An Approach to a Patient with Post-Operative Endophthalmitis

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Endophthalmitis is a condition in which the internal structures (inner layers) of the eye are invaded by replicating microorganisms, resulting in an inflammatory response. All the structures may get involved ultimately with resulting loss of function.

Only rarely do the organisms get across the intact cornea and sclera. Exogenous endophthalmitis (Post-operative and traumatic) occurs when the integrity of the outer wall is breached. We will focus our discussion on the post-operative endophthalmitis.

Cataract is the most common intra ocular procedure performed and hence the incidence of endophthalmitis is highest. Approximately 90% of post-operative endophthalmitis occur following cataract surgeries. Other causes are intra vitreal injections, trabeculectomies, penetrating keratoplasties and pars plan a vitrectomies.

Intravitreal injections of anti VEGF agents represented 8.5% of all cases of endophthalmitis. Cultures yielded positive results in 75% of cases, majority of them were aerobic coagulase negative staphylococcus.

In **Trabeculectomy** the overall incidence of endophthalmitis vary with the surgical technique and use of metabolites, in the range of 0.12 to 1.2 percent per year. Commonly isolated organisms are Streptococci (acute), Haemophilus influenzae (delayed). Gram negative organisms and fungus are also isolated in post trabeculectomy endophthalmitis. Use of mitomycin increased the risk of endophthalmitis. Glaucoma valve related endophthalmitis have similar isolates as in post cataract endophthalmitis.

After **Penetrating keratoplasty** the incidence of reported endophthalmitis ranged from 0.382 to 0.67%. Factors associated with endophthalmitis were donor cause of death (infection), high risk cases and indication for corneal transplantation (infections). In 60% donor buttons were the likely source of infection and the most common organisms were gram positive cocci.

Post **pars plana vitrectomy** the incidence of end ophthalmitis is 0.05%. The risk of end ophthalmitis was lesser in sutured sclerotomies and in tamponade agents other than BSS.

The type of operation, onset of symptoms, clinical presentation, duration, age of patient, geographic location and other co morbidities etc. may indicate, with reasonable accuracy towards the causative organism. Intuitively a broad spectrum therapy is initiated while awaiting the specific microbiological reports from the laboratory.

The normal conjunctiva harbours commensals, in conjunctival swab cultures most commonly isolated are aerobic coagulase negative Staph. epidermidis. Predominant anaerobic isolates were Propionibacterium. Children harbour less number of organisms and the predominant isolates were streptococcus species.

The culture positivity rates vary from 30% to 70%. The culture results in EVS (endophthalmitis vitrectomy study) showed 69% with confirmed bacterial growth, 18% with no growth and 13% with equivocal growth. 94.2% of culture positives were gram positive bacteria, of them 70% were gram positive coagulase negative, 9.9% Staph. aureus, 9% Streptococcus species, 2.2% Enterococcus and 3% others. Gram negative species were involved in 5.9% cases.

A survey in India reported 53% of post-operative endophthalmitis were gram positive and 26% were gram negative . In another study from the same institute in south India 60% culture positive cases were Nocardia.

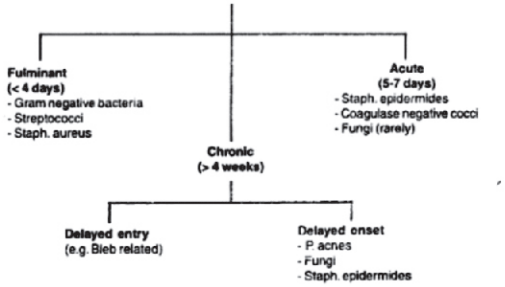
Among the gram negative, P. aeruginosa though reported as the most frequent organism has until never been reported as the single most common organism in studies. Other gram negative isolates are E. coli, Klebsiella, Sphingomonas paucimobilis etc.

Clinical features

The incidence of post-operative endophthalmitis though has sharply declined over the past 50 years, it is still the one of the most catastrophic complications of eye surgeries.

The presentation can be fulminant, acute or delayed as shown in the chart.

Chart-1
Post-Surgical Endophthalmitis



Blurred vision, sudden increase in pain 1 to 7 days after surgery, though absent in 25% of cases are the commonest presenting symptoms.

