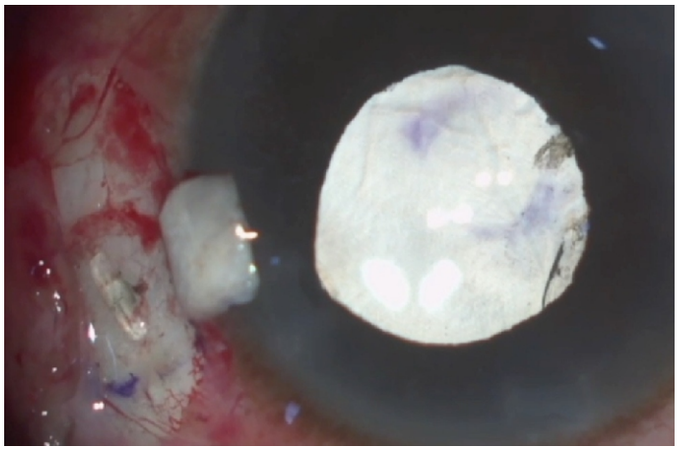

Figure 4. After fixation, a well-centered IOL is seen. The scleral flap on the left has been elevated to demonstrated anchoring of the "T" shaped haptic to the sclera.

On day 1 after surgery, visual acuity (VA) was 6/24. The intraocular pressure (IOP) was measured as 16 mm Hg. The IOL was well centered with no optic capture or IOL tilt. The patient was followed up at 45 days and 90 days when the VA was 6/9p and 6/9 respectively.

At 1 and 2 years, the VA was 6/6. Ocular exam showed a well-centered IOL with covered haptics and a round pupil. The vitreous was clear with no evidence of inflammation. There was no macular edema on optical coherence tomography.

Discussion

In managing aphakia, ophthalmologists have a variety of IOL options.[5,6] SFIOLs are among the more popular types employed because of various advantages like closer approximation of anatomical position to in-the-bag IOL and non disturbance of the iris. Scharioth published his innovative technique of sutureless scleral fixation of an IOL using external scleral pockets.[7] Subsequently, to enhance stability and reduce exposure of haptics, the flap and glue technique was introduced by Agarwal et al.[8] The flanged technique of Yamane has seen increased interest in recent years owing to its simplicity and reproducibility.[9]

The techniques hitherto mentioned have their use in various overlapping scenarios and have found wide acceptance among surgeons. A common thread connecting all the said sutureless techniques is the use of 3-piece IOLs. These IOLs have prolene haptics that are relatively more flexible and forgiving of manipulation to the optic-haptic junction. That said, the haptics themselves are thin and are often noted to bend, break or deform during the performance of complex maneuvers required to secure it to the sclera. This would then require removal and replacement of the IOL. In short, sutureless scleral fixation of a 3-piece IOL is a complex surgery with a steep learning curve.

With the aim of specifically addressing these concerns and simplifying the process of scleral fixation, the CM-T Flex IOL was designed.[3,4] The unique haptic style provides of self- anchoring once exteriorization is completed. The surgeon does not have to perform special maneuvers to firmly secure the IOL or stabilise the optic in its correct anatomical position behind the pupil. The CM T-Flex IOL provides for a simple grasp, pull and release technique which is sufficient for IOL fixation. A "U" shaped based provided for the haptics allows for use in eyes of varying diameters and the hydrophilic material allows for pliability.

In conclusion, this report demonstrates that the CM T-Flex IOL helps to simplify SFIOL surgery. Complex suturing and haptic manipulation techniques are avoided. Apart from intraoperative ease, we have noted that this IOL has long term stability with no undesirable events like haptic exposure, IOL tilt or inflammation upto 24 months after surgery.

