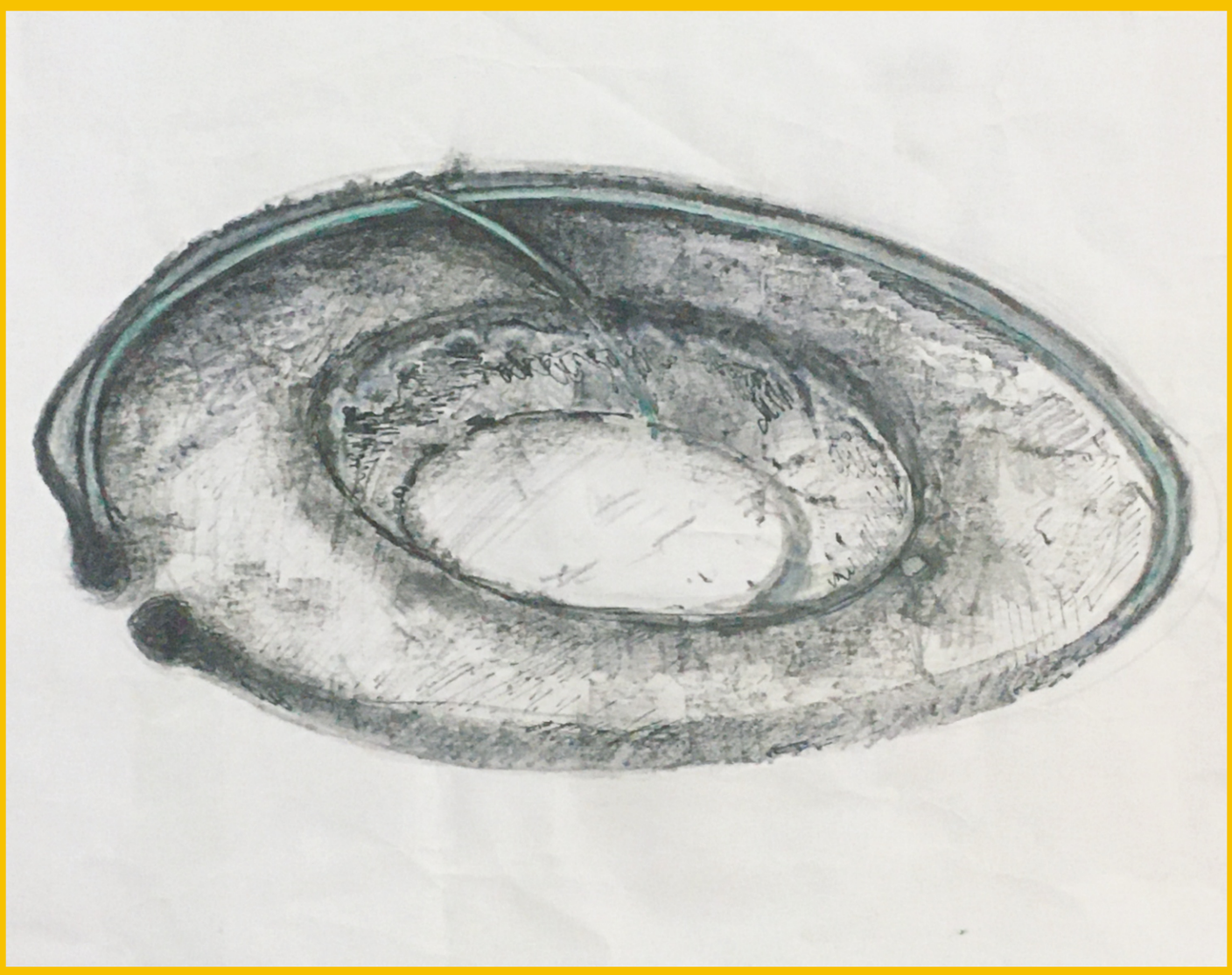
DECEMBER 2020

The Official Newsletter of the

VITREO RETINAL SOCIETY-INDIA



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Contents

From the President's Desk

Dr. Shobhit Chawla
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Dear Friends and colleagues,

Best wishes for the festive season and a very happy Deepawali. The Final VRSI Newsletter of this year is here by the efforts of Dr. Anand Rajendran , the scientific convenor. Let us all contribute with enthusiasm and think of the best possible ways for keeping the pace with which our society has grown and achieve new milestones.

The issue is dedicated to the all important topic of Endophthalmitis, which presents us with challenges always.

The Stalwartspeak views on Endophthalmitis are by none other than Michael Stewart on Endophthalmitis management in 2020. The interesting spotlight on the same topic is moderated by Vivek Dave, Avinash Pathangey and Anand Rajendran.

Let us hope 2021 brings with it a new order leaving the gloom of Covid times behind. With this let us all pray for peace, health and happiness for all.

Regards
Dr. Shobhit Chawla
President
Vitreo-Retinal Society of India

From the Honorary Secretary's Desk

Dr. Raja Narayanan
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Dear Friends

I hope that you all are doing great and have picked up patient volumes in your practice. It seems that we are entering a new 'normal' phase in our lives, with online meetings becoming the accepted modality to interact and learn. VRSI will be conducting a shortened version of a series of exciting sessions from Dec 10-13, 2020. Our dynamic Scientific Convenor has tirelessly worked to create an excellent program with stalwarts and subject matter experts sharing their latest updates in the management of retinal diseases. You would be delighted to know that we have received an overwhelming number of abstract submissions for the online meeting.

An excellent issue of VRSI Newsletter on Endophthalmitis, anchored by Dr. Avinash Pathengay and Dr. Vivek Dave, has been compiled by Dr. Anand Rajendran. All of them are leading experts and teachers in the field of Endophthalmitis, and I am sure that you will find their articles extremely valuable for your daily practice. I take this opportunity to request you all to submit your interesting images, cases, articles and innovations to the VRSI newsletter, which will help improve the scientific knowledge base of our members. Stay safe, and we shall meet soon online.

Regards
Dr. Raja Narayanan
Hon. Secretary
Vitreo-Retinal Society of India

From the Convenor, Scientific Committee's Desk

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Dear Friends and Colleagues

It has been a pleasure bringing out the September edition of the VRSI Newsletter. In this issue, we have Dr. Michael Stewart, an internationally acclaimed retina specialist, giving us his take on “Endophthalmitis Management in 2020” in the 'Stalwart Speak' section. The Spotlight article of the issue, anchored by Dr. Vivek Dave, Dr. Avinash Pathangey and yours truly, is focussed on the same theme Endophthalmitis, with an eminent panel of national experts holding forth on a slew of challenging situations. The Retina Tech Section has Dr. Abhishek Kothari highlighting the role and value of PCR based diagnostics in endophthalmitis. In the Innovator's Isle section, Dr. Prabu Baskaran, a retinal specialist with a passion for innovation, describes his creation the XNIT device for sutureless scleral fixation of IOLs. Finally a couple of interesting case reports from Dr. Kushal Agrawal and Dr. Sangeet Mittal, Dr. Rajeev Gupta adorn this Issue.

We look forward to contributions from all members to future issues. It has, however, 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.

An enthralling Virtual VRSI Meet from December 10th-13th 2020, is around the corner and promises to be a scientific fest. 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 Medical and Surgical Challenging Cases, with theme based sessions such as OCTA Cocktails, Macular Mélange, Choroidal Conundrums, Jail Breakers, Surgical SWAT making the programme unique.

We are thankful to all the members for the appreciation and hope to see the same enthusiastic response and support to VRSI activities.

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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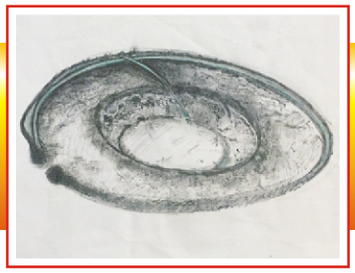

VRSI Retinal Image Winner November 2020 - Dr. Rajkumar Sharma, Jaipur

- An artist's impression of a dislocated IOL-CTR-Bag complex in his eye!

STALWART SPEAK

Endophthalmitis Management in 2020

Dr. Michael W. Stewart, MD
Professor and Chairman of Ophthalmology
Mayo School of Medicine
Florida, USA

For centuries physicians have battled, and for a long time failed, against the ravages of endophthalmitis. Though ophthalmologists frequently speak of endophthalmitis as a single disease entity, the term actually refers to several diseases, each of which can be caused by a plethora of organisms. As such, making generalizations about diagnostic strategies, management approaches, and visual prognosis is not possible.[1] With each case we should not just reflexively reach for antibiotic syringes, but instead we should formulate a thoughtful differential diagnosis with a list of the most likely organisms. Despite research spanning several decades, most of which has been retrospective and uncontrolled, many important management questions remain unanswered. The ubiquitous presence of pathogenic organisms combined with our limited ability to maintain a perfectly sterile surgical field mean that endophthalmitis will never become a "never event".[2] As a consequence, we will always confront cases of endophthalmitis, which highlights the need for continuing research and underscores the importance of optimal case management. The limited space afforded an editorial prevents a comprehensive discussion of endophthalmitis, so I will fill most of my space discussing our standard approaches to post-cataract surgery endophthalmitis, highlight some of the unresolved problems, and propose a common-sense approach to endophthalmitis management that may be possible if we can prove its efficacy - in the near future.

Most cases of endophthalmitis have been post-operative (40-80%), followed by post-traumatic (25%), and endogenous (5-15%), but the rapid adoption and widespread use of vascular endothelial growth factor inhibitors has catapulted post-injection endophthalmitis to second position on the incidence list.[3] Though the incidence of post-injection endophthalmitis trends lower than post-operative endophthalmitis, the volume of intravitreal injections for chorioretinal vascular conditions produces enough cases to rival the number resulting from surgery. A meta-analysis that included 105,536 intravitreal injections found that *Streptococcus* species, a component of oral flora, are three times as likely to cause post-injection as post-operative endophthalmitis.[4] Physicians were advised to either refrain from speaking while injecting or wear a face mask to prevent dispersion of bacteria. In a recently reported series of 483,622 injections from a single center, endophthalmitis rates in the "no talking" group resembled those in the face mask group (0.0371% vs. 0.0298%; $P = 0.527$), but cases of oral flora were found exclusively in the "no talking" group (16 vs. 0; $P = 0.302$). Since *Streptococcus* produces more severe endophthalmitis than does *Staphylococcus epidermidis*, efforts to limit *Streptococcus* endophthalmitis should be considered. Now that the COVID-19 pandemic has us wearing face masks during all encounters, physicians should continue wearing masks while performing intravitreal injections even after the pandemic abates. Expired air is preferentially directed through inadequate

seals with poorly fitting masks, particularly over the bridge of the nose,[5] so patients receiving injections should not wear masks for fear of directing their own respiratory droplets onto the eye.
Preventing postoperative endophthalmitis has become a hot topic among cataract surgeons. An increasing trend toward the routine use of prophylactic intracameral antibiotics (cefuroxime, moxifloxacin, and vancomycin) approximately 47% of American Society of Cataract and Refractive Surgery membership use them[6] - has lowered endophthalmitis rates to approximately 0.02% in largeretrospective studies.[7]Careful attention to operative suite ventilation, instrument processing, and sterile technique can also produce an endophthalmitis rate of 0.02%,[8]so surgeons should optimize their operating suite processes before reaching for intracameral antibiotics.

Results from the landmark Endophthalmitis Vitrectomy Study[9] (1995) established the major principles of post-cataract surgery endophthalmitis management, most of which are followed to this day. Intravenous antibiotics are no longer administered, vitrectomy is performed for only the most severe cases (light perception), and vancomycin and ceftazidime are injected empirically. These 25-year-old standards have served us well, but advancements in surgical instruments and techniques, improved understanding of the biochemical processes that accompany intraocular infections, and changing microbial profiles mandate that we re-evaluate these long-held principles.

Ninety-nine percent of the microbes cultured in the EVS were sensitive to either vancomycin or ceftazidime, which suggests that there is no need to changeempiric antibiotic use, and implies that identifying the responsible organism with aqueous tap or vitreous biopsy may not be necessary. The EVS was performed in the United States, but pertinentmicrobial profiles differ throughout the world. For example, the proportion of infections due to gram negative organisms varies from 9% in Australia, to between 10.7% and 18.5% in the United States, and to 18.2% and 23.9% in New Zealand and India. During the past 25 years antibiotic resistance among organisms has increased; only 8% of gram negative organisms in Australia are resistant to ceftazidime butresistance increases to a worrisome 40.3% in India.[10] Therefore, “location matters”, and surgeons should know the antibiotic sensitivities of infecting organisms in their area so that they can make appropriate antibiotic choices.

The EVS reported that vitrectomy benefits eyes with light perception visual acuity, whereas eyes with hand motions or better do equally well with a vitreous or aqueous tap and antibiotic injections. Nonetheless, many authors recommend that early vitrectomy be performed more frequently for several reasons: 1) The high viscosity of native vitreous frequently prevents the acquisition of an adequate sample through small needles for gram stain and cultures; 2) Vitreous samples are more likely to produce positive cultures than are aqueous samples (64.9% vs. 37.1%);[11] 3) Debulking the vitreous of microbial load and inflammatory mediators may accelerate resolution of the infection and limit inflammation-mediated retina damage.

Since most responsible organisms are sensitive to vancomycin or ceftazidime, do we actually need toobtain an intraocular fluid sample? Despite their sensitivity to first line therapy, some virulent organisms fail to respond completely to the first set of injections, thus leaving the surgeon with incomplete data while pondering the next management step. An intraocular sample may be useful for only a small group of eyes, but timely culture and sensitivity (C&S) information mayenable the surgeon to shorten disease duration by a couple of days and prevent catastrophic vision loss.

What if vitreous samples provided us with better and immediately actionable information? Whole-genome sequencing (WGS) and polymerase chain reaction (PCR) techniques may be useful in more severely affected eyes.[12] Whole gene PCR sequencing can identify the inciting organism in 76% of culture-positive cases and 33% of culture-negative cases. Higher bacterial loads of organisms other than *Staph epidermidis* were associated with worse outcomes and co-infection with torque teno virus (found in half of samples) had a greater need for secondary vitrectomy. VITEK 2 is a commercially available susceptibility test, and the use of MALDI-TOF MS is experimental but it promises to quickly identify organisms. Immediate diagnoses could enable the use of species-specific injections more quickly and, if needed, more frequently.