On examination the signs are lid edema, conjunctival chemosis, yellowish exudates in the cul de sac, corneal edema – infiltrate, AC cells, flare, hypopyon, exudates and fibrin membrane on either side of IOL.

Posterior segment examination shows vitreous exudates, retinal phlebitis (earliest sign). Sometimes only a red reflex is visible obscuring all the other details, poor dilatation and media opacity are major limitations to posterior segment evaluation.

Ultrasound B-scan is a useful tool for evaluation in such severe cases. Vitreous membranes filling the cavity and their density are indicative of severity. Status of retina, choroid and optic nerve head is very well defined in opaque media. Follow up USG is done at same gain settings to evaluate the response of treatment with reasonable accuracy.

Bacterial endophthalmitis

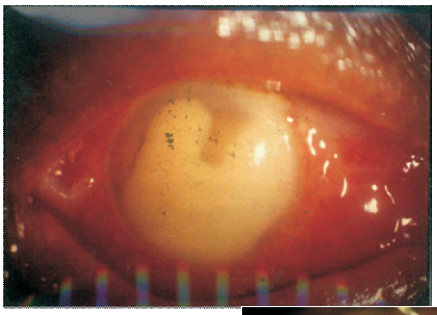


Figure 1 : Bacterial (gram negative)

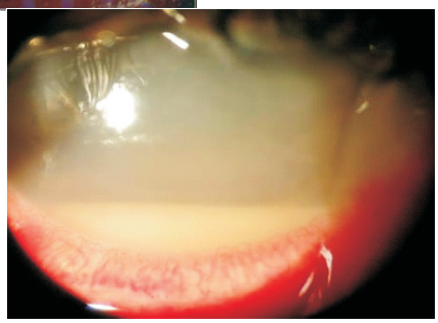


Figure 2: Bacterial (gram positive)

Onset is within 24 to 48 hours. There is marked visual loss and pain. On examination conjunctival hyperaemia and chemosis is noticed, there could be corneal edema and infiltrate with increasing AC reaction and hypopyon. There can be no red glow and the fundus details may be obscured. A rapid progression of signs usually occurs.

Fungal endophthalmitis

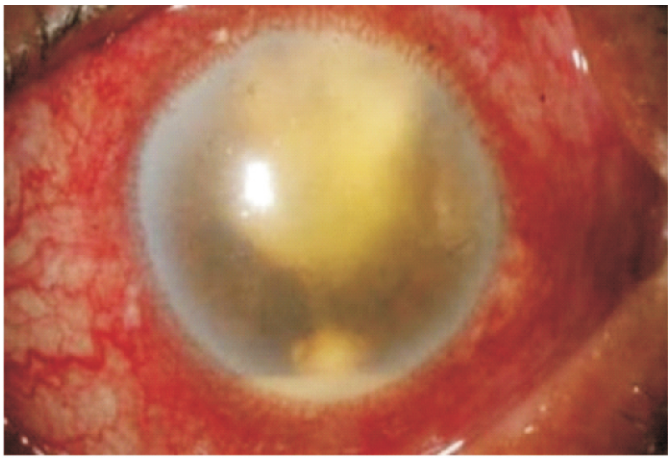


Figure 3: Fungal exudates

Presentation is usually late (after 4weeks) but can occur after one week. There are mild symptoms and minimal discomfort, visual discomfort may as well be minimal. Fibrinopurulent AC exudates, vitreous snow balls and vitreous abscess are suggestive of fungal infection. Most commonly isolated species are Candida albicans, Aspergillus and Fusarium.

Nocardia

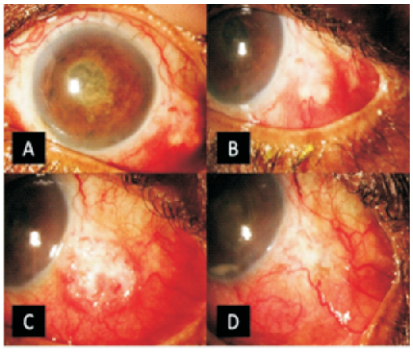


Figure 4a: Scleral exudates in Nocardia infection

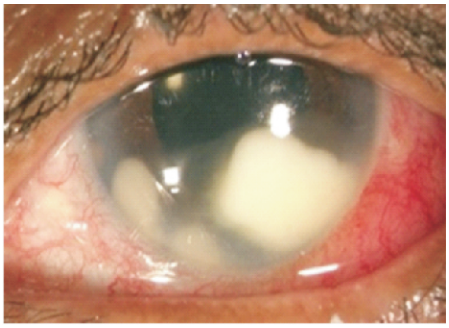


Figure 4b: Nodular exudates in Nocardia infection

The exogenous variant involves the anterior segment, since the vitreous is not a good medium for growth. The bare foot habits of the geographic location should be kept in mind while evaluating a case of post-operative endophthalmitis. Identifiable nodular exudates in AC are quite characteristic.