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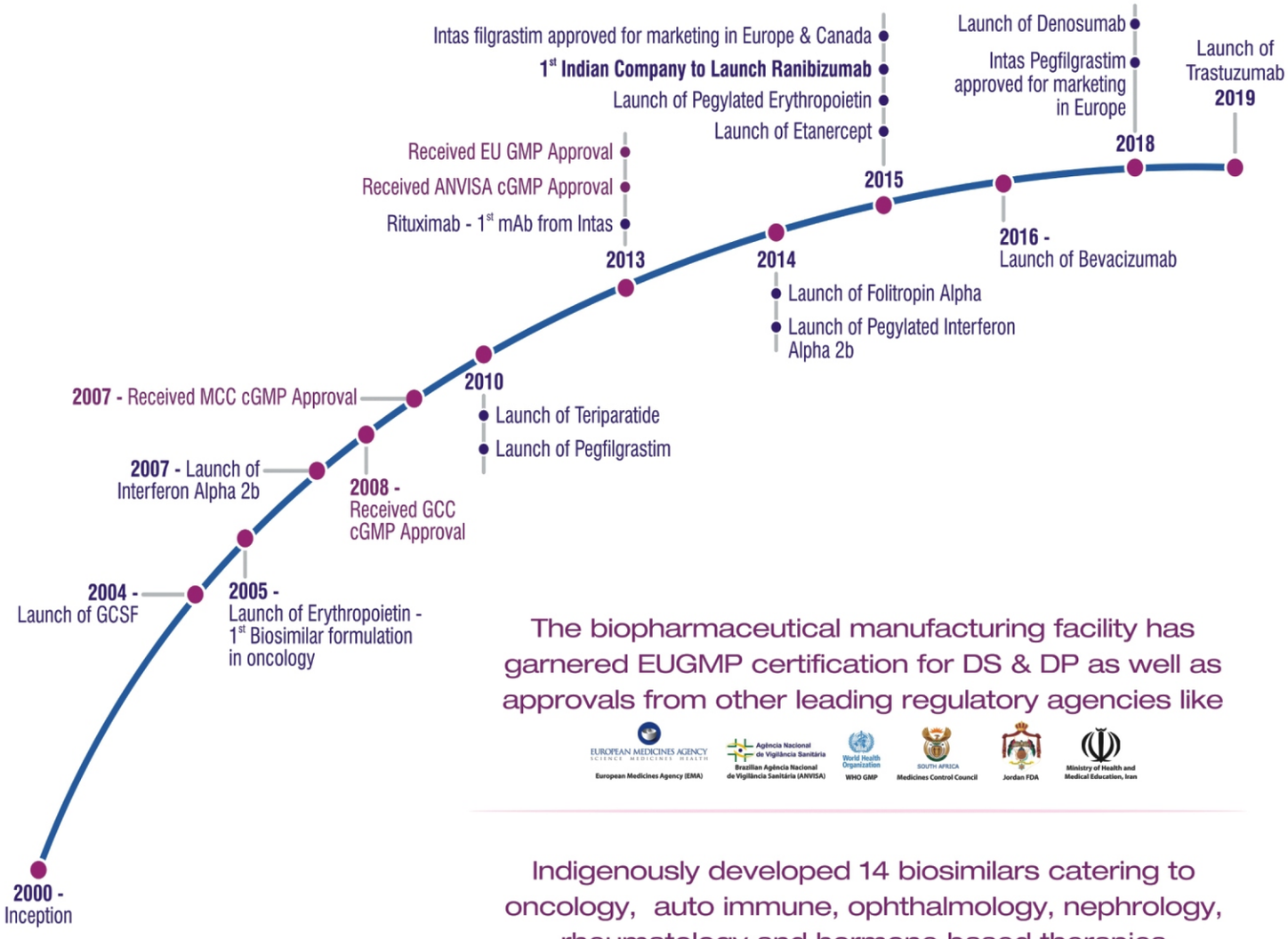

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INNOVATOR'S ISLE

PVRS - post vitrectomy recovery system

Dr. Ashish Ahuja,
Vitreo - Retina Surgeon,
DNB, FICO, FAICO (Retina), FAICO (uvea), FVRS.

Vitrectomy surgery has evolved dramatically in the past 50 years since the time Robert Machemer introduced it in the year 1972 . We live in a country with a population of 1.3 billion people , and if we take an average incidence of 10 cases per 1 lakh population for developing retinal detachment annually , then the incidence of cases reaches about 1.3 lakh/year . [1]

Along with good surgical intervention, the postoperative period is also equally important for patient recovery and treatment success .Post operative positioning in cases with retinal detachment , macular hole , diabetic vitrectomies has been a preferred practice pattern for many surgeons.

