Original Research Article

Management of microbial keratitis

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Abstract

Microbial keratitis is the one of the common causes of corneal blindness. It is defined as an epithelial defect with infiltrate. It can be caused by bacteria, virus, fungus, acanthamoeba. Detecting the exact causative organism to ensure prompt treatment is important. In this article we describe the evaluation, management (medical and surgical) of the microbial keratitis. We focus predominantly on bacterial and fungal ulcers in this article.

Key Words: Microbial keratitis, bacteria, fungus, keratoplasty.

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INTRODUCTION

Management of Corneal Ulcers: In developing Countries Corneal Ulcers constitute major cause of unilateral blindness, whenever we come across a patient with microbial keratitis, it is important to thoroughly evaluate the patient and try to pin point the causative organism by using micro biological facilities in order to direct the treatment according to the causative organism and distinguish between non healing due to in appropriate medications and non healing due to severe infection.

Pre Operative Evaluation: Through history of any previous corneal trauma, contact lens use, any history of corneal surgery, history of disorders like Steven's Johnson Syndrome, Pemphigoid has to be taken. In all the patients of microbial Keratitis through evaluation of the eye including the adnexa is to be done. Lid margin diseases, dacryocystitis have to be ruled out in all the patients. The size of the epithelial defect, infiltrate and its location in relation to the limbus has to be documented in order to see for the progression of the disease. Extent of thinning or perforation if any has to be documented. Status of the lens [phakic, pseudophakic, aphakic] should be noted. Fundus examination if visible has to be done. In cases where media is hazy B Scan Ultrasonography needs to be done to rule out posterior segment involvement. General systemic diseases like diabetes, immune deficiency if any have to be documented. It is also important to examine the fellow eye thoroughly to note for any scarring vascularization. Microbiological investigations including scraping from the edges and the base of the ulcer has to be done in all cases. The scraped material is subjected to grams stain, KOH – Calcoflour mount in all the cases. Speical Stains like Zeihl Neelsen Acid fast Stain is used for identifying atypical microbacterium, actinomyces. Nocardia Stains with 1% Acid Fast Stain. The material is also inoculated into culture media like Blood agar, Chocolate agar, Sabroud Dextrose Agar[SDA]. In cases where acanthamoeba is suspected the inoculum is placed on non nutrient Agar with E.Coli. When the material for scraping is sparse it is ideal to inoculate the material in liquid medium like Thioglycolade Broth, Brain Heart Infusion Broth. In cases where a typical mycobacterium is suspected LJ Medium[Lowenstein Jensen] can be used. The results of the scrapping are usually available immediately. The culture results however take 48 hours and usually the sensitivity of the drug is mentioned in the culture report. The causative organisms can be bacterial [staphylococcus, streptococcus, pneumococcus, enterococccus, pseudomonas, gonococcus,

mycobacterium, nocardia etc.,] fungal [filamentus, candida], acanthamoeba.

Medical management of microbial Keratitis: Fortified antibiotics [cefazolin 50mg/ml], ciprofloxacin 0.3% drops are started half an hourly in cases of suspected bacterial keratitis. The drugs are modified based on the smear reports and the culture and sensitivity reports. In cases of nocardia, atypical mycobacterium, fortified amikacin[40-100mg/ml] is given. In cases of fungal keratitis natamycin is given hourly. Oral ketakonazole 200mg twice a day or itraconazole 100mg twice a day are also given. Base line Liver Function Test are to be done prior to the Prescription of these imidazoles Cycloplegic, oral analgesics are added to elevate the pain of the patient. In acanthamoeba keratitis chlorhexidine 0.02% and poly hexa methylene biguanid [0.02%] are given hourly. Monitoring the sugar levels and treatment accordingly has to be done to avoid delayed wound healing.

Monitoring and follow up: It is advisable to examine these patients every 24 hours. Subjective improvent of the sysptoms reduced swelling of the lid, reduced size of epithelial defect, size and density of the infiltrate, anterior chamber reaction on set of scaring indicate positive response to the treatment. In cases where the healing response is not adequate it is advisable to re evaluate for the common causes of non healing. Wrong medications inadequate dosage, poor compliance, mixed infections, secondary glaucoma, missed chronic dacryocystis, flag of lagophthalmos, dry eye, neuro trophic cornea, drug toxicity, persistant inflammationare the common causes for non healing ulcers. In such cases repeat corneal scraping after a drug holiday may pinpoint to the causative organism.

Surgical management of Microbial keratitis: In cases refractory to medical treatment, surgical management is the resort In Patients with severe thinning [80-90%] and perforations less than 2mm, cyanacrylate glue application with bandage contact lens, is done to tectonically stabilize the globe. For larger perforations a corneal patch graft, Therapeutic Keratoplasty is performed. In refractive fungal keratitis intra stromal and intra cameral voriconazole[50micro gram/0.1ml] has been tried. The disadvantage with this modality includes need for multiple injection and the patient might eventually need a therapeutic keratoplasty. Therapeutic Keratoplasty is a term used for the procedure which is used either to remove an infection or infl ammatory process in cornea or to give tectonic support to the eye.

Indications of therapeutic Keratoplasty: Non resolving microbial keratitis after maximum medical therapy, Perforated corneal ulcers Descemetocele formation, Scleral involvement adjacent to limbus. It is also done in cases where the etiology could not be established and the keratitis is worsening.