Propionibacterium acenes

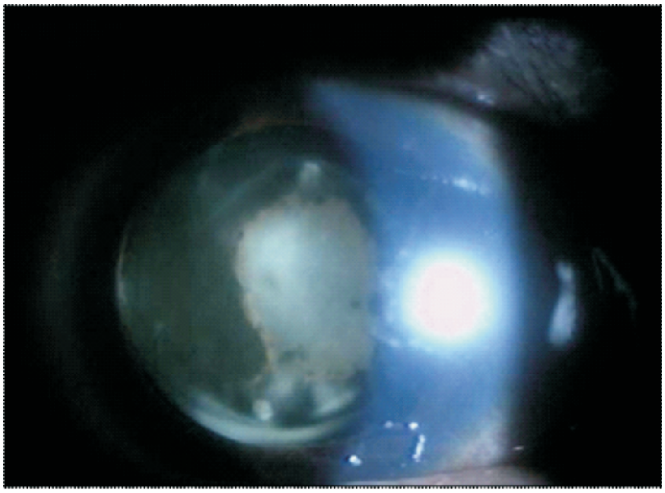


Figure 5: Posterior capsule plaque in P. acenes

A normal commensal of the conjunctival sac ,anaerobic gram positive bacillus, causes late post-operative endophthalmitis because of routine post-operative uses of steroids. Exacerbation of inflammation is noticed each time steroids are tapered. Presents as equatorial white plaques mimicking posterior capsular opacification. YAG capsulotomy exacerbates the reaction and can lead to vitreous reaction and full blown endophthalmitis.

Sterile post-operative endophthalmitis

Here the symptoms are less intense. Intra ocular drugs, gas, chemicals from sterilisation, mechanical irritation of iris ciliary body by IOL, autoimmunity to retained lens matter or excessive iris or vitreous manipulation are the usual causes of sterile endophthalmitis. Retained lens matter and endophthalmitis may occur concurrently and one should suspect infection in any post-operative ocular inflammation with retained lens material

Work up sheet

History

Visual acuity

Examination of lid and adnexa

Examination of specific area of interest (wound site, bleb etc)

IOP

Ocular movements

Anterior segment examination

Fundus examination

Systemic examination

Complete hemogram, blood sugar viral markers (optional with consent)

Informed consent for further management

The role of meticulous history taking and thorough systemic examination cannot be over emphasised. The co morbidities like diabetes, tuberculosis and other immuno compromised states due to disease or treatment must be addressed and managed simultaneously, one cannot wait until completion of the treatment and subsidence of signs of the co morbidity.

Examination of the periocular structures, lids, naso lacrimal system need be done to identify the possible source of infection.

Wound abnormalities like wound leak, vitreous wick, inadvertent filtering bleb, suture abscess etc should be looked for. Other surgical risk factors are vitreous disturbance, exteriorised haptics / sutures as in scleral fixated IOL.

Newer studies have not confirmed higher incidence of endophthalmitis following clear corneal incisions compared to scleral incisions.

Diagnosis

Confirmation of infective etiology depends upon the identification of microorganism. The best chance will have 70% isolation of organism, still 30% will remain unidentified. The samples from aqueous aspirates yield upon 36- 40% positive cultures whereas vitreous aspirates/ biopsy are positive in 56-70% cases.