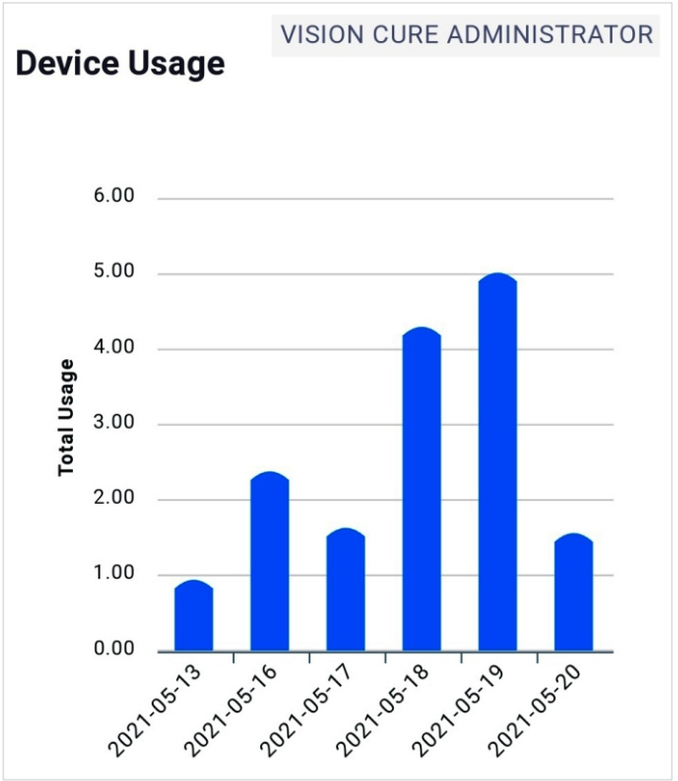
Kelly and Wendel in their paper reported macular hole surgery (MHS) outcomes with Face down positioning (FDP) used for 1-week. [2] And since then many studies have evaluated the role of FDP in cases of macular hole surgeries.

The real world scenario is that it is very difficult for the patients to maintain FDP for a prolonged period of time . Also the duration for which the prone positioning is maintained is also a guesswork based on what the patients inform in the follow up period.

We have developed a device called PVRS - post vitrectomy recovery system after 3 years of research and development, which has a patent pending technology that helps to track the duration for which the prone position was maintained in real

time on daily basis .The device consist of a supportive furniture system (Image 1) , a sensor embedded in the headrest of the cushion (Image 2) and a mirror.

To use the device, patients have to just connect the device to the power bank and place the forehead on the cushion . Data relay to our online server starts when the patients place their forehead on the cushion . Doctors or the patients can themselves track the duration for which prone positioning was maintained through our website and the data is represented in the form of a bar diagram for easy interpretation (Image 3). The height of the supportive furniture system can be easily adjusted and the entire device is lightweight and portable .



To use the cushion in the lying down position , it has to be detached from the supportive device and connected again to the power bank so the data relay can happen in the lying down position as well . This technology would help us to accurately track the duration for which the FDP was maintained by the patients.

The angled mirror provided with the device helps to reflect images in front of the patients when placed below the eye level so patients may talk to their relatives and do other other activities without the change in posture. A central supportive stand is also provided with the device that will help to place the mirror below patients eye level .

This device would also help the doctors medico legally and incase of re surgeries, to track patient compliance for FDP as an added risk factor for failed or repeat surgeries.

The pilot study that we conducted has shown encouraging results. Within our pilot study, we investigated the use of a (patent pending) pressure sensor embedded in the headrest of a supportive furniture with data-logging function to measure the compliance of patients after vitrectomy surgery . All surgeries were performed by a single surgeon and the patients positioning was evaluated in post operative period upto 12 days . Patients were given the devices to be carried home with them in the postoperative period .

13 patients were evaluated but 2 patients had to be excluded as they could not maintain FDP in the post op period . 11 patients were evaluated in this pilot project , out of which 6 were male and 5 were females with the age group ranging from 28 - 71 years . The duration of prone position maintained , varied from 4 days to 12 days . The average duration of face down positioning was 5.5 hours in the first 24 hours . Compliance for FDP reduced over the next few days . The adherence was significantly better after MH surgery than after RRD surgery. Adherence was higher in female than in male patients.