Donor cornea: Donor cornea selection is very crucial for favourable outcome of the procedure and also to prevent iatrogenic spread of infections. The donor blood sample should be investigated for HIV and HBs Ag. Cause of death of the donor and any associated sepsis should be noted. The donor cornea should be evaluated thoroughly, noting specifi cally, the size of the epithelial defects, stromal edema, infi ltrates, scars, stress lines, if any. Specular microscopy should be done on all tissues. Preferably, good-quality donor tissue should be used in cases of therapeutic keratoplasty. Postoperatively, the healthy donor endothelium maintains a clear graft despite the associated infl ammation and elevated intraocular pressure. Use of healthy donor tissue with an intact epithelium also minimizes the risk of graft re-infection. Our criteria for donor tissue quality are not as stringent as for optical keratoplasty. This situation is due to paucity of good-quality donor tissue in developing countries such as ours, as well as the emergency situation under which this surgery is often performed. Donor cornea with fair quality may be used in case of emergency, to attain tectonic stability. After the integrity of the globe is preserved and ocular infl ammation has subsided, a smaller diameter optical keratoplasty may be performed later for visual rehabilitation.

Anaesthesia: In small grafts up to 10 mm diameter, local anaesthesia can be given if the patient cooperates. Careful peribulbar block with a mixture of 1% lidocaine and 0.50% Bupivacaine is given to achieve akinesia and analgesia. Good preoperative hypotony is desirable, however use of excessive massage and application of pinky ball should be avoided in cases where there is a suspected thinning or perforation. In perforated corneal ulcers and in cases with extreme thinning it is advisable to apply tissue adhesive before proceeding with the block to avoid any expulsion of intraocular contents during anaesthesia. General anaesthesia is preferred in cases where there is pre- existing corneal perforation or when the surgical time may be prolonged, as in large grafts, and in young children or very old frail elderly patients who might not cooperate with local anaesthesia.

Surgical procedure: The surgical procedure includes the following steps[1].

Exposure: Self retaining speculum is used to get adequate exposure of the eye. In cases of excessive thinning of cornea or frank perforation, the placement of the speculum should be gentle so as to avoid expulsion of contents of the eye

Extent of the ulceration should be clearly delineated and a careful peritomy is done to rule out any scleral involvement when suspected.

Fleringa ring (18 to 20mm) is used to avoid any possible distortion or collapse of the globe during surgery. It is useful especially in aphakia, in eyes with high myopia, pediatric age groups and situations where anterior vitrectomy may be needed during the surgical procedure. The ring is sutured to the episclera with 6-0 silk taking care to provide equal traction in all the four quadrants.

Recipient bed preparation: The primary goal of therapeutic keratoplasty is to excise all the infected tissue. The size of the recipient bed should be measured with callipers. It is essential to remove all the infected tissue with a 1mm of healthy rim all around. Simple disposable hand held trephines are used most often for this purpose. To check the appropriateness of the recipient bed the trephine is placed over the cornea and the epithelium is indented and globe is examined in all directions to look for the clear margins in all directions

Perforated corneas: Recipient bed preparation is aided by the use of tissue adhesive, cyanoacrylate glue, to seal the perforation. The pressure applied should be minimal so as to avoid any expulsion of intraocular contents. In such cases suction trephines like Hessberg Baron trephines are useful.

Eccentric grafts: Peripheral or eccentric grafts in the form of patch graft, banana shaped graft or crescent grafts may be needed in cases where the pathology involves the peripheral cornea such as corneoscleral tunnel infection, extreme cases of peripheral ulcerative keratitis. These could be done with small sized trephines or could be shaped with free hand dissection. Corneal scraping may be repeated on table preoperatively. It is very important especially in those cases where the etiological diagnosis could not be made earlier, as it will aid in the postoperative management

Entry into anterior chamber: It is achieved using a MVR blade. Entry should be very gentle in cases of perforated corneas. Side port entry is also used to sweep the incarcerated iris from the site of perforation with a cyclodialysis spatula. The recipient bed is trephined up to 80% depth with the trephine and anterior chamber entry is made with the help of 11 number surgical blade or MVR blade. The recipient bed is then excised using Castroviejo's right and left corneal scissors. Left over posterior ledge may be trimmed with vannas scissors, however, leaving a larger posterior ledge may be useful in large grafts to prevent wound leak. In cases of presence of vitreous in the site of perforation, proper anterior vitrectomy should be done to avoid any postoperative vitreous in anterior chamber. The excised corneal specimen should be divided into two parts and sent for microbiological and histopathological examination.

Clearing the anterior chamber of exudates: Irrigation of the anterior chamber is done to remove exudative material from the eye. Membranes over the iris should be carefully peeled off. Intracameral antibiotics or antifungals may be used if needed. Two or three large peripheral iridotomies are done to avoid postoperative pupillary block. Trauma to the lens should be avoided as much as possible. Careful vitrectomy should be done if any vitreous loss is suspected. Vitreous tap with intravitreal antibiotics injection is done in cases of suspected endophthalmitis.

Donor cornea preparation: The donor cornea preparation in therapeutic keratoplasty is done after the preparation of the recipient bed to achieve the correct size of the graft. The size of the graft is taken generally 0.5 mm more than the recipient to improve cooptation and decrease the risk of glaucoma. In larger graft, it may be up to 1mm more than the host bed. The donor tissue is placed on the Tefl on block and centred under the microscope and is punched using a corneal punch. In cases of sclerokeratoplasty and large grafts occasionally free hand cutting of the tissue may be required.

Suturing of donor cornea to the host tissue: Suturing techniques in infl amed, infected eyes should always be interrupted. Full thickness sutures should be avoided to prevent entry of infection into the anterior chamber. The sutures should be taken approximately at 75% depth. Longer bites should be taken to achieve proper wound closure. The sutures should be in moderate tension so as to avoid cheese wiring of the tissue. Interrupted sutures also allow early suture removal in case of excessive sectoral infl ammation, vascularisation or suture infi ltration. In case of small grafts, 16 sutures are taken and in large grafts, 24 sutures are taken

Additional procedures: Vitreous