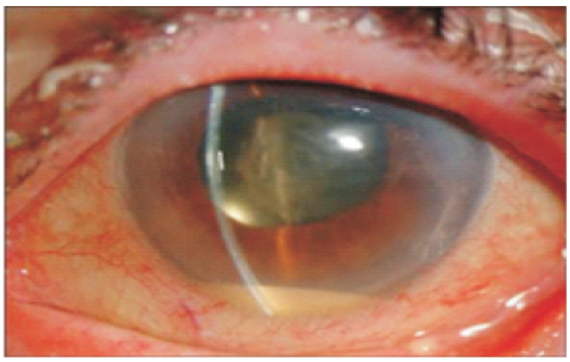


Figure 6: Post operative AC reaction

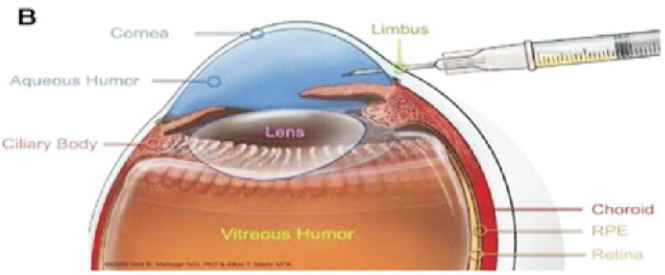


Figure 7: 26 G needle AC TAP

Aqueous fluid / hypopyon 0.1 – 0.2 ml is obtained by paracentesis using 23 g needle, 26 g needles are to fine to

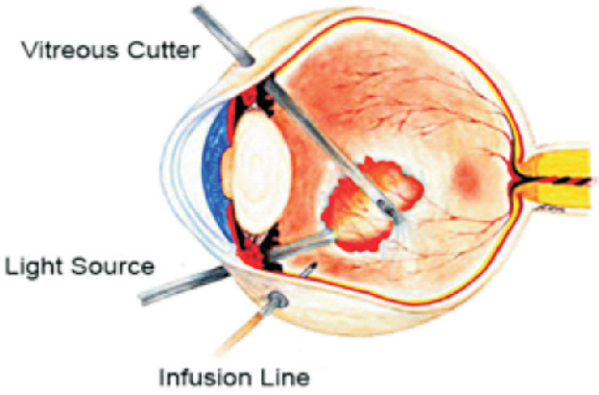


Figure 8: Vitreous biopsy

Vitreous samples of 0.2 – 0.3 ml are obtained by aspiration through pars plana with the help of 23 g needle. In most of the severe cases there is high probability of a dry tap, hence biopsy with the cutter has the highest probability of getting adequate sample and yield.

Biopsy can be performed with 2 pars plana ports, without opening the infusion vitreous sample is collected in a syringe connected to the aspiration tube. (alternately the infusion can be through a 26 g needle instead of a canula). The cutter is placed behind the lens/ IOL and tip should be visible though hazy. In case of IOL a piece of posterior capsule may be taken in the sample.

Other samples could be IOL, suture, abscised tissue etc.

Best is to inoculate immediately in the operation room, loss of precious time in transport of samples would have poor yield. First Gram and Giemsa stain is done, inoculations are done on blood agar, choclate agar, saburouds and Maconky agar for aerobic organisms and thioglycolate broth for anaerobic bacteria.

The reasons for a poor yield could be fastidious organisms, insufficient sample, sterile endophthalmitis or prior administration of antibiotics. Repeat cultures may be needed in poor response to treatment, presence of contaminants in the media or presence of fungi which are likely to be missed in the initial examination.

Newer microbial detection methods

FISH (florescent in situ hybridisation)

MICROARRAYS – large scale screening system for simultaneous diagnosis and detection of many pathogens

LAMP (loop mediated isothermal amplification)

DNA sequencing

MALDI-TOF MS (matrix assisted laser desorption ionisation time off light mass spectrometry)

PCR & MULTIPLEX PCR – it is a technique that has led the way into this new era by allowing rapid detection of microorganism that were previously difficult or impossible to detect by traditional microbiological methods. A quick, highly transport tolerant, highly sensitive and specific test. Unlike other tests which detect immune response, this detects pathogens. Valuable in detecting fastidious organisms, Mycobacterium, Bacillus cereus, Nocardia, Hemophilus etc.

Not without limitations though, false positive tests due to contaminants and dead organisms. The test is costly, has limited availability and cannot comment on antibiotic sensitivity as well.

Current perspective on endophthalmitis management

Endophthalmitis vitrectomy study (EVS 1995) guides us to the management of endophthalmitis, however re-evaluation of the EVS recommendations seem appropriate as treatment modalities have changed since then.