Out of 11 patients, 5 underwent macular hole surgeries which showed a successful closure of MH in all cases . Out of 5 patients of retinal detachment, 4 cases achieved anatomical success and one case required re surgery in the postoperative period .We observed a good acceptance of our device to measure compliance of patients after vitrectomy surgery to maintain FDP

. Further studies are needed to analyse how much time of FDP is sufficient to improve the surgical success in the indicated cases .

The limitation of this pilot study was the small sample size . But further validation studies are being planned in the future .

Although many surveys have analyzed and debated the need for and the duration of a face-down posture [3-5], there is a lack of compliance controls. In most cases, the intervention being tested was advice to posture rather than posturing itself.

In cases of macular hole the question is what is the optimal duration to keep the macula dry to allow healing to occur? This is not known. Optical coherence tomography studies have demonstrated that retinal flattening, reabsorption of fluid from the intraretinal cysts, reapproximation of the retinal dehiscence can take place as early as the first postoperative day. [6,7] This would be more commonly observed in cases where MH size would be less than 400 microns in base diameter .

MH cases in which the holes are larger in size (more than 1000 microns), post traumatic MH, MH with localised neurosensory detachment, some secondary MH, surgeon preference would be more towards FDP in the postoperative period .

We are moving into an era where the patient expectations are increasing, we have better surgical equipment and instruments at our disposable, the use of scleral explants has been reducing over the past decade in cases of retinal detachment. In this scenario the surgeon preference may be towards the use of postoperative posturing as required to improve the surgical outcome.

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PRACTICE PEARL

Insurance and beyond for Intravitreal injections – the current status in India

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The prevalence of retinal diseases is increasing in India with nearly 5% population suffering from neovascular age related macular degeneration and more than 9% diabetics having diabetic macular edema.[1,2] Most of these conditions require intravitreal injections of antiVEGF agents on a repeated basis. This leads to a heightened treatment and financial burden and non-compliance with injections in the long run. Recent data suggest that less than a third of Indian patients complete injections recommended by their physicians at one year follow up.[3] There are a number of ways to improve compliance of intravitreal injections. In this write up we will discuss some of these strategies including insurance.[4]

Currently about 50 crore people in India have health insurance of which roughly 70% is covered by the Government of India, another 19% is by group insurance that is usually offered by corporate houses and individual (retail) insurance comprises of about 8% of the total share.[5] However, there has been a 14% growth in numbers insured from 2014 to 2020 and this is expected to increase by further 19% by the end of 2024.[5] This growth can be attributed to rising awareness and affluence, increasing incidence of lifestyle related diseases, tax incentives, proactive Insurance Regulatory and Development Authority of India (IRDAI) and increasing competition with increasing number of insurance providers offering sophisticated products at competitive prices. Keeping these trends in mind the IRDAI has released a master circular on standardization of health insurance products on 22nd July 2020 that is applicable from 1st October 2020.[6]

Some of the key developments included in these guidelines are:

1. All monoclonal antibodies to be given as injections and all intravitreal injections have been covered, either as inpatient or as part of day care treatment.

2. Coverage has been extended up to 50% of the sum insured specified in the policy schedule annually.

3. There is a waiting period of 24 months after enrolment into the policy before claims for cataract and other age related eye ailments including intravitreal injections can be settled.

4. Reimbursement claims for hospitalization or day care should be submitted within thirty days of the day of discharge from hospital

5. Reimbursement for post hospitalization expenses should be submitted within 15 days from the completion of hospitalization.

6. Routine documents that should be submitted for reimbursement that the physician needs to provide are medical practitioners prescription advising admission/treatment, original bills with itemised break up,

payment receipts, discharge summary including complete medical history of the patient along with other details, investigations and diagnostic test reports such as optical coherence tomography (OCT) and fundus fluorescein angiography if performed.

A meeting was organised in June 2021 by the VRSI called **"Dialogue on Retinal Insurance (DORI)"** and included an array of senior retinal surgeons across India as well as participants from the insurance industry. During the meeting we learned that more than 75% insurance products now covered intravitreal injections and 72% products cover up to 50% of the sum insured value for antiVEGF as mandated by the IRDAI regulations. Given these encouraging numbers we should definitely ask our patients with insurance to apply for reimbursement of their claims for intravitreal injections. It is highly likely that their claims will be settled either entirely or partly, based on the terms of their policy, including repeat injection claims. I have personally witnessed more than 25 settled claims from my own patient pool over the past few months.