Since publication of the EVS, surgical techniques and diagnostic modalities have improved, and new antibiotics have been developed, yet we still use the same management recommendations. Some surgeons worry that the EVS tap-and-inject recommendations have been inappropriately expanded to include light perception eyes, to the detriment of outcomes. Vitrectomy may not influence the final outcome for most eyes but some surgeons argue that today's vitrectomies differ

significantly from those in the 90s.Faster, smaller gauge cutters combined with improved fundus visualization may enable more precise surgery with less collateral damage. Importantly, the rate of retinal detachment in the CEVE study,[13] in which early vitrectomies were frequently performed, was comparable to that in the EVS (6.4% vs. 8%).

In rabbit models of endophthalmitis, retinal damage occurs after the eradication of bacteria, thereby implicating bacterial toxins and the host's inflammatory response.[14-16]Removal of purulent material in human eyes, particularly from the surface of the macula, mightlimit inflammatory-medicated damage and improve outcomes. This technique, referred to as Complete and Early Vitrectomy (CEVE), produced excellent visual acuity results (79% achieved 20/40 or better).[13] Vitrectomy was performed in eyes with sufficient inflammation to obscure fundus detail, and patients were positioned face-down after surgery to prevent pooling of inflammatory material over the macula. Unfortunately, the retrospective study design and lack of a control group limit the generalizability of this strategy.

So how do we put all this together? I closely follow EVS guidelines but I am frustrated with the poor morphologic and functional results achieved by many eyes. Below I propose an updated treatment paradigm based on currently used guidelines, as-yet unproven (lack of level 1 data) management strategies, and not-yet widely available technologies. My *wished-for* management of post-cataract extraction endophthalmitis would be as follows:

1. Severity of inflammation mild (visible retinal detail but no retinal vascular damage):

a. Perform an aqueous tap for gram stain, C&S, and qPCR or other available microbial identification method.

b. Forego a primary vitrectomy.

c. Treat with broad spectrum intravitreal antibiotics.

2. Severity of inflammation severe (cannot rule out retinal and retinal vascular damage by ophthalmoscopy):

a. Urgent vitrectomy

i. Sample taken for C&S and qPCR.

ii. Broad spectrum intravitreal antibiotics at end of surgery.

b. Face down positioning until retina can be visualized.

c. Sequential (daily) vitreous taps for gram stain, C&S, and qPCR until demonstrable improvement in inflammation.

d. Repeated injections of antibiotics (every 24-48 hours), depending on tap results and antibiotic toxicity profile.

e. Corticosteroid administration: daily intravitreal dexamethasone and oral prednisone beginning when the infection is eradicated and continuing until retinal detail can be visualized.

This represents an aggressive treatment strategy that requires new technology and improved clinical trial data before it can be implemented. I propose this not to change the reader's current approach to endophthalmitis but rather to encourage researchers to address gaps in our knowledge and developers to provide us with accurate, rapidly available techniques to identify microorganisms. Until these deficiencies are rectified, I will continue to follow widely agreed upon management strategies, but I long for the day that we can better treat the 50% of eyes that suffer from final visual acuities of worse than 20/40.

DISCLOSURES:

Allergan: Institutional Research Support
Alkahest: Consultant
Bayer: Consultant
Kang Hong: Institutional Research Support
Santen: Institutional Research Support

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SPOTLIGHT

Endophthalmitis Management

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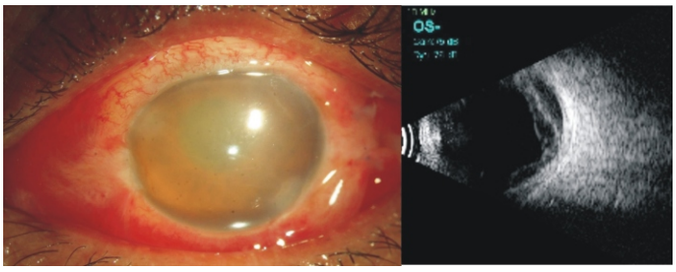
Q1. A 60 yr old one eyed male presents with uncontrolled diabetes develops endophthalmitis of 2 days duration with vision of PL following cataract surgery with the above clinical picture. Vitreous tap on culture grew Pseudomonas aeruginosa which was multi-drug resistant. How would you manage this case?

HF & NRB: Since the patient is pseudophakic with visual acuity of light perception only, we would recommend core vitrectomy



after removal of fibrin and opacities from the anterior chamber. Would prefer a 6mm pars plana infusion cannula over a 4mm. No vitreous base shaving would be attempted. Repeat administration of intravitreal antibiotics could be considered since it is MDR. In view of the MDR, alternative antibiotics like intravitrealimipenem and aminoglycosides could be considered if these classes of drugs have demonstrated efficacy. Would administer intravitreal dexamethasone along with the antibiotic towards which the organism has shown efficacy (clinical and microbiologic). Simultaneously, the diabetic status of the patient should be considered for appropriate control of blood sugar. The fluoroquinolones are not generally used but ciprofloxacin would be the most effective for *Pseudomonas*. Antimicrobial susceptibility report in these cases is very helpful in selecting appropriate intravitreal antibiotic. In culture proven cases of bacterial endophthalmitis, intravitreal steroids may be considered along with repeat antibiotics to which the organism is susceptible as per antimicrobial susceptibility report.

The use of systemic antibiotics is of questionable value in this setting. The penetration into the vitreous cavity for most antibiotics is less than ideal and the use of these antibiotics may create systemic side effects. The use of silicone oil could be considered if there is retinal involvement causing a high risk of retinal detachment.
If endoscopic vitrectomy armamentarium and skill is available, it can be used to bypass anterior segment opacities and perform an effective core vitrectomy.

AP: There are 3 key factors which have to be considered in the management of this patient.

1) **Uncontrolled Diabetes :** Patients with uncontrolled diabetes could be associated with fulminant inflammation especially if they were to be associated with virulent organism. EVS also reported patient with virulent organism had to undergo additional procedures compared to patients with non virulent organism. In patients with uncontrolled diabetes it would also serve as a challenge when we have to counter the fulminant intraocular inflammation with oral corticosteroids.

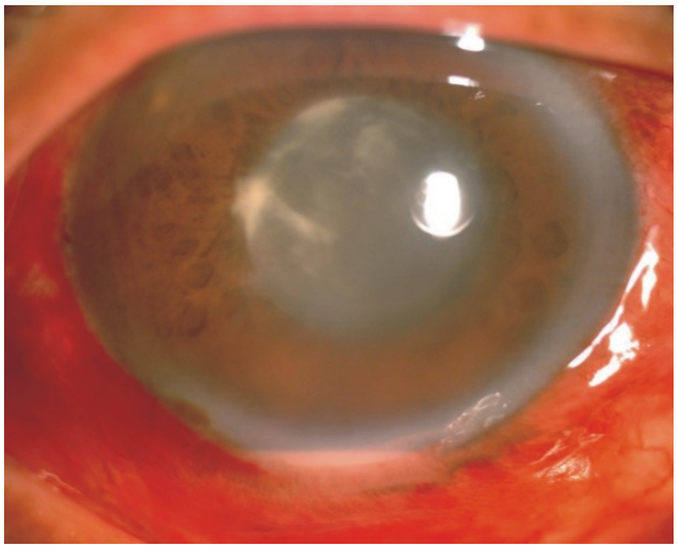
2) **Presenting with Light perception within 2 days of cataract surgery :** According to EVS this is frequently seen in virulent organism causing endophthlamitis like Gram negative and Gram positive organism like Streptococcus and Staphyloccusaureus. These patients can be associated with other comorbidities in the cornea which will influence the visualisation during PPV. It is also observed that visual outcomes of patients with these organisms are poor. These patient have better visual outcome when vitrectomy is performed over vitreous biopsy. In situation when PPV becomes nearly impossible vitreous biopsy can only be considered . Presence of endoscopic vitrectomy would be more favourable. Prefer to inject intravitreal dexamethasone along with intravitreal antibiotics. My personal preference would be to use intravitrealvancomycin and imipenem as the empirical antibiotics. Imipenem because of increase in ceftazidime resistance observed in our study. These patients also would require multiple anitbiotics injections based on sensitivity.

3) **Pseudomonas and multidrug resistance :** Outcomes of endophthalmitis due to this organism is very unfavourable in spite of administration of sensitive antibiotics. One of our study concluded Pseudomonas as the commonest organism to cause MDR in our setting. My personal recommendation is to include both intravitrealimipenem and colistin in the management of MDR due to Pseudomonas. Pandrug resistance could entail usage of silicone oil even in the absence of RD.

AR: A challenging, but not altogether an uncommon situation. With the PL Vision at presentation and the fact that 2 days have already lapsed, without presumably any definitive treatment, I would be inclined to take this patient directly for surgery. The cornea appears reasonably clear to take this approach. An anterior chamber clearance of exudates would be mandated before proceeding with MIVS. However, if the Blood sugars are excessively high and the patient is not immediately cleared for surgery, I would not hesitate in immediately instilling intravitreal antibiotics-intravitrealPiperacillin with Tazobactum (225 micrograms) or Imipenem (5 micrograms). I would, be partial to fortifying the patient with Intravenous Piperacillin and

Tazobactum or Imipenem too, to aggressively address what is a very severe endophthalmitis with the pathogen being a formidable one a multi-drug resistant Pseudomonas aeruginosa. This would have the dual advantage of treating the patient in the interim period prior to inevitable surgery, as well as aiding final visual outcomes. Lack of improvement or worsening of the clinical picture within 24 hours would compel me to take up for surgery. The same combination of intravitreal antibiotics with intravitreal dexamethasone would be preferred. In the event that the retina is very friable and necrotic (likely to be the case, or has detachment), I would not hesitate to use Silicone oil as a tamponade.

Q2: A 54 year old diabetic female presented as below 5 days post a vitrectomy for retinal detachment. The eye had an oil fill. How do you diagnose and manage a case of endophthalmitis in an oil filled eye?



VD: Such cases have minimal visible exudation in the posterior segment as it is filled with oil. Thus all the exudates aggregate anteriorly. Hence in an endophthalmitis, the reaction in the anterior chamber will be grossly disproportionate to “the usual expected post-op reaction” in such cases. While this may relatively easy to judge in one's own cases as we have an idea of our own usual post-op reactions, it can be little difficult for cases operated by a different surgeon. In case of a doubt, I would start the patient on topical steroids without antibiotics (to prevent masking of the infection) and review again after 12 hours. I take slit lamp photos at each examination to compare and pick up subtle or evident worsening or improvement. Status quo or deterioration of reaction at 24 hrs on observation would tilt the diagnosis in the favor of endophthalmitis for me. I would take these patients up for AC Tap and AC wash along with anterior chamber and intravitreal antibiotic injection. I do not reduce the dose from the standard one. As visibility improves in the anterior segment, posterior segment needs to be evaluated carefully to look for layering of exudates in the sub silicone space. If there is no or minimal layering one can repeat intravitreal antibiotic after 48 hours. Significant layering if noted/ or non-resolution if noted with the above approach will require silicone oil removal and lavage of the posterior segment. In view of the pre-existing posterior segment pathologies for which these eyes are operated before, these eyes have a relatively low visual prognoses inspite of early and appropriate treatment. Leaky ports and hypotony at the end of the primary surgery is a risk factor for this occurrence and should be prevented.

RB:1st line of management:

Intravitreal antibiotics in half the standard dose (vancomycin 0.5 mg/0.1 mL + ceftazidime 1 mg/0.1 mL)

Intravenous antibiotics (ciprofloxacin 200 mg BD x 5 days) till vitreous aspirate culture report is available

Topicals as for exogenous endophthalmitis:

- If culture-proven endophthalmitis, 'sensitive' antibiotic (fortified when applicable) drops 1-2 hourly
- If culture negative, broad spectrum antibiotic drops (moxifloxacin) with the above-mentioned frequency.
- Topical corticosteroids 1-2 hourly/day (usually betamethasone-N eyedrops) to reduce inflammation/ fibrin
- Cycloplegic (Atropine) drops TID.

2nd line of management:

If minimal or no response by 2nd day:

oil removal + re-vitrectomy + silicon oil tamponade + injection of intravitreal antibiotics (half the standard dose)

Continue intravenous and topical treatment.

CR:

1. When there is a disproportionate anterior chamber reaction signified by fibrin exudation with or without hypopyon associated with HIGH IOP.

2. Disproportional paraocular or periorbital reaction which could include conjunctivalchemosis, lid edema, restricted extra-ocular movement, proptosis and corneal edema in the form of descemet's folds all of which is associated with the anterior chamber fibrin.

3. There will be insufficient resolution of the above findings despite increasing the topical steroids frequency with or without a trial of oral steroids.

4. If fundus view is present, there may be multiple blot hemorrhages in the retina (which is unusual when the surgery was done for retinal re-attachment) and pre-retinal exudates in the inferior periphery.

If the above signs develop in the first 2-3 post-op day then initially increase the topical steroids (every 15 minutes for a few hours) with supervision. Reassess after 6 hours and if the fibrin reduces, iop reduces and fundus view improves then consider close supervision to monitor for deterioration.

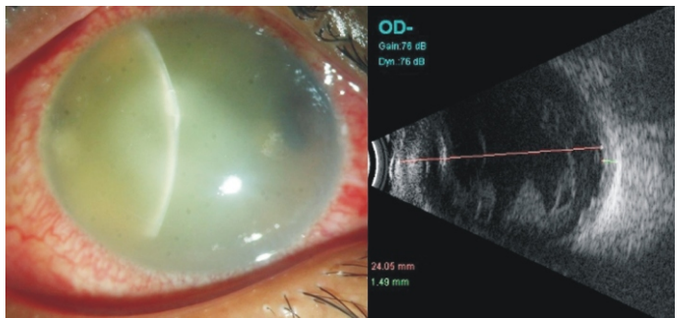
If the signs are worsening, then consider it as infection and then do anterior chamber tap for microbiological analysis and inject intravitreal broad spectrum antibiotics with steroid. Usually the preferred medicine would be Vancomycin 1 mg, Ceftazidime 2.5 mg and 400 microgram dexamethasone. Get a physician clearance for oral steroids and start oral steroids with blood sugar monitoring by the internist and start systemic broad spectrum antibiotics like a 3rd generation cephalosporin intravenous or oral ciprofloxacin.