EVS recommends management on the basis of visual acuity and the media clarity, on the visibility of retinal structures. Recommends vitrectomy in eyes with severe media opacity and PL, PR vision. It also recommends that systemic antibiotics have no added benefit (excluding traumatic, bleb related and endogenous endophthalmitis).

On confirmation of endophthalmitis by clinical examination before confirmation of organism a broad spectrum antibiotic is chosen which is non-toxic to the ocular structure in the required doses. Unfortunately not a single agent is effective against gram positive, gram negative cocci and bacilli. The intra vitreal doses of commonly used drugs-

For **gram positive organisms**

Vancomycin- 1mg/0.1 ml

Cephazolin – 2.25 mg/ 0.1ml

Cefuroxime – 1mg/0.1 ml

Ceftriaxone – 2.25mg/0.1ml

For **gram negative organisms**

Amikacin - 400µg/0.1ml

Ceftazidime 2.25mg/0.1ml

Gentamicin 200µg/0.1ml

Role of intra vitreal vancomycin remains a standard choice for gram positive organisms though increasing number of resistant strains are emerging.

For gram negative organisms intra vitreal amikacin is the most effective of all but has toxic effects on the retina, ceftazidime is

safe but many organisms are resistant to the drug.

Dexamethasone 400µg/ 0.1 ml, is administered concurrently to minimise the inflammation caused.

Less commonly used intra vitreal drugs-

Piperacillin - tazobactam - 250µg/0.1ml – effective against P. aeruginosa, Enterobacter, klebsiella

Colistin – 0.1mg (1000IU)/0.1ml

Imipenem 50-100 µg/0.1 ml

Carbenicillin – 2000µg/0.1 ml

Ticarcillin - 3000µg/0.1 ml

Aztreonam -100µg/0.1 ml

Ciprofloxacin 100µg/0.05 ml

For **fungal infection** sintravitreal drugs used are

Amphotericin B - 5µg/0.1 ml

Voriconazole 100µg/0.1 ml

Intra vitreal drugs as per the culture/ sensitivity reports (if available) or the broad spectrum antibiotic combination are administered. The fungal filaments are seen on smears, and subsequently antifungal drugs are administered. Half the normal doses are administered in vitrectomised eyes.

Oral administration of moxifloxacin 400 mg once daily, linezolid 600 mg twice daily (for resistant organisms) have been found to be effective, wasn't studied in the EVS.

Every treating centre shall have a treatment protocol based on the scientific background and their own experiences as per the review of their results/ outcome. The decision to undertake a surgical procedure (core vitrectomy) is imperative to the prevailing conditions like severity, media clarity (corneal infiltrate, opacity are limitations to vitrectomy), accessibility etc.

Intra vitreal injection at the outset has advantages of improvement without further intervention, clarity of media and sometimes spontaneous induction of PVD.

Core vitrectomy is undertaken if the intravitreal injection is not effective or minimally effective in 24 to 48 hrs post injection. Sometimes also undertaken for removal of residual vitreous opacities after the control of infection. The debate between early vitrectomy vs deferred is still on. With the introduction of small gauge trocar canula system the incidence of peripheral retinal tears has come down significantly. Minimal efforts should be made to induce PVD, though PVD ensures near complete removal of vitreous. Posterior capsulectomy is generally performed for better capsular bag lavage, better drug penetration and media clarity.

Decision of repeat surgery depends upon poor response and persistence of infection. Removal of IOL and capsular bag with vitreous lavage is done in repeat procedures.

Use of silicone oil is not done frequently. Used in cases of retinal breaks and retinal detachments. It may prevent retinal detachment in untreated superior breaks for a while. To an extent prevents the growth of microorganism as well.

Retinal detachment is the most dreaded complication and once it happens visual outcome is severely compromised. Thorough examination of the retinal periphery must be done, a hazy media and opaque vitreous cuff hinders the peripheral view. A low infusion pressure allows easier indentation for a better visualisation.

Late complications

Although some of the problems resolve on its own in due course of treatment some may lead to fixed/ progressive visual loss and ocular morbidity. Delayed vitreo retinal pathologies are high risk factors for poor outcome.

Anterior segment complication are corneal opacification, posterior/ anterior synechia, subluxation/ dislocation of IOL, secondary glaucoma, bullous keratopathy etc. Ocular hypotony and band shaped keratopathy are ominous signs.