It is also important for us to drive education and awareness among relevant stakeholders to maximise the impact of the new IRDAI guidelines. Patients and caregivers must be made aware of reimbursement possibilities, hospital counsellors must bring this up during discussions with patients, healthcare providers, approvers in TPAs and insurance companies should also be aware of the need for recurrent injections and corporate employers should also be aware about reimbursements that are highly likely through their group insurance policies.

What an insurance company looks for in the claim are clear treatment guidelines, usage of approved drugs, network availability, clear documentation, background diagnostics (viz. OCT), discharge summary etc and confidence from a submission that there is no fraud. Corporate group policies have a higher probability of reimbursement. For individual insurance policies, if rejected then one should ask for ICD code and rejection reason in writing and also ask for the clause under which the case is denied. If not satisfied, the policy holder can raise the concern under grievance redressal forum of the insurance company. If still not satisfied with responses, then approach area specific ombudsman's office. Litigation should be used as the last resort.

Some alternate channels to improve patient affordability include:

1. Patient support programs from drug manufacturers,
2. Crowd funding,
3. EMI options for payment.

Patient support programs are extended by drug manufacturers that offer some subsidized injections after a minimum number of injections have been administered. Crowdfunding options are also coming into vogue (example impactguru.com) and may be viable options in the future. Patients could also be made aware of paying for their injection costs through EMI options such as those offered by Bajaj Finserv and others. They should also be made aware of reimbursement options through their corporates, or PSU's or private insurance or through their government sector insurance. There are also some paid services on resolving insurance complaints that are evolving such as Insurance Samadhan, Claim Body and Sure Claim who charge a small fee but go a long way in resolving insurance complaints. Some drug manufacturers (e.g. Novartis, Intas) are also providing hotlines that help patients claim their insurance reimbursement.

In summary, it is important for us to understand the new IRDAI standardization guidelines, make our patients aware of these options that may improve compliance of repeated injections and make our staff counsellors aware. Insurance for intravitreal injections should be as common and well known as insurance for cataract surgery in the coming few years.

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CASE REPORT

Direct laser photocoagulation to the dilated right-angled vessel in the management of proliferative type 2 macular telangiectasia

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Introduction:

Type 2 macular telangiectasia (MacTel) is an occult, acquired, idiopathic, bilateral disease affecting the macular capillary network seen in elderly with a dual pathogenesis, i.e., neurodegenerative and vascular.[1] In 2006, Yannuzzi et al simplified the classification proposed by Gass and Blodi into two distinct stages: non-proliferative and proliferative.[2,3]The occurrence of secondary neovascularcomplex in type 2 MacTel may overall be considered a rather rare but serious complication, as it may result in a rapid loss of visual acuity.[1,3] In type 2 MacTel, anti-vascular endothelial growth factor agents seems to be effective in the treatment of choroidal neovascularization complicating the disease.[4] Promising results have been noted in the regression of choroidal neovascularisation due to age related macular degeneration, polypoidal choroidal vasculopathy and retinal angiomas following direct feeder vessel photocoagulation.[57]In advanced proliferative type 2MacTelcases, dilated vertically running vessels identified as right-angled vessels (RAV) can be seen connecting the inner retinal vasculature to the deep neovascular complex on optical coherence tomography angiography.[8]In this report, we describe a case of proliferative type 2 MacTel treated successfully with direct laser photocoagulation to the RAV. To the best of our knowledge, there are no reports published in literature showing reduction in activity of the neovascular complexin type 2 MacTel following direct laser photocoagulation to the RAV.