If in the next 24 hour there is no resolution of the anterior chamber reaction and peri-orbital reaction, the surgeon should do an anterior chamber washout, assess the fundus and if there are exudates which are usually seen in the sub-silicone oil space coating the retina or in the peripheral vitreous, then remove the oil, do a lensectomy or iol removal (if pseudophakic), a thorough peripheral vitrectomy to remove all the exudates upto the parsplana area, re-inject oil and give full dose intravitreal Vancomycin, ceftazidime and dexamethasone and continue oral steroids and systemic antibiotics.

Monitor the case and give intra-cameral injection of antibiotics with steroids and continue the broad spectrum systemic antibiotics and if there is a culture positivity and sensitivity available alter the medications as per the sensitivity.

Most cases of endophthalmitis post vitrectomy are due to staph aureus or streptococcus epidermidis, bacillus cereus or gram negative bacilli and some may progress to scleral involvement and eventually evisceration despite treatment.

Q3: This was a 7 year old female with a small corneal tear and corneal infiltrate and echoes on B scan. Initial vitreous tap grew *Enterobacteraerogenes*. How do you treat such cases? How would you decide between just a vitreous tap, a PPV with keratoplasty or an endoscopic approach?



VD: Enterobacterspp are fulminant Gram-negative organisms. The corneal as shown has an immune ring infiltrate which is a sterile inflammatory response to the toxins released by gram-negative organisms. This warrants topical steroids for its clearance along with topical antibiotics. The B scan shows significant echoes. In a fulminant presentation (Gram negative, trauma, pediatric population) I prefer debulking infection from the posterior segment in all cases. The options here would be PPV with a temporary K-pro or an endoscopic approach. In my practice over the last 3 years, I have shifted exclusively to endoscopic surgeries in such cases. The advantages of endoscopy over the conventional K-pro approach include non-requirement of a cornea surgeon simultaneously, ability to see the retina and posterior segment at the first go to be able to judge prognosis, ability to abandon surgery immediately if needed, without the complex work of regrafting the cornea. Most importantly, it gives the native cornea an opportunity to clear which happens in quite a few cases in our experience (results published recently) and avoids making a patient unnecessarily a post-PK patient for life.

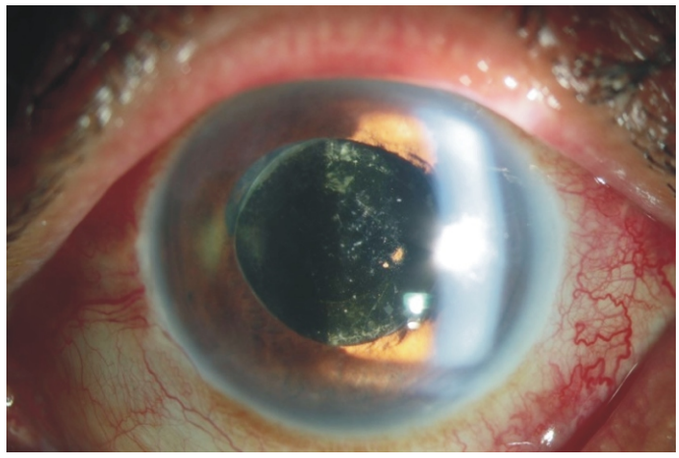
AR: A paediatric, traumatic endophthalmitis involving an organism as virulent and fulminant as Enterobacter mandates urgent intervention. The B-scan reveals significant vitreous exudates hence it would be prudent to opt for direct vitrectomy at the earliest (rather than an intermediate measure like a vitreous tap, if possible). The cornea does not appear too hazy to completely preclude vitrectomy. Topical steroids along with antibiotics, would have a beneficial role in clearing the immune infiltrate ring seen here and help improve corneal clarity. Topical glycerine may also be used. In the event of severe corneal infiltration and corneal opacification , a temporary K-Pro and Corneal Graft along with Vitrectomy would be resorted to. Clearance of anterior chamber exudates would precede vitrectomy. If very severe exudates or necrotic retina is noted, a radical vitrectomy with Silicone Oil would be opted for. Halving the dose of intravitreal antibiotics would be called for in that event. Imipenen may be administered to cover for resistant cases, as this being a paediatric case under general anesthesia, the possibility of repeat interventions needs to be kept to a minimum. We have limited experience with Endoscopic vitrectomy but would advocate the same as an alternative, which would have the additional benefit of circumventing an opaque cornea and a grafting procedure.

RC: Cases of Enterobacter are fulminant and may not have a good prognosis . I would prefer to go ahead with vitrectomy. To improve visualisation in such cases we have tried using 50% glycerine (sterile) after epithelial debridement. This is available from our corneal preservation laboratory. It works in some cases. Else we make resort to putting a temporary k pro followed by vitrectomy and replacement with corneal graft. Personally I have not performed many cases of endoscopic vitrectomy.

- Another issue is use of silicon oil at the end of surgery. In fulminant cases, especially post traumatic cases, we do inject silicone oil after performing a careful vitrectomy which is more than a core vitrectomy but not a radical vitrectomy.

- I would inject intravitreal antibiotics (usual dose) after vitrectomy if leaving under air. If injecting silicon oil then half dose. Choice of drug in this case may be Imipenem as chances of it being resistant to Ceftazidime.

Q4: A 60 year old male presented with a delayed-onset endophthalmitis with low grade inflammation, capsular opacities and circumcorneal congestion. The explanted IOL grew *Aspergillus spp*. In your practice how do you decide on IOL explantation in these cases?



HF & NRB: In this setting, the organisms are growing inside the capsular bag and generally do not respond to topical or intravitreal antimicrobials. By removing the IOL and the entire capsular bag, the correct diagnosis can be established (*Aspergillus*sp in this case) and the likelihood of recurrence is reduced. In a one-chambered eye, the delivery of additional antimicrobials can be more easily accomplished either by limbal or pars plana delivery of additional medications.

Vitreous biopsy and injection of antibiotics (into the capsular bag and intravitreally) can be tried but have limited role due to low culture positivity and high rates of recurrence. Other conditions including immune-mediated and intraocular malignancies can masquerade as delayed-onset endophthalmitis. The IOL-capsular bag complex removed from the eye should be sent for histopathological and microbiological evaluation. It is important to not use intravitreal steroids in these patients until the causative organism can be identified. The causative organisms are typically *Cutibacterium acnes*, coagulase negative *Staphylococci* (i.e. *Staphylococcus epidermidis*), and Mycobacterium spp but also fungus. Our group has previously reported cases, that resembled *Cutibacterium acnes* but subsequently were found to have a fungal etiology.

AR: In this clinical scenario of a low-grade inflammation in a long-standing pseudophakic eye with presumably minimal visual

acuity reduction and mild symptoms, I would initially resort to an intravitreal antibiotic injection. Recurrence of inflammation with the invariable mild vitreous involvement would then prompt me to opt for a core vitrectomy with a vancomycin capsular bag wash after opening up the posterior capsule with the vitrectomy cutter. This would have the beneficial effect of clearing the pathogens (P.acnes usually a posterior capsular plaque or sedimented deposits in the bag ; fungal microbes). Persistence or recurrence after two such interventions of escalating effort would then entail a more radical procedure of explanting the IOL and capsular bag remnant. In the event of the presentation being more severe with intense exudates in the bag or vitreous, I would proceed directly with Core vitrectomy and IOL-Bag explantation with intravitreal antibiotics. Once the eye is quiescent for 6 months or more, a secondary scleral fixated IOL implantation can be considered.

PS: The rationale of IOL explantation in treatment of endophthalmitis has been a topic of debate for both bacterial and fungal etiologies. Management of these chronic cases where deposits over IOL and posterior capsule are present with persistent inflammation despite multiple intravitreal injections and/or surgeries necessitates IOL explantation not only for improving visualization during repeat pars planavitrectomy (PPV) but also to reduce the organism load. Fungal spores are known to get sequestered over the IOL surface and in the capsular bag especially inferiorly and these may be responsible for multiple recurrences. Acrylic and hydrophobic IOLs are particularly known to favor adhesion of microorganisms. Also, the posterior capsule may serve as a protective barrier for the fungal spores against the intravitreal antifungal injections given. Repeat surgery with more radical vitrectomy and IOL and capsule removal may be required for eradication of infection.

Having said that, one must always remember the underlying lurking danger of retinal break formation leading to a rhegmatogenous retinal detachment which can rapidly reverse the benefits of a more radical surgery to cure recurrent endophthalmitis. Trimming of the capsular remnants without pulling them off the zonules can allow opening of this potential space without an undue traction on the peripheral retina. Also, direct irrigation of the capsular bag remnants to deliver antifungals as well as to dislodge any sequestered fungal spores can be tried.

When facing a sight or a globe threatening scenario, a vitreoretinal surgeon should not hesitate in sacrificing the IOL in the larger interest of the patient. And of course adequate patient counselling makes this decision easier.

Q5: How would you rate the efficacy of PCR in the etiological diagnosis of infectious endophthalmitis as against routine smear culture techniques?

PS: Identification of causative organism in endophthalmitis is important not only to establish diagnosis but also to initiate a rationale and appropriate treatment regime with minimal unwanted side effects. The rate of positive bacterial identification in cases of endophthalmitis has been reported to be around 40-50% using conventional culture methods. PCR followed by gene sequencing can increase this rate to about 6395% according to various reports. Also, PCR requires only a small amount of specimen and usually results in rapid identification. PCR can be particularly useful in chronic or recurrent endophthalmitis which has already been treated with various antibiotics. In these cases, prior treatment with antibiotics may not allow a significant growth of causative organism on culture but PCR may still detect some DNA. PCR also is known to increase the rates of detection for fastidious organisms like E. faecalis and Haemophilus influenza. E. faecalis can be difficult to identify in conventional plate culture methods because of its ability to enter a viable but nonculturable (VBNC) state.

But if you ask me, can we replace our culture techniques with only PCR, I would say they are actually complementary. In some cases, we do come across instances when cultures are positive, yet the PCR doesn't identify an organism. This could be because of lack of a specific set of primers or too small an inoculum. Also, the equipment required can be costly and facility may not be universally available. Additionally, this method can at times give a high rate of false-positive results which of course need to be interpreted with clinical relevance.

JJ: **While the isolation of microorganisms in smear/ culture is the reference method for determining the etiology of endophthalmitis, its positivity varies from 30 - 50%. There are many reasons for cultures being negative which include, over-diagnosis, low microbial load, prior antibiotic therapy, sequestration of microorganisms in the capsular bag and delay in processing the samples. These difficulties are overcome by polymerase chain reaction (PCR) and its variants such as the real-time PCR (RT-PCR) or quantitative PCR (qPCR). PCR reaction is highly specific and sensitive and is used to amplify**

the DNA of microorganisms in clinical samples. Some studies (Therese et al. BJO 1998) have reported that PCR increased the sensitivity from 46.5% to 75.8% for proving infectious aetiology in vitreous specimens. PCR techniques are thus more sensitive and rapid than culturing, particularly for slow-growing and fastidious microorganisms and are especially useful in culture negative specimens. Hence, the available evidence shows that panbacterial PCR and standard cultures are complementary in microbiologic identification.

LP: In spite of low sensitivity, conventional microbiological methods of direct smear examination and culture have been the gold standard for diagnosis of infectious pathogens. Multiple factors may affect the sensitivity of detection of microorganisms on culture, including less sample volume, prior antibiotic treatment, and slow growing or fastidious nature of the pathogen. Polymerase chain reaction (PCR) assays can overcome these limitations due to its inherent amplification of minute amounts of genetic material of organisms and is able to identify non-culturable, slow-growing or even dead organisms in only a small amount of specimen more rapidly. PCR is more sensitive than culture method with a reported positivity rate as high as 75%. However, one disadvantage is the high rate of false-positive results.

In our experience, over the last three years from 2017 to 2019, in post-operative endophthalmitis and traumatic endophthalmitis respectively, the positivity rates of culture were 15.3% and 16.7% and PCR were 29.7% and 37.5%. PCR showed 51.43% and 44.4% sensitivity in post-operative and traumatic endophthalmitis respectively and 100% specificity in both.

So, to rate the efficacy of PCR in the etiological diagnosis of infectious endopthalmitis as against routine smear culture techniques, there is an added advantage in using PCR. Clinical correlation is important for diagnosis of infectious bacterial endophthalmitis. It is necessary to exercise caution when interpreting bacterial identification results, because environment contamination and previous infections may also result in positive identification of bacteria.

Q6: Do you use intravitreal steroids commonly in your practice? What are the indications? Would you recommend it in fungal endophthalmitis also?

RC: We prefer to give oral steroids post-operatively to most cases (unless systemically contraindicated) as they can be stopped if there is a fungal growth detected. So we definitely avoid oral or depot steroids in cases of fungal endophthalmitis. In cases where oral steroids are contraindicated intravitreal dexamethasone (0.4mg) is used. I have not used depot triamcinolone for endophthalmitis.

CR: I use Intravitreal steroids for treatment of bacterial endophthalmitis, most preferably dexamethsone and is used in combination with antibiotics and repeated as short an interval as 24 hours. I do not prefer intravitreal steroids for fungal endophthalmitis and would consider it only if I see low iop due to ciliary body atrophy or traction with concomitant signs of resolution of fungal endophthalmitis evidenced by no new growth of fungal mass on the iris, angle of anterior chamber or ciliary body.

Q7: What are the challenges that one would face while managing an endophthalmitis in a private setting as against an institute setting?

RJ: Microbiology backup

- Finding the right microbiologist with good set up and experience in ocular microbiology is a big challenge.
- Other challenges include delay in the sample transport chain and inadequate or inappropriate plating of the sample at labs

Cross referrals :

Sometimes time is lost due to delays in getting opinion of cornea/glaucoma consultants especially if the practice is run by single retina specialist

Financials :

- Though it may not be much of an issue at institutions, private practitioners have to spend lots of energy in this.
- Cost of Injections and surgery
- Have to spend lots of time with the referring anterior segment specialist and the patient in negotiating the cost of the surgery. Anterior segment colleagues at times want us to operate free of cost or at basic minimal cost, which

again is a major hinderance in giving the right care to the patient.

- Despite informing about all the pros and cons of injections/surgery, if patient develops retinal detachment following injection/vit, then again no one is willing to pay and since it is caused after our intervention, we as a retina specialist has to operate for free. This all leads to cutting corners in giving the right care to the patient like not using fresh cutters and instruments for surgery (though I personally use fresh cutters now for all my endophvits and patient/referring doctor pays for it).