Posterior segment complications can involve macula, optic nerve, retina and the choroid- ciliary body. Inflammation, endotoxin and drugs are responsible for the deleterious effects.

Macular pathologies

Cystoid macular edema (CME) –A common cause of vision loss caused by inflammatory or mechanical factors. Persistent edema causes disruption of the neural networks leading to gliosis and atrophy resulting in permanent vision loss. Inflammatory process can be treated by systemic or periocular, supra choroidal, intra vitreal steroids. Epiretinal membranes are the cause for mechanical traction and persistent macular edema. Removal of the cause (ERM) treats such persistent edema.

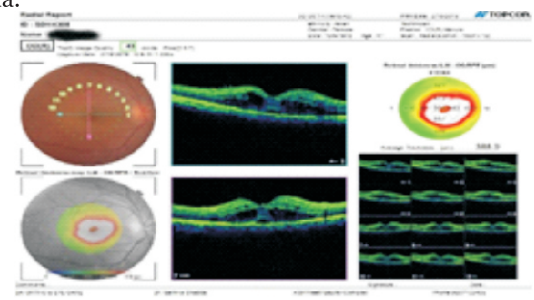


Figure 9: Macular edema

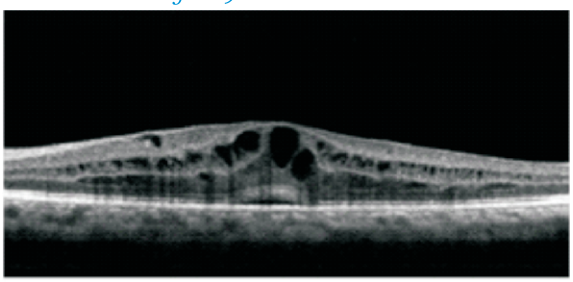


Figure 10: Cystoid Macular Edema

Retinal toxicity though not very common are due to drugs (aminoglycosides, amphotericin), seen as whitening of macular area with intra retinal haemorrhage at the posterior pole.

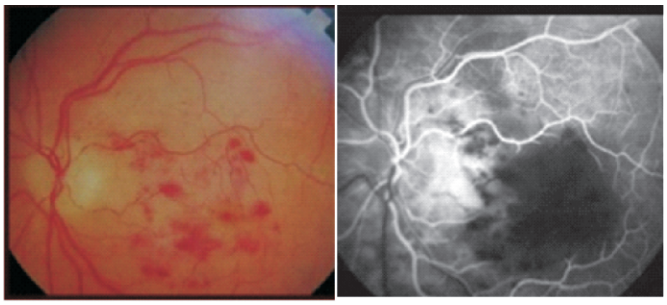


Figure 11: Drug Toxicity

Haemorrhagic occlusive retinal vasculitis (HORV) –a rare but devastating complication is due to delayed hypersensitivity to vancomycin. Early intensive steroid can salvage a few.

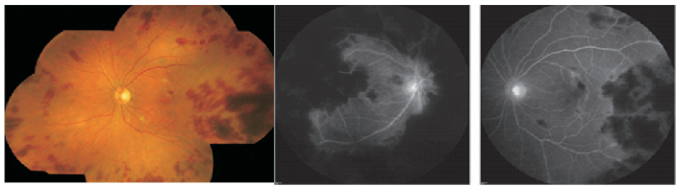


Figure 12 : Haemorrhagic occlusive retinal vasculitis (HORV)

Retinal detachment a feared complication has risk of 7.4 to 8.4 % after treatment of endophthalmitis. Usually encountered in infection by virulent organisms with poor presenting visual acuity. Anatomical success was reported in 78% in EVS, but the occurrence was correlated with poor visual outcome.

Prevention of endophthalmitis

Prevention of endophthalmitis is much cheaper than its management. Pre-operative instillation of antibiotics (moxifloxacin, gatifloxacin), application of 5% povidone iodine 3 minutes before surgery, intracameral moxifloxacin have been found to be effective.

The sterilisation of instruments and operation theatre, quality of consumables and clean practices are important aspects in prevention of endophthalmitis.

Documentation of each and every event and the advice to the patient should be meticulously done and kept in the records to safeguard practices.

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