Case description:

A 61-year-old male, with no past medical history, diagnosed and treated previously elsewhere for bilateral proliferative type 2 MacTel was referred to our retina clinic for further management. He was treated with three intravitreal ranibizumab0.5mg in 0.05 ml injections in each eye with last injection given 3 months before presentation. He complained of recent onset decrease in vision in his right eye forlast 2 months. At the time of presentation to our clinic, his corrected distance visual acuity in

the right eye was counting fingers at 3 metres and left eye was 6/18. There was grade 1 nuclear sclerosis in both eyes. Anterior segment examination and intraocular pressure were within normal limits in both eyes. On fundus examination, both eyes showed features of type 2 MacTel and presence of subretinalneovascular complex at the temporal macula. Retinal pigment clumps were identified in the right eye. Documentation of the fundus findings was done using the Topcon TRC 50 Dx colour fundus camera'(figure 1)'and by the multicolour imaging

Figure 1: Clinical fundus photographs of both eyes using the Topcon TRC 50 Dx colour fundus camera:

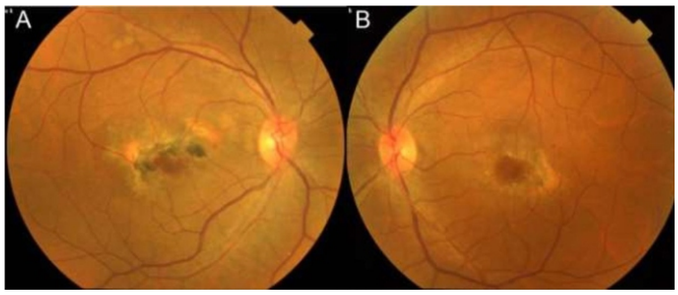


Figure 1A, B: Clinical fundus image of both eyes showing perifoveal greying, superficial retinal crystals, right angled vessels (all veins and three in number) and presence of subretinalneovascular membrane. In the right eye, the neovascular membrane is extending from 8 o'clock to 2 o'clock meridian superiorly while in the left eye, the subretinalneovascular membrane is located temporally. Retinal pigment clumps are seen in the right eye.

Figure 2: Optical coherence tomography (OCT) angiographyscan of the right eye using Optovue, Avanti RTVue-XR (Fremont, CA, USA):

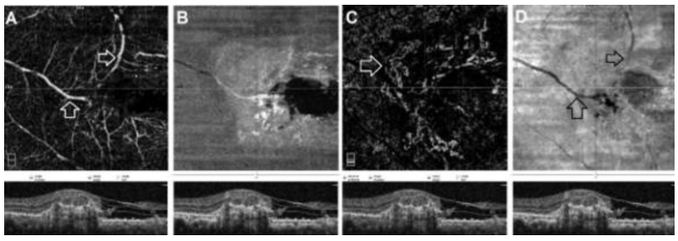
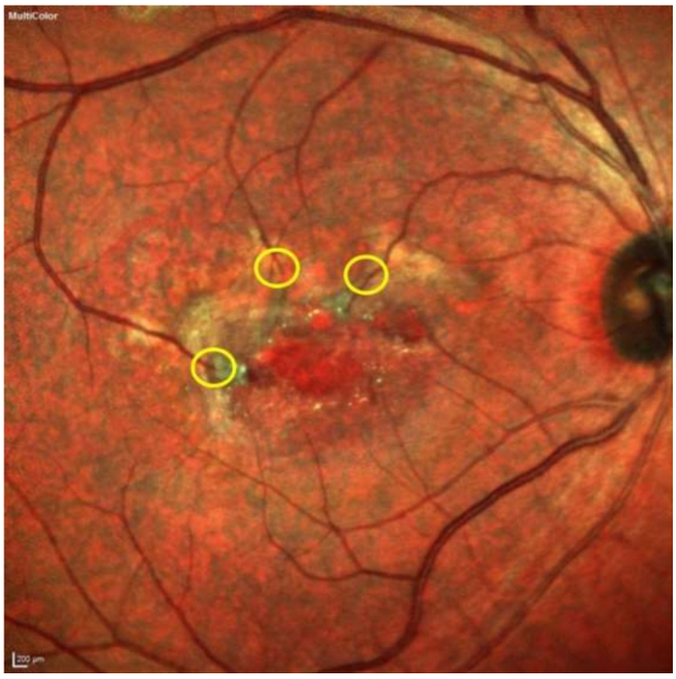


Figure 2A and B: OCT angiography and enface OCT slabs of the right eye through the deep capillary plexus shows the abruptly ending large dilated venules (white arrows) suggestive right-angled vessels temporal and superior to the fovea. **Figure 2C and D:** OCT angiography and enface OCT slabs of the right eye passing through the outer retina slab showing the right-angled vessels dipping into the subretinalneovascular complex. The extent of the subretinalneovascular complex is best seen on the OCT angiography image (white arrow) while the dilated right-angled vessels are seen on the structural enface OCT outer retina slab (black arrows).