Medicolegal liability :

- Sometimes even if we see a gross mismanagement by our referring colleague (like giving subconjmoxi for suspected endohthalmitis for first few days, giving subtenons steroid and antibiotics without taking another opinion, complications like dropped nucleus/cortical matter/IOL and not informing the patient) we try to make up for their mistakes without realizing that after starting the treatment we are also a party to it.

- We are equally or may be more liable for loss of eye following our management of endophthalmitis for a referred patient. This leads to referring the patient to institutes which results in delays in management / treatment.

SS: There are definitely a few extra challenges that one would encounter when managing endophthalmitis in a private practice setting:

1) Timely suspicion, diagnosis and immediate referral of an exaggerated post-operative anterior chamber reaction as endophthalmitis by a cataract surgeon is severely limited by a day care set up and fixed hours of work where emergencies are invariably postponed to the next morning. Moreover, referral to a retina specialist amounts to a) extra expenses for an injection or vitrectomy which the patient would not prefer to bear, especially after hearing about the apparent lapse of asepsis incurred in the primary surgery and b) performing a more elaborate procedure this time under injection of local anesthesia and patching the eye compared to the less ostentatious primary procedure performed under topical eyedrops and no eye patching c) no immediate wow effect, an added apprehension of performing multiple surgical procedures with no assurance of recovering lost vision d) stigma associated with tarnished credibility of the cataract surgery set up and surgeon skills following an expensive premium IOL implant in a seemingly smooth uneventful procedure.

For a retinal surgeon in a private set up, the challenges are a) emergency availability of staff to help set up and assist a high end vitrectomy amounting to intravitreal injections being the primary management option, irrespective of the severity of endophthalmitis b) compulsion to perform a high end vitrectomy with a poor promise of outcome, remuneration and returns on the surgical consumables, most of which having now become non-recyclable on account of patient contamination c) added expenses and relative unavailability of performing high end diagnostics such as PCR in case of atypical and poorly responding endophthalmitis.

Q8: What is the role of topical antibiotics in the management of infectious endophthalmitis?

HF&NRB: Topical antibiotics have limited role in the management of endophthalmitis, due to low penetration into the anterior chamber and vitreous cavity. They may however be useful in bleb associated endophthalmitis or in endophthalmitis cases with a corneal or scleral wound infection. Fortified topical antibiotics are preferred compared to commercially available topical antibiotics in the treatment of endophthalmitis. Topical fluoroquinolones may not be as effective because of increasingly reported high rates of resistance. However, the use of intravitreal antibiotics is far more important than topical antibiotics. In fact, some physicians use only intravitreal antibiotics without supplement topical antibiotics.
RB: Very important in exogenous endophthalmitis. Limited role in endogenous endophthalmitis.

- If culture-proven exogenous endophthalmitis, 'sensitive' antibiotic (fortified when applicable) drops 1-2 hourly

- If culture-proven endogenous endophthalmitis, 'sensitive' antibiotic (fortified when applicable) drops QID

- If culture negative, broad spectrum antibiotic drops (moxifloxacin) with the above-mentioned frequency.
- Topical corticosteroids QID (usually betamethasone-N eyedrops) to reduce inflammation/fibrin
- Cycloplegic (Atropine) drops TID.
- If repaired corneal laceration (in case of exogenous endophthalmitis), tear substitutes to reduce suture-induced foreign body sensation.

AP: Usage of topical antibiotics in the management of endophthalmitis over the years, has become the norm, since the landmark EVS study. Topical antibiotics may not achieve sufficient levels to exceed MIC 90 in vitreous, this is rather more pronounced for fluroquinolones. With this hypothesis we at LVPEI asked a question if usage of topical antibiotics could benefit the outcome postoperative endophthalmitis. Retrospective comparative chart review of two cohorts of endophthalmitis (other than those associated with open-globe injury, keratitis or wound site infection), one managed with topical antibiotics and one without topical antibiotics were done .Topical antibiotics do not give any added advantage in the management of endophthalmitis otherwise being treated with intravitreal antibiotics and standard vitrectomy techniques.

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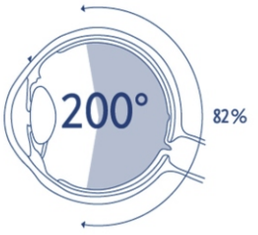

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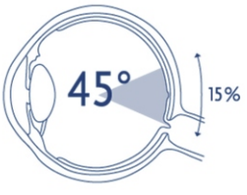

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RETINA TECH

New Tools for Pathogen Discovery in Infective Endophthalmitis

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Pink City Eye and Retina Center
Jaipur

Endophthalmitis is a grave complication of intraocular surgery. Timely, appropriate intervention is critical in minimizing intraocular damage and ensuring good outcomes in these cases. Current clinical management of endophthalmitis has evolved from the previous guidelines based on the Endophthalmitis Vitrectomy Study[1]. Patients with endophthalmitis routinely undergo aqueous and vitreous tap, with the sample being which are subjected to routine microbiology. Empirical treatment is given at first contact and treatment is subsequently modified according to microbiology results. The threshold for surgical intervention has been steadily falling as surgical techniques and results of small gauge surgery improve.

Despite their limitations, traditional stain and culture techniques are widely available and relatively inexpensive, and have a long history of use. However, routine microbiology yield from samples of endophthalmitis patients is known to be poor[2] due to a variety of reasons. More often than not, definitive diagnosis is delayed because cultures can be slow to grow, or may not grow at all. As a result, many cases of suspected intraocular infections are treated empirically. A delay or uncertainty in etiological diagnosis results in continuation of empirical therapy, based on clinical features alone, which can be fallacious and can frustrate treatment efforts.

Polymerase chain reaction (PCR) based diagnostics offer higher yield and sensitivity in a very short period. Routine PCR techniques have been available for some time now[3] and have been employed in management of viral retinitis, keratitis and uveitis. Their application in endophthalmitis management[4-9] had previously been limited due to restricted pathogen detection capability, lack of specificity, vulnerability to contamination and availability of the tests.

In 'standard' clinical PCR, test for each organism or class of organisms under consideration must be ordered individually and requires its own portion of sample (typically 10 to 50 ul). Initial PCR diagnostics used in endophthalmitis were based on identifying conserved ribosomal sequences in the two main class of pathogens- bacteria and fungi- and would only allude to the presence of either in the specimen. This information alone offered little advantage in the management of disease. Detection of such targets also had low specificity, which would compound treatment dilemmas. Identification of specific pathogen involved in a particular case was needed for the test to be of clinical use in guiding treatment better.

For a pathology like endophthalmitis, there may be insufficient material to test for all suspected pathogens individually. Previously used PCR techniques depended on a priori knowledge or suspicion of a particular species to choose appropriate primers, tags, and targets for analysis. There is no commercially available kit that looks for the full breadth of pathogens associated with endophthalmitis, as the range of pathogens is

extremely large. The practical considerations for making a sufficiently reliable test dictate testing for a limited number of pathogens. Composite data from various published series on postoperative endophthalmitis has led to the recognition that a few (25-30) organisms are the causative factors in more than 90% of such cases. Therefore, tests currently in use are targeted at this select group of pathogens that are commonly identified offending agents in intraocular infections.

Improvements in DNA extraction and purification have facilitated the recovery of DNA that is free of the molecules and proteins that normally decrease the yield of PCR techniques.

Multiplex PCR, or PCR using novel primer sets for a panel of common pathogens, has enabled simultaneous performance of PCR for multiple pathogens with minimal loss of sensitivity and with high specificity.[10] This makes it possible to concomitantly run one high-quality PCR reaction for the detection of multiple organisms in the place of several separate reactions, saving both time and resources and expediting the results of these tests. Post-amplification identification of species has been attempted using various in-situ hybridization techniques. A visual identification of color change is one of the easiest and quickest to perform (Fig 1).

A patented tool (Syndrome Evaluation System (SES) earlier called asXCytoscreenDNA Macrochip, XCyton Diagnostics Pvt

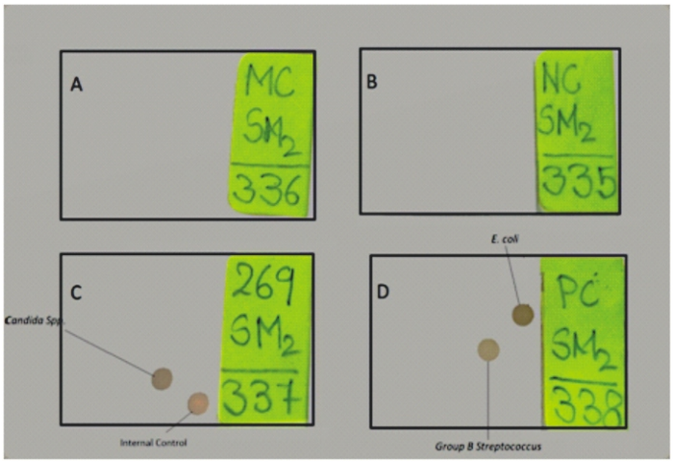
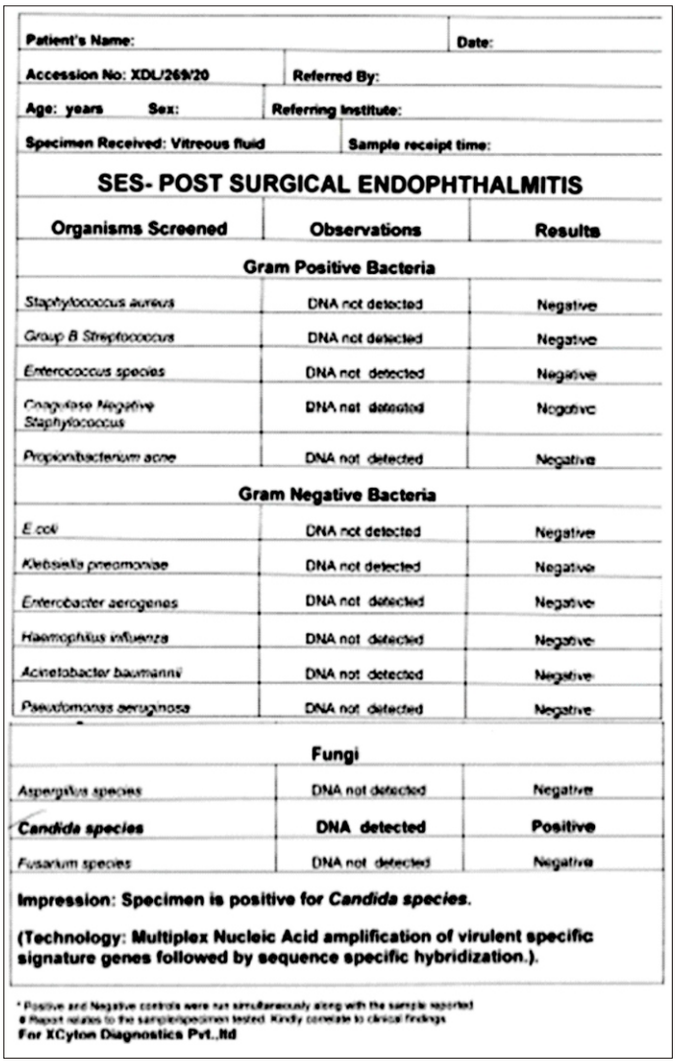


Figure 1. Results of SES Endophthalmitis test visible as macroscopic blots with color changes
A - Method control
B - Negative control
C - Patient's Vitreous samples showing Candida Spp. and Internal control
D – Positive control showing E. coli & Group B Streptococcus



Patient's Name: Date:
Accession No: XDL/269/20 Referred By:
Age: years Sex: Referring Institute:
Specimen Received: Vitreous fluid Sample receipt time:

SES- POST SURGICAL ENDOPHTHALMITIS

Organisms Screened	Observations	Results
Gram Positive Bacteria		
Staphylococcus aureus	DNA not detected	Negative
Group B Streptococcus	DNA not detected	Negative
Enterococcus species	DNA not detected	Negative
Coagulase Negative Staphylococcus	DNA not detected	Negative
Propionibacterium acne	DNA not detected	Negative
Gram Negative Bacteria		
E coli	DNA not detected	Negative
Klebsiella pneumoniae	DNA not detected	Negative
Enterobacter aerogenes	DNA not detected	Negative
Haemophilus influenza	DNA not detected	Negative
Acinetobacter baumanni	DNA not detected	Negative
Pseudomonas aeruginosa	DNA not detected	Negative
Fungi		
Aspergillus species	DNA not detected	Negative
Candida species	**DNA detected**	**Positive**
Fusarium species	DNA not detected	Negative

Impression: Specimen is positive for *Candida species*.

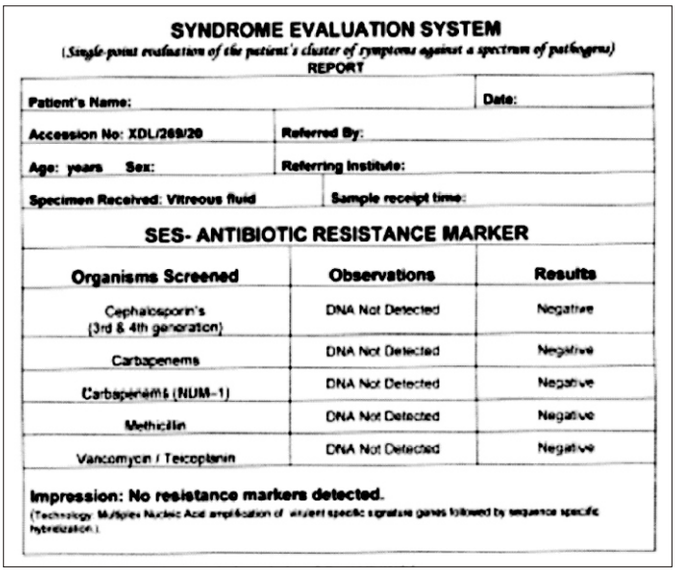
(Technology: Multiplex Nucleic Acid amplification of virulent specific signature genes followed by sequence specific hybridization.).

* Positive and Negative controls were not simultaneously along with the sample reported
# Report relates to the sample/specimen tested. Kindly correlate to clinical findings
For XCyton Diagnostics Pvt..ltd

Figure 2. Sample report of the specimen tested and demonstrated in Fig 1.

Ltd, Bangalore) is available for clinical use in India which offers rapid species specific identification covering upto 40 common pathogens involved in postoperative endophthalmitis. The test was developed under the auspices of NMITLI (New Millennium Indian Technological Leadership Initiative) Project of CSIR (Council for Scientific & Industrial Research), Government of India as a collaborative project between several ophthalmic institutes and XCyton Laboratories, Bengaluru and has been found both sensitive and specific in preliminary testing. Of note is the fact that this is the only such test of its kind available for widespread use anywhere in the world.

Identification of the pathogen alone (e.g. Staphylococcus aureus or Pseudomonas spp) confers a distinct advantage to the vitreoretinal surgeon in terms of directing appropriate antibiotic therapy (Figure 2). Knowing the antibiotics it is most likely to



SYNDROME EVALUATION SYSTEM

(Single-point evaluation of the patient's cluster of symptoms against a spectrum of pathogens)

REPORT

Patient's Name:	Date:
Accession No: XDL/269/20	Referred By:
Age: years Sex:	Referring Institute:
Specimen Received: Vitreous fluid	Sample receipt time:

SES- ANTIBIOTIC RESISTANCE MARKER

Organisms Screened	Observations	Results
Cephalosporin's (3rd & 4th generation)	DNA Not Detected	Negative
Carbapenems	DNA Not Detected	Negative
Carbapenems (NDM-1)	DNA Not Detected	Negative
Methicillin	DNA Not Detected	Negative
Vancomycin / Teicoplanin	DNA Not Detected	Negative

Impression: No resistance markers detected.

(Technology: Multiplex Nucleic Acid amplification of virulent specific signature genes followed by sequence specific hybridization.)

Figure 3. Antibiotic Resistance gene detection report for the common antibiotic resistance patterns encountered

respond to multiplies this advantage manifold. Conventional microbiological culture isolation allows testing of sensitivity of an organism to several antibiotics. This enables detection of resistance to certain antibiotics and helps tailor appropriate therapy. Erstwhile PCR techniques did not give this very useful information. Most antibiotic resistance characteristics are carried on genes or plasmids, which are nucleic acids capable of being picked up by PCR techniques. Currently, multiplex PCRs are available to detect the presence of resistance genes in isolates. While conventional culture and sensitivity testing may take 48 hours or more to give species and antibiotic susceptibility information, PCR techniques can provide this information in a matter of 7-8 hours. The XCyton endophthalmitis panel has an optional resistance gene panel to detect the common and serious antibiotic resistance in samples from endophthalmitis patients. When requested, the resistance panel is run simultaneously with the detection panel to get information on both in an aqueous or vitreous sample (Figure 3).

Our Study:

We conducted a study to evaluate clinical utility of SES Endophthalmitis in infective endophthalmitis in terms of i) identification of causative organisms, ii) Correlation between DNA macrochip, routine microbiology& clinical picture and iii) effect on number of antibiotics, interventions and duration of hospital stay. Patients with endophthalmitis following intraocular surgery were included in this study. Paediatric patients, those with endophthalmitis following trauma andthose with corneal pathology or other pathology affecting visualization were excluded. All patients included in the study underwent aqueous and vitreous taps and empirical treatment (intravitreal antibiotics) was given at first contact. In this case control study design, samples from cases (group A) were subjected to both routine microbiology and DNA macrochip analysis. Samples from controls (group B) were subjected to routine microbiology alone. 10 controls (Spiked with 5 positive known pathogens and 5 negative sterile samples) were also sent for DNA macrochip testing for validation.

SES testing was done by XCyton Ltd, Bengaluru. Samples were sent through ordinary courier to the company, with no need for cold chain maintenance. The testing is a multi-stage process beginning with DNA extraction. This is followed by the amplification stage employing multiplex PCR on the specimen (<0.10 cc) of intraocular fluid. Subsequently, hybridization over a Macrochip platform (with embedded signature sequences of pathogens) is performed. Through enzymatic processes, color changes develop on the platform identifying the pathogen (reverse dot-blot type reaction). The whole process takes appx 7-8 hours.

The DNA macrochip results were available within 24 hours of the sampling and intravitreal injection. Following this first contact treatment, Group A patients (cases) underwent subsequent treatment modified on the basis of DNA macrochip results. Group B patients (controls) continued treatment based on routine microbiology and clinical picture alone.

Data was collected in both groups on the microbiology, clinical correlation, number of interventions, and duration of hospital stay. Intravitreal injections, core vitrectomy, repeat vitrectomy and evisceration were counted as interventions. Statistical analysis was done using the SPSS ver11.0 package.

Results:

All 5 positive controls were identified correctly by SES Endophthalmitis testing. There was one false positive out of 5 negative controls (sensitivity- 100%, specificity-80%, positive predictive value= 0.83).

22 cases of postoperative endophthalmitis were recruited into the study. There were 10 cases and 12 controls in the study.

Average age of patients in group A was 67.5 yrs and group B was 62.3 yrs. Anterior chamber cells and vitritis scores were similar in both groups (p=0.648). Mean BCVA in group A was 0.04 and in group B was 0.10 (p=0.381). One patient in group A had late endophthalmitis following filtration surgery. All the other patients had endophthalmitis after cataract surgery.

Routine microbiology identified the causative organism in 1 of 10 cases (10%) in group A and 3 of 12 cases in group B (25%). DNA macrochip testing revealed the causative organism in9 out of 10 cases in group A (90%). 6 cases had bacterial agents identified, and 5 cases had fungal agents detected (2 cases had polymicrobial results).

Results of SES testing showed high correlation with clinical picture. Identical result was obtained in the case that had both routine microbiology and SES Endophthalmitis tests positive. Clinical response to treatment (antibiotic selection) correlated well with SES results.

There was a significant difference in the number of interventions, duration of hospital stay and number of antibiotics used between the groups (Table 1).

Discussion:

Table 1. Effect on clinical course

Parameter	Group A (DNA Macrochip)	Group B (Routine microbiology)	P value
Number of interventions	1.5	2.67	0.007
Duration of hospital stay/daily visits after results	2.8 days	10.5 days	<0.001
No. of antibiotics prior to test results	2.2	2.3	0.502
No. of antibioticsafter test results	1.2	2.3	0.003

In our study, we sent positive controls (suspensions of known cultured organisms) to test the diagnostic accuracy of the SES Endophthalmitis test. Negative controls (vitreous samples from patients operated for diabetic vitreous hemorrhage, macular hole) were also sent for the test. Very high degree of accuracy was noted for the positive controls. Among negative controls, one sample was reported weakly positive for *staph. epidermidis* (false positive).

In our study, controls were selected to match cases with respect to ocular inflammation characteristics at presentation. This was done to ensure similar starting points in both groups. Such matching would reveal the effect of SES test results on the course of treatment and disease given similar initial clinical scenarios.

Detection of pathogens by routine microbiology was very low in our study (overall 18.2%). This was significantly lower than the detection rate ofSES testing (90%). There was good correlation between clinical picture and SES results. Accurate species identification of causative organism enabled confident tailoring of the antibiotic therapy and avoiding unnecessary multiple drugs. Treatment based on SES results showed excellent clinical response, resulting in reduced number of interventions and thereby, reduced hospital stay.

We did not include vision improvement as a parameter in this study. Vision in cases with endophthalmitis depends on a number of factors other than microbiology and the treatment (e.g. corneal damage, IOL status, condition of retina and vitreous after microbiological sterility, late complications).

Conclusion:

Negative microbiology reports of samples from endophthalmitis patients are exceedingly common. In such situations, empirical treatment guided by clinical features has been the mainstay. Considerable variability exists, however, in presentations of

endophthalmitis even with the same organism and may perplex the treating ophthalmologist. Expeditious and accurate identification of infective organism leads to better clinical assessment of the condition and enables precise therapy. Though PCR testing offers these advantages, it has not entered routine clinical use due to limitations of conventional PCR techniques, availability and cost concerns. SES testing offsets most of the technical disadvantages that have prevented the widespread adoption of PCR techniques for endophthalmitis diagnosis and management. A concern about the use of DNA macrochip testing is its cost. However, less interventions and shortened hospital stay reduces the economic burden of the disease on the patient and the attendants. Eventually, an eye salvaged from endophthalmitis with very useful vision more than compensates for the cost of treatment. Vitreoretinal surgeons in India are in a uniquely enviable position compared to the rest of the world with regard to the ease of availability of this game-changing 'Make-in-India' tool, and should utilize the same to their advantage to achieve the best possible recovery in every single eye with endophthalmitis.

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INNOVATOR'S ISLE

Extraocular Needle Guided Haptic Insertion Technique for Scleral Fixation Intraocular Lens Surgery (X-NIT for SFIOL)

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None of the authors have any financial or proprietary interest in the subject matter discussed

Introduction:

Aphakia is one of the most dreaded complications during cataract surgery. Scleral fixated intraocular lens (SFIOL) surgery is a widely accepted mode of surgical management of aphakiain patients with no capsular support. SFIOL techniques have evolvedover the yearsfrom a complex and time consuming sutured procedures to simpler and quicker sutureless procedures. There are various methods described for sutureless SFIOL and each has its own learning curve[1,2,3]. The exteriorisation of haptic and its fixationare two challenging steps in SFIOL. The conventional handshake techniques involve intraocular manipulations which might be difficult for a beginner and in patients with corneal scars or poor pupillary dilatation.

Extraocular needle guided haptic insertion technique (XNIT) simplifies the exteriorization of haptic by shifting the intraocular handshake to a safe extraocular docking.[4] The conventional XNIT technique uses 26 G needle which is bent to 60 degrees close to its hub. Silicone stopper was obtained using cut pieces of #240 band used in retinal detachment surgery. The XNIT device is novel product, first of its kind, designed exclusively to perform XNIT technique of SFIOL surgery.[5] The device is incorporated with features like pre bent needle, pre-loaded&dual protection silicone stopper, customized 26 G needle with increased shaft length, ergonomic handle with finger grip and sclerotomy markers.

The steps of XNIT device assisted SFIOL technique:

Scleral Groove& Sclerotomy marking:

A limited conjunctival peritomy is made. Adequate cautery is done to prevent intraoperative bleeding. A toric marker is used to get an imprint of 2 meridians that are 180 degree apart (Figure1). A bent 15 degree side port knife is used to create scleral grooves on either sides starting from meridians marked (counter clock wise direction) and 1.5 mm away from the limbus (Figure 2). By doing this, a triangular scleral groove is created with broad entry for easy tucking and narrow distal end for fixing the haptic intrasclerally.

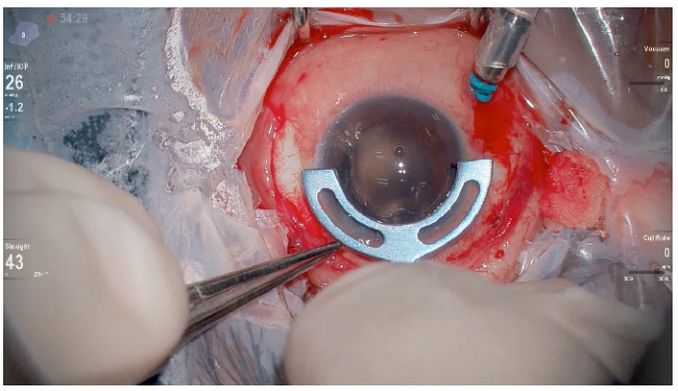
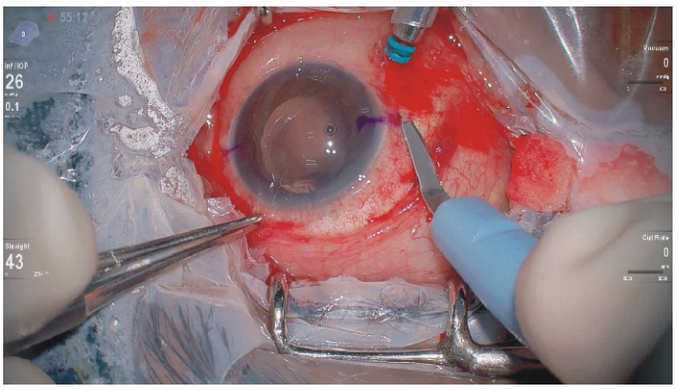
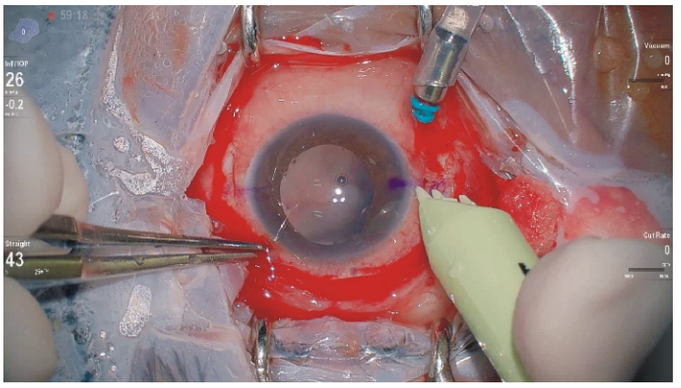


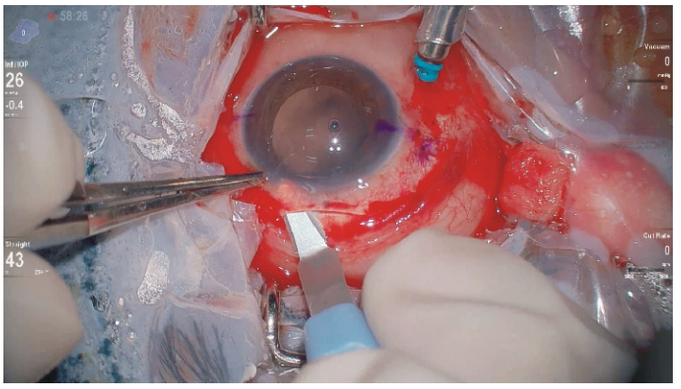
Image shows toric marker being used to mark the meridians 180 degree apart



Bent side port knife being used to create triangular scleral grooves.



Picture shows the sclerotomy marker incorporated in XNIT device

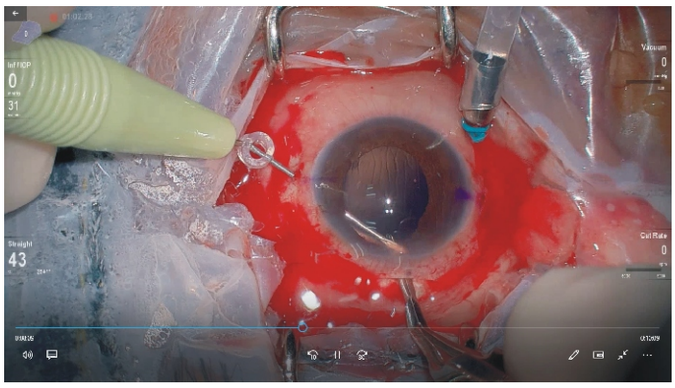


Sclerocorneal section for the main entry

Either a pars plana infusion or anterior chamber maintainer is used. An adequate anterior vitrectomy is done. A 5.5 mm corneo scleral tunnel is made (Figure 3). The sclerotomy marker of the XNIT device is used to mark 1.5 mm point away from limbus (Figure 4).

Scleral entry & goextraocular:

Then the tip of the 26 G needle is used to pierce the sclera. The direction should be initially towards the mid vitreous. Once pierced, the direction is changed more anteriorly and advanced towards the pupillary plane. Once the tip of the needle is visualized through the pupil, the direction of the needle is further changed and brought out through the corneoscleral section. To prevent the sharp tip damaging the surrounding

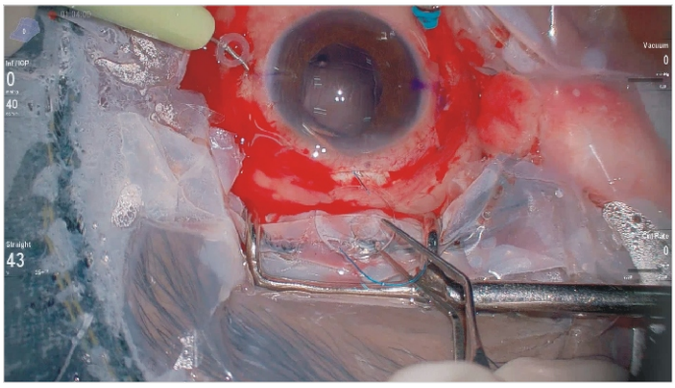


The needle is swept over the McPherson forceps to bring its tip out

structures, a MC phersons forceps is used to depress the posterior lip of the corneo scleral section (Figure 5). It is a good idea t to avoid penetrating movement while attempting to bring the needle tip outside. Rather it is recommended to adopt a sweeping movement from inside out, so that when the arc of the movement is completed, the tip of the needle will be extraocular. Also it is important to check if the needle is free from entanglement by attempting side to side movements.

Extra ocular docking:

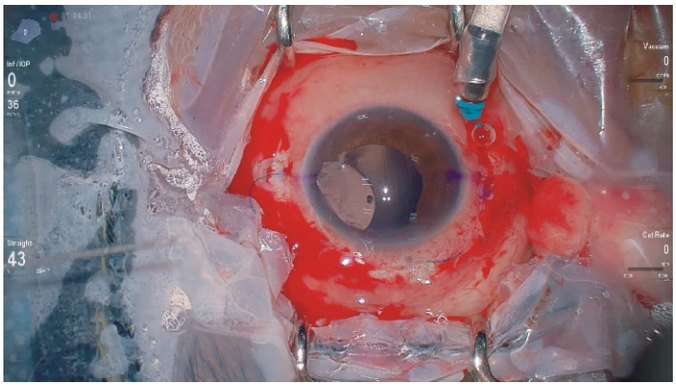
The tip of the leading haptic is then docked into the lumen of the 26 G needle (Figure 6). A docking of 3 4 mm is generally needed to prevent any slippage. Once docked, the needle is retracted gently and the intraocular lens with the haptic is pushed. This should happen as a single unit to prevent disengagement.



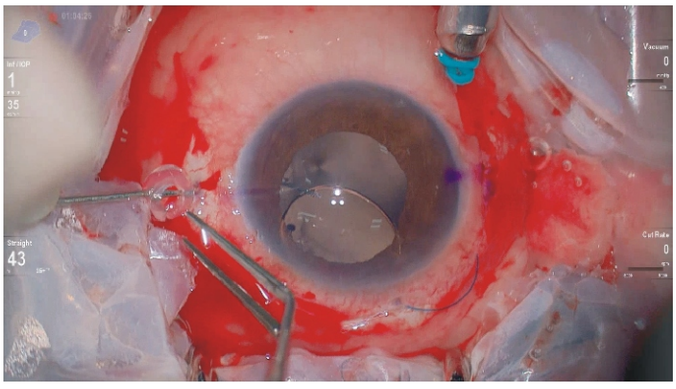
Extraocular docking of the tip of the needle into the lumen of 26 G needle

Silicone stopper:

The dual protection silicone stopper is simply slid over the shaft of the needle and kept close to the sclera. A Mc Pherson forceps it kept inside the foramen of the dual protection silicone stopper and wait to visualize the haptic (Figure 7). Once haptic is seen, it is gently held using the forceps and the needle is disengaged slowly. This avoids undue pressure on the haptic and thereby prevents distortion of the haptic (Figure 8).



Exteriorized leading haptic is kept safe using the stopper



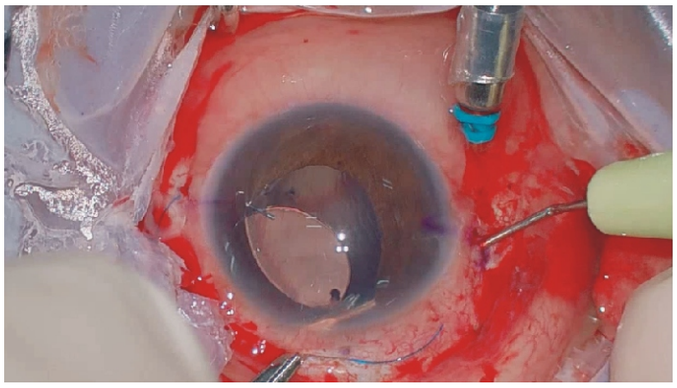
Silicone stopper is being used while exteriorizing the leading haptic

Now the silicone stopper is retracted to the very tip of the haptic and kept close to the sclera. This increases the intraocular portion of the haptic and helps better maneuvering while docking the trailing haptic. The advantage of a silicone stopper is

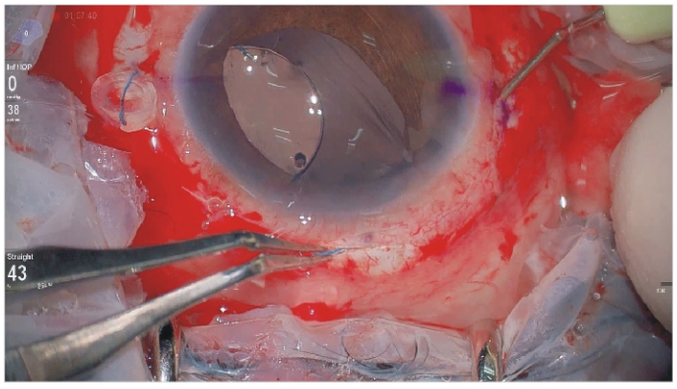
to temporarily stabilize the leading haptic while the trailing one is maneuvered (Figure 8). Also this avoids the surgeon's dependency on the assisting nurse which can sometimes become unreliable. The dual protection stopper enhances the safety at this crucial moment.

Trailing haptic exteriorization:

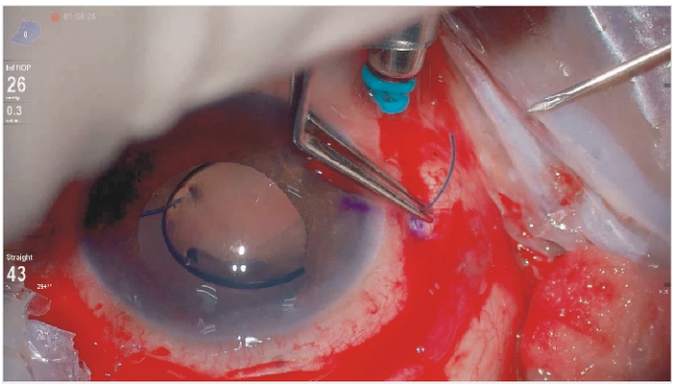
The XNIT device is now used to pierce through the opposite side sclerotomy point1.5 mm away from limbus using the inbuilt marker. The tip of the needle is advanced towards the corneo scleral section. It is recommended to keep the needle plane above the haptic optic plane to avoid any tissue entanglement. Now a Mc Pherson forceps is used to depress the post lip of corneo scleral section like before and the needle is brought out (Figure 9). The trialing haptic is retracted slightly using the McPherson forceps and docked inside the lumen of the needle.



Similar step as Figure 5 for the trailing haptic



Flight landing position of the trailing haptic tip helps in easy docking



A McPherson forceps is used to gently exteriorize the trailing haptic

It is a good idea to orient the haptc in such a way that the tip of the trailing haptic faces down like an aeroplane landing on the runway (“flight landing sign”)(Figure 10). Once adequate docking of 3-4 mm is done, the needle is retracted to exteriorize the trailing haptic. A Mc Pherson forceps is used to hold the haptic and then needle is disengaged gently. Any violent pull of haptic at this stage can transfer the force to the haptic optic junction and may cause breakage (Figure 11).

Haptic Fixation:

Once both haptics are exteriorized, SFIOL forceps or Mc Pherson forceps is used to tuck the haptic into the preformed scleral grooves. It is important that the only the tip of the haptic is held while tucking.

The XNIT is all about simplified exteriorization of haptics. Once exteriorized, it can be combined with any described technique for haptic fixation (Gabor Scharioth technique of intrascleral tunnel, Glued IOL technique of scleral flaps, and Yamane's technique of flange creation).What we describe in this article is a modification of Chariot fixation method.

Advantages of XNIT device:

The device is customized in such a way that a surgeon can directly perform the surgery without any preparatory steps like bending the needle to 60 degree angulation, procuring # 240 bands and cutting into pieces to make the silicone stopper and loading the same onto the needle shaft.

Since there is very minimal intraocular maneuver involved, we believe XNIT is safe for beginners.

Also XNIT can be performed even if there is dense corneal scar or small pupil. XNIT can be easily combined with all keratoplasty procedures as corneal opacity is not a deterrent for XNIT.

The only limitation is that the technique requires a large 5.5 corneo scleral section and hence we do not recommend the current version XNIT device in a clear corneal section.

To conclude we believe XNIT device is a safe and cost effective device designed to simplify SFIOL procedures especially for the beginners.

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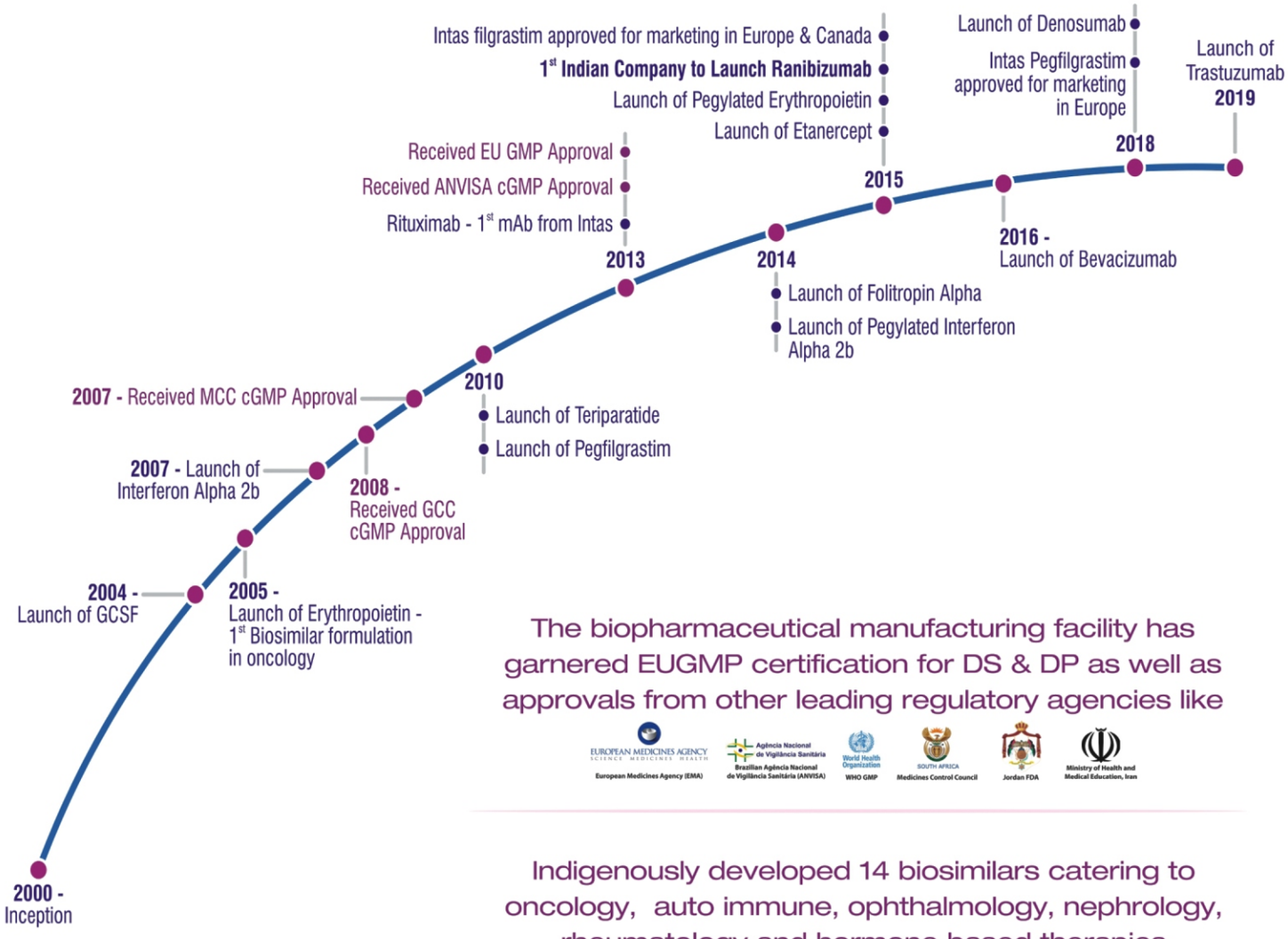

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CASE REPORT

Exudative Retinal Detachment post Pan Retinal Photocoagulation in Diabetic End Stage Renal Disease patient on Dialysis

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Consultant - Vitreo-Retina surgeon and Uveitis Spcialist,
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Abstracts

Exudative retinal detachment post panretinal laser photocoagulation is known complication, but rare nowadays. Here we mention a case of patient with Diabetic End Stage Renal Disease (ESRD) who was on dialysis. He was having Proliferative Diabetic Retinopathy in Right eye and dense vitreous haemorrhage in other eye. He developed exudative retinal detachment post laser in right eye. Here we also explain factors associated in development of exudative retinal detachment in ESRD patients post laser, concept of fluence in laser and how case was managed.

Key Words

End Stage Renal Disease, Exudative Retinal Detachment, Pan Retinal Photocoagulation, Fluence

Introduction

Diabetes is major cause for End Stage Renal Disease (ESRD) and patients with ESRD requires dialysis or renal transplant **(1)**. ESRD patients with diabetes have high chances of severe Diabetic Retinopathy including Proliferative Diabetic Retinopathy (PDR) **(2)**. Pan Retinal Photocoagulation is most commonly used treatment modality for PDR. Exudative Retinal Detachment following Laser therapy is well known complication but quiet rare in present scenario **(3)**. Here we discuss a case of Diabetic ESRD patient who is on dialysis, developed Exudative RD post laser, it's possible associated factors and follow up.

Case

A 56 years old male patient came with complaint of diminution of vision in Both eyes since last 6 months. He is diabetic ESRD patient who is on dialysis since last 2 years. On examination his best corrected visual acuity in right eye was 6/12 and in left eye HM+. He was having left eye dense Vitreous hemorrhage for which he was planned vitrectomy. In right eye he was having PDR and advised laser treatment for same. (Figure 1)

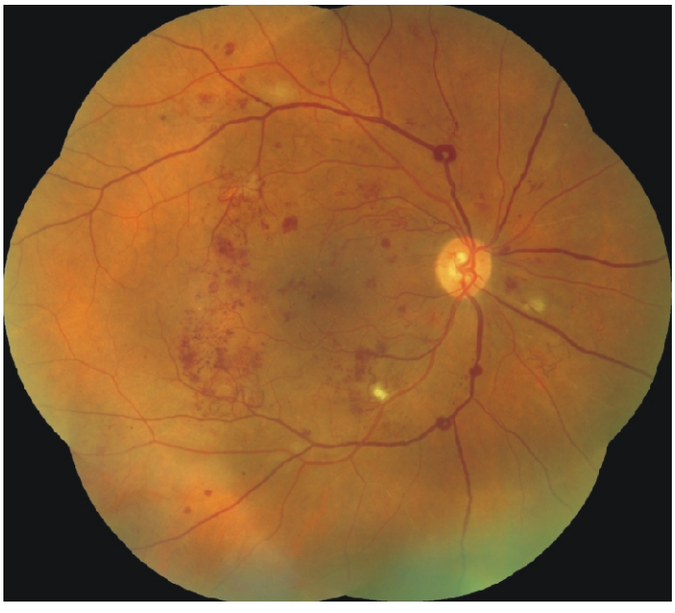

Figure- 1 Pre-LASER Fundus Photo RE

Pan retinal Laser Photocoagulation was performed by frequency doubled Nd: Yag laser (wavelength 532nm) on Zeiss green laser machine. Laser parameters were Spot size-200 u, Power 130-150 mw, Duration 120-140 ms, Interval-200 ms and No. of spots around 1500-1700 in each session. Immediate After 2nd session of laser, patient complaint blurring of vision and on examination Exudative Retinal Detachment noted over posterior pole and peripheral retina was attached. (Figure 2) Patient was started on Prednisolone Actetate eye drops, Nepafenac and Atropine eye drops and reviewed after 4 days.

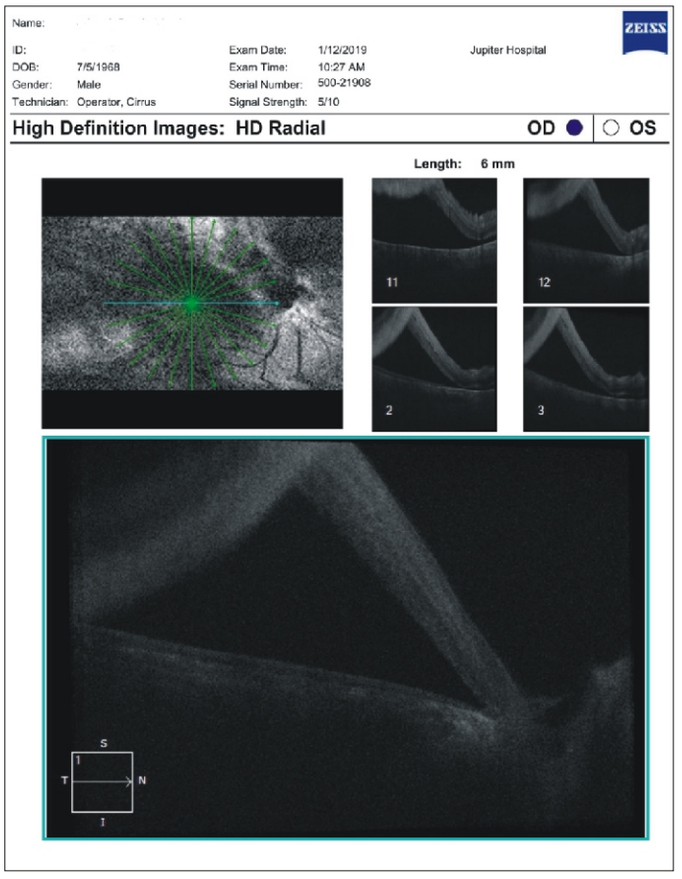

Figure 2 - OCT-Immediate Post 2nd Session of LASER

After 4-5 days patient came with complaint of persistent increase in blurring of vision and Exudative RD had become very bullous over posterior pole, peripheral retina was attached. (Figure 3& 4) Vision in Right eye was Hand Movements+.

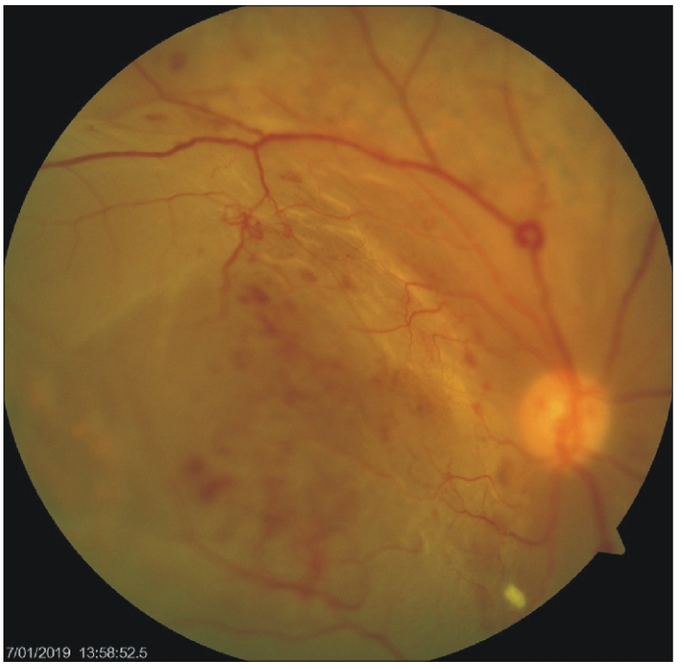

Figure 3- Post 5 days of 2nd session of LASER (Significant increase in SRF)

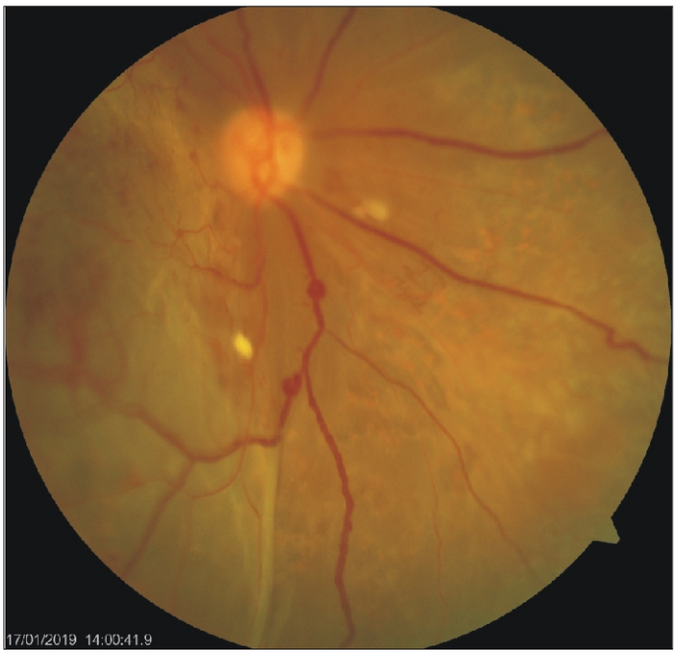

Figure 4- Post 5 days of 2nd session of LASER (Peripheral Retina attached)

Patient was advised to be in follow up, continued on same topical medications and reviewed after 2 weeks , at this time significant resolution of exudative RD noted with minimal SRF over macula and vision improved to 6/60. (Figure 5&6)

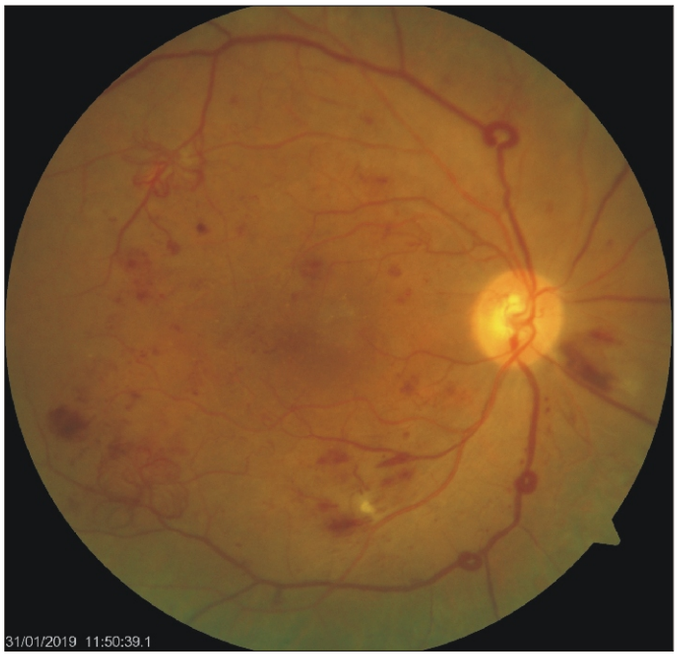

Figure 5- Post 2 weeks of Exudative RD development

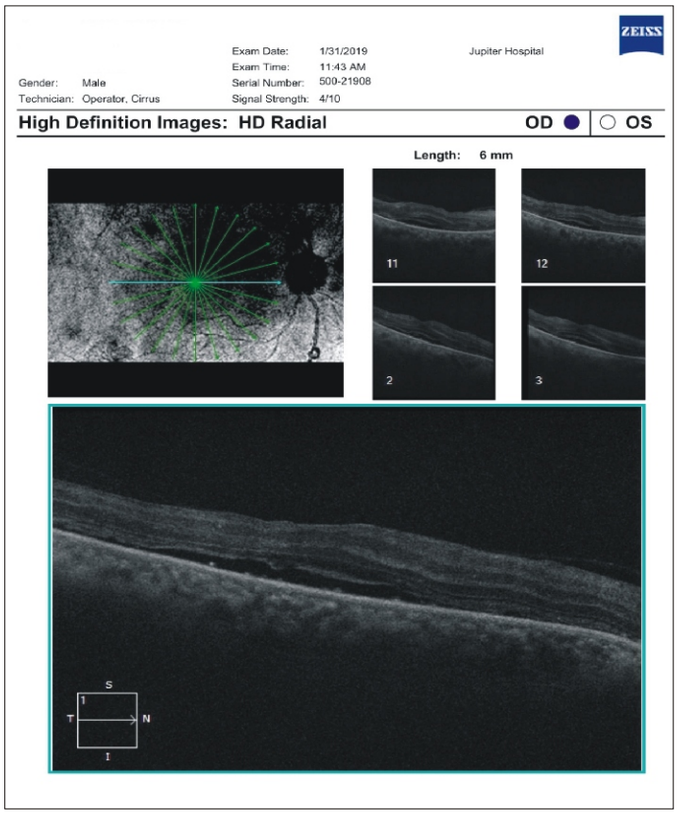

Figure 6- OCT- Post 2 weeks of Exudative RD development

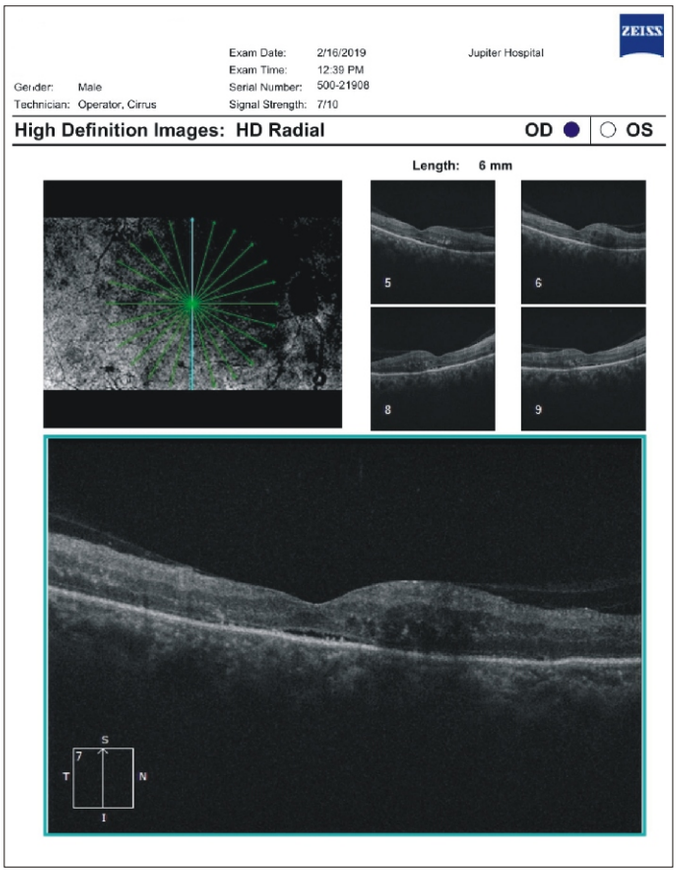

Figure 7- OCT- POST 1 month of Exudative RD

One month post laser, patient was having vision of 6/24 and minimal SRF at posterior pole. (Figure 7)In view of macular edema on OCT, patient was advised intravitreal Injection Bevacizumab. 1 month post injection patient developed improvement in vision of 6/18 and no fluid at macula. (Figure 8 & 9)

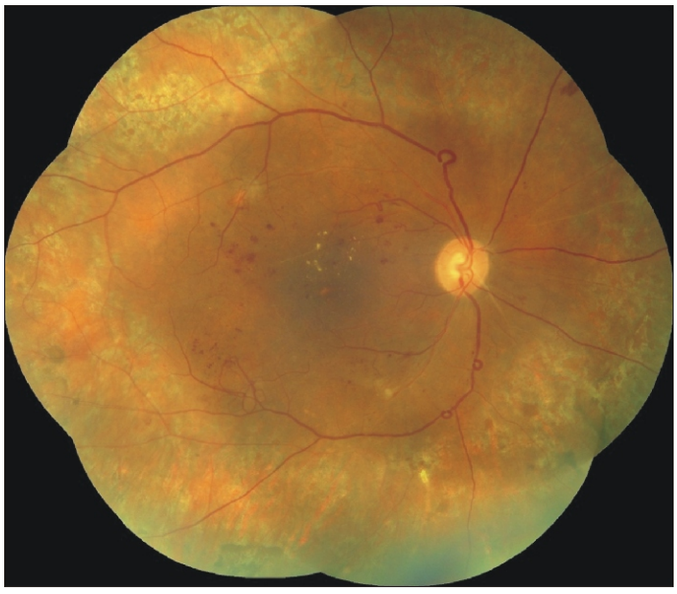

Figure 8- Fundus Photo- 1 month post Inj. Bevacizumab

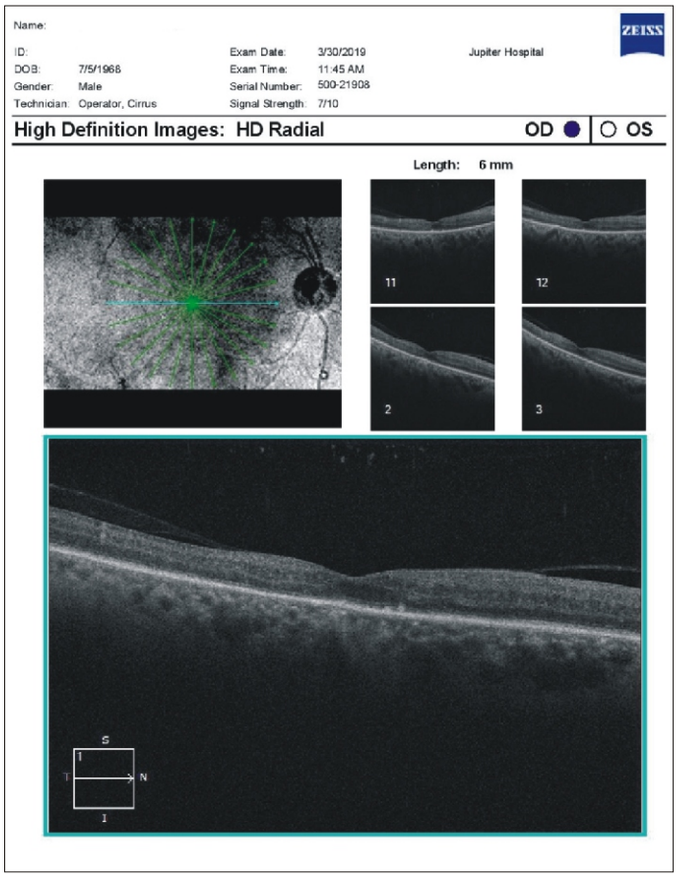

Figure 9 OCT RE- 1 month post Injection Bevacizumab

Discussion

1. In patients with ESRD on dialysis chances of serous retinal detachment is 3.86 times higher as compare to normal population **(4)**. ESRD can cause increase in choriocapillary permeability and that can lead to increase **r**isk of serous retinal detachment.

2. Chorioretinal inflammation induced by laser can lead to breakdown of blood-retinal barrier and that also increases choriocapillary permeability, and can lead to serous retinal detachment **(4)**. In our patient relatively higher number Of laser shots given per sitting which might also be associated with increased chorioretinal inflammation.

3. Pascal uses about one fourth fluence (Energy delivered per unit area) as compared to conventional laser machine **(5)**. So, energy delivered by conventional laser machine is higher as compare to pascal for same number of laser shots. This laser was done on zeiss conventional laser machine.

All these factors are possible association with Exudative Retinal Detachment post laser in Diabetic ESRD patient on dialysis.

Exudative RD post laser usually resolves well with observation and rarely requires intervention. **(3)**.

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CASE REPORT

Morning Glory Disc with Contractile Optic Nerve

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Abstract Page:

Morning Glory Syndrome is a well-established entity with early descriptions seen in 1900 AD. It results from an abnormal closure of embryonic ocular fissure allowing herniation of retinal and optic nerve head tissue leading to excavation of optic disc. It consists of funnel shaped excavated optic nerve head with an annulus of chorio-retinal pigmentary disturbances. Multiple, narrow and straightened retinal vessels are seen emerging from the optic nerve head in a spoke like manner. It is frequently associated with white fibrous tissue overlying the disc. Rarely the optic disc in Morning Glory Syndrome exhibits contractile movements during which the change in size of the disc is seen. We present three cases of rare congenital malformation i.e. morning glory syndrome with contractile optic nerve.

Introduction: Morning Glory Syndrome is a well-established entity with early descriptions seen in 1900 AD.[1] It results from an abnormal closure of embryonic ocular fissure allowing herniation of retinal and optic nerve head tissue leading to excavation of optic disc. It consists of funnel shaped excavated optic nerve head with an annulus of chorio-retinal pigmentary disturbances. Multiple, narrow and straightened retinal vessels are seen emerging from the optic nerve head in a spoke like manner. It is frequently associated with white fibrous tissue overlying the optic disc. Rarely morning glory disc is associated with contractile movements of optic nerve head.[2] Here, we present 3 cases of morning glory disc anomaly in which the optic nerve showed undulating and contractile movements.

Case 1:

A 34 years old male presented with poor vision and squint in his right eye since childhood. On examination, his best corrected visual acuity was 6/24 in right eye and 6/6 in left eye. He had 40 ΔD of exotropia in right eye. Pupil of right eye revealed relative afferent pupillary defect. The intraocular pressure was 16 mmHg in both eyes. Slit lamp examination was unremarkable. Fundus examination of left eye was normal. Fundus examination of right eye revealed a morning glory disk anomaly. The right optic disc was enlarged with central tuft of glial tissue. The disc was surrounded by an annulus of pigmented chorio-retinal atrophy. Spoke like radial vessels were seen arising from the edges of the disk.

During examination, the optic disc was seen to contract and expand alternately resulting in undulating movements (Fig 1). These contractions were seen to occur at irregular intervals.

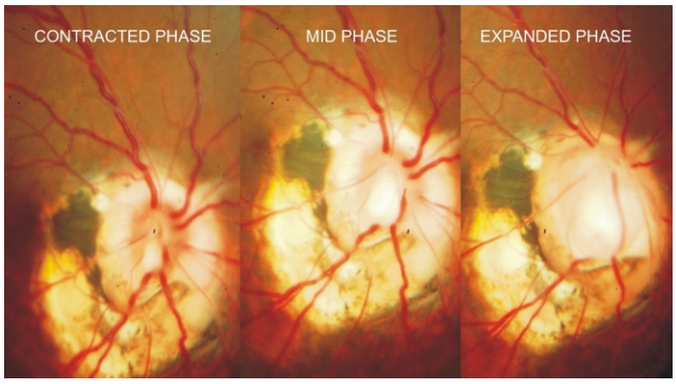

Fig 1: Fundus Photo of Case 1 Morning glory anomaly showing contractions of the disc in various phases

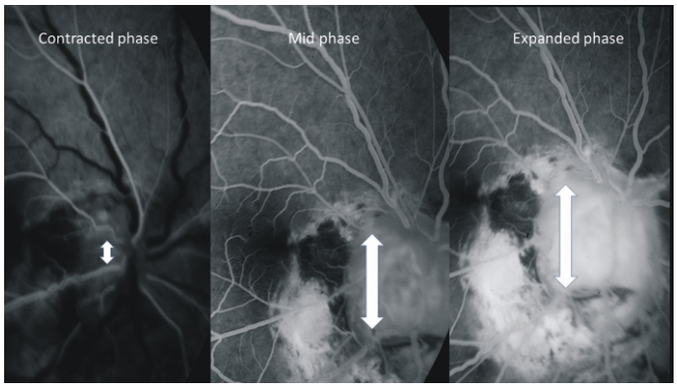

Fig 2: FFA of Case 1 showing increase in the distance between vessels during contractions

During contracted phase, the disc became smaller and the retinal veins became hyperaemic and dilated. After remaining contracted for a few seconds, the disc rapidly expanded to its original size. Fundus Fluorescein angiography (FFA) showed contracted disc in the early phases with blood vessels present close to each other. The blood vessels were seen to move apart in the later phases of angiography (Fig 2).

Case 2:

A 9 years old female presented with poor vision and exotropia in right eye. On examination her best corrected visual acuity was counting fingers@1 metre in right eye and 6/6/ in left eye. She had 40 ΔD of exotropia in right eye. External examination revealed a wide nasal bridge. Slit lamp examination was normal. Fundus examination of right eye revealed morning glory disc

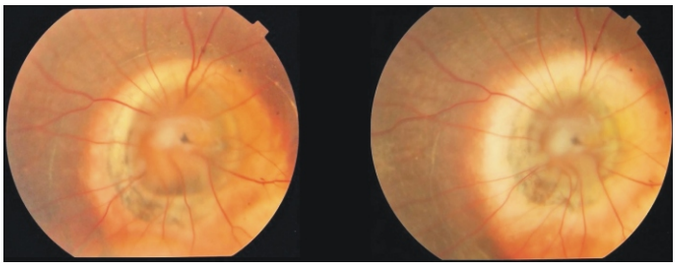

Fig 3: Fundus Photo of Case 2. On the left side the disk is large and the cup is small. On the right side the disk is getting smaller and the cup is getting enlarged.

with contractile optic nerve (Fig 3). Fundus examination of left eye was normal.

Case 3:

A 2-year old female was brought for examination with complaints of exotropia. She had 25 ΔD of exotropia in right eye. Dilated fundus examination of right eye showed a large excavated optic disk with spoke like radial vessels suggestive of morning disk anomaly. On careful examination contractions of the optic nerve were seen (Fig4). Left eye was within normal limits.

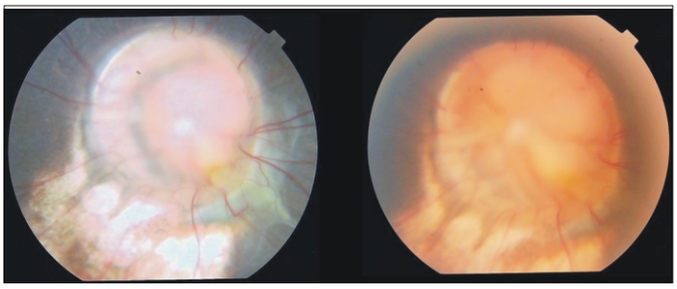

Fig 4: Fundus Photo of Case 3. Notice the distance between the edge of the disk and the staphyloma getting reduced as the optic nerve head expands.

Discussion:

Morning glory syndrome is a rare congenital malformation of the optic nerve.[1] Its exact pathogenesis is still unknown but a few theories include primary mesenchymal abnormality, defective closure of the embryonic fissure or dynamic disturbance between the relative growth of mesoderm and ectoderm.[3] Rarely, the morning glory anomaly can be associated with a

contractile optic disc.[2] Few theories have been put forward to explain the mechanism of contraction. The first hypotheses proposes the presence of anomalous communication between the subarachnoid space and the subretinal space. Changes in transient pressure gradient result in the flow of fluid back and forth along optic nerve causing the contraction and expansion.[4] Sugar et al proposed that the contractions were related to the respiratory cycle and followed changes in venous pressure.[5]

Wise et al. suggested the presence of an atavistic retractor bulbi muscle lying alongside the optic nerve.[6] This muscle pulls directly on the optic nerve and squeezes it within a cone of muscle. Lee et al proposed another muscle-related mechanism in which heterotopic smooth muscle is present in the posterior sclera which contracts due to the influence of parasympathetic cholinergic neurons.[7]The heterotopic muscle was considered to be a ciliary muscle because the contraction was provoked by strong light stimulation and accommodation effort. Kral and Svarc suggested the presence of a sphincter iridis type muscle in the coloboma area that results in contraction evoked by light stimulation a hippus-like movement which simulates pupillary contraction.[8]Rajendran et al described SD-OCT images of contractile movements of optic disk during various phases of contraction.[9] They ruled out presence of subretinal fluid at any stage of relaxation or contraction. They also demonstrated anterior movement of optic disk and surrounding posterior staphyloma during contraction of optic nerve.

Morning glory syndrome is a well-established entity with early descriptions in 1900. Very few cases of contractile morning glory disc have been reported so far in the literature. Actually the appearance of morning glory syndrome is so striking that we just have a look, label it as morning glory and never give a second thought to it. The message here is just to spend a little more time and we may sometimes see some things which we miss otherwise. To conclude, we report and describe features of the three cases of morning glory disc anomaly with contractile optic nerve. This may help ophthalmologists to recognize and understand this rare anomaly.

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Notes

Notes

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