Figure 3: Direct laser photocoagulation to the right-angled vessel in proliferative type 2 macular telangiectasia:



Single-spot green laser photocoagulation was performed to the right-angled vessels marked areas as yellow circles with the PASCAL SynthesisTM (Topcon Medical Laser System), 532nm wavelength. Light grey-white burns were delivered at the tip of the right-angled vessels dipping towards the outer retina. The power of the burn was 175mw set at a duration of 30ms and 100µm spot size.

Figure 4: Spectral domain optical coherence tomography (OCT) images of the right eye at presentation, 1-month post laser therapy and 6-month post laser therapy:

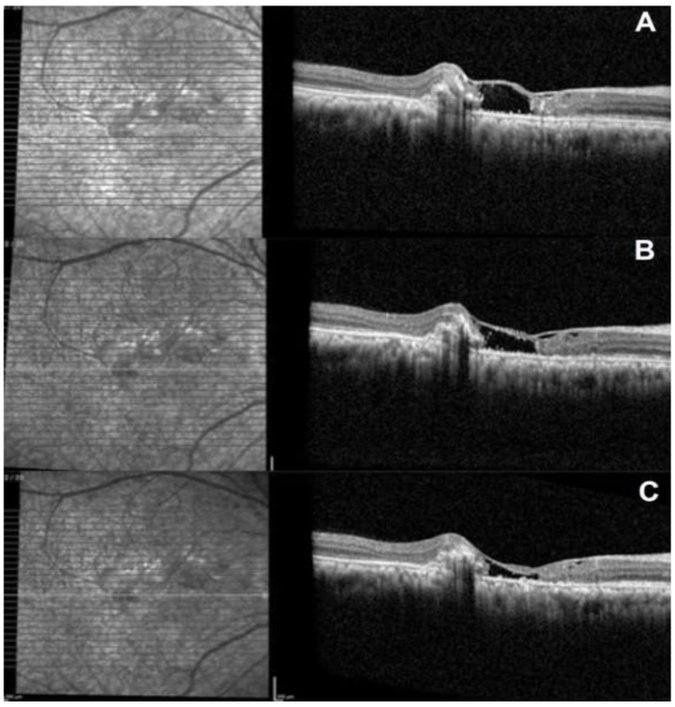


Figure 4A: Right eye horizontal OCT scan at presentation shows irregularity in foveal contour, internal limiting membrane drape sign and degenerative inner and outer retinal cavities and subretinalneovascular complex. The height of the hyporeflectivespace is 114µm. **Figure 4B:** 1-month post direct laser therapy to the dilated right-angled vessel, there is reduction in the height of central foveal thickness to 85µm. **Figure 4C:** At 6-month final follow-up visit, there is a further reduction in the height of the central foveal thickness to 49µm. The rest of the structural features on OCT remain the same.

Figure 5: Change in vascularity of neovascular membrane on optical coherence tomography angiography before and after treatment:

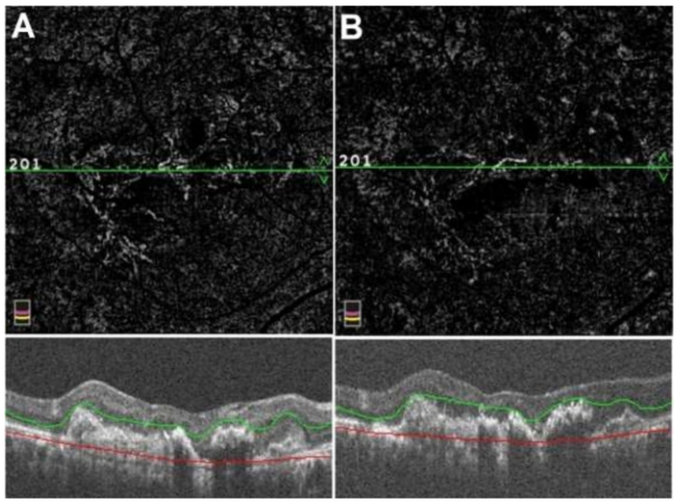


Figure 5A, B: Reduction in the vascularity of neovascular membrane on the outer retina slab on OCT angiography is noted 1-month after direct laser photocoagulation to the dilated right-angled vessels.

technology from the Heidelberg Spectralis machine. Avanti spectral domain SD-OCT angiography (RTVue-XR Avanti; Optovue, Fremont, CA, USA) was used for retinal vessel imaging at the macula which showed the dilated right-angled vessel in the deep capillary plexus dipping to the subretinalneovascular membrane in the outer retina slab '(figure 2)'. Spectral domain optical coherence tomography (OCT) was performed using Spectralis OCT machine (Heidelberg Engineering, Heidelberg, Germany). Both eyes showed irregularity in foveal contour, internal limiting membrane drape sign and degenerative inner and outer retinal cavities and subretinalneovascular complex extending underneath the retinal pigment epithelium. Retinal pigment clumps with shadowing were noted in the right eye. The height of the hyporeflectivespace at the fovea was 114µm when measured from the outer boundary of the internal limiting membrane to the outer boundary of the retinal pigment epithelium. In view of the recent onset decrease in vision and non-responsiveness to multiple intravitreal anti- vascular endothelial growth factor injections, direct laser photocoagulation to the RAV was planned on the same day. No treatment was given to the left eye. Single-spot green laser photocoagulation was performed with the PASCAL Synthesis™ (Topcon Medical Laser System), 532nm wavelength. The power of the burn was 175mw set at a duration of 30ms and 100µm

spot size. Light grey-white burns were delivered at the tip of the RAV dipping towards the outer retina '(figure 3)'. At one-month post laser, patient had expressed improvement in visual acuity and the visual acuity had improved to 6/60. There was reduction in the height of central foveal thickness to 85µm on OCT and the superficial retinal crystals had reduced '(figure 4)'. On OCT angiography, reduction in the vessel density in the neovascular membrane was noted in the outer retinal slab '(Figure 5)'. At the final follow-up visit at 6 months post laser, there was further reduction in the central foveal thickness to 49µm and the visual acuity improved to 6/36, 6/18RS in the right eye. The left eye vision was maintained at 6/18, 6/12RS. No worsening or scarring was noted at the lasered area.

Discussion:

With this case report, we demonstrated a successful reduction in the central retinal thickness at the fovea on OCT with no worsening of the neovascular complexor need for further anti-vascular endothelial growth factor injections and visual acuity improvement following direct laser photocoagulation to the RAV in type 2 MacTel.

The neovascular membranes in type 2 MacTel are usually less aggressive and a stabilisation or fibrosis of neovascular complex may occur even without any treatment.[9]On the other hand, neovascular complexes secondary to type 2 MacTel are most commonly located temporal to the fovea, thus making it amenable to thermal laser therapy.[9] Before the anti-VEGF treatment became available, improvement, stabilisation and deterioration in vision have all been documented after argon laser photocoagulation to the neovascular membrane. The risk of scotoma due to fibrosis or scar formation and the potential to trigger further growth of neovascular membranes has not favoured this treatment approach, despite the membranes being extrafoveal in location.[1]According to the current knowledge, there is a definite association between RAV and neovascular complex in type 2 MacTel.[8]The degenerative space at the fovea in the presence of proliferative disease could occur due to contribution from the active subretinalneovascular complex or could just be a degenerative outer retinal cavitation. Treatment of proliferative type 2 MacTel with anti-vascular endothelial growth factor agents shows improvement, but recurrence after cessation of therapy is common and the risk of further atrophy with repeated injections.[10]Feeder vessel laser photocoagulation achieved regression of the neovascular complex by noting reduction in the height of central foveal thickness and no recurrence of the disease or need for anti-vascular endothelial growth factor therapy up to6-month follow-up visits. Also, there wasimprovement in the visual acuity at the final follow-up visit. The reduction in the central foveal thickness on OCT could have occurred as a part of the natural history of the disease; however, there was no recurrence of the activity and visual improvement was satisfactory.

To conclude, direct laser photocoagulation to the RAV could be considered as alternative treatment option for proliferative type 2 MacTelespecially in patients non-responsive to anti-vascular endothelial growth factor therapy. However, long-term follow-up studies in a larger cohort are required to ascertain sustained efficacy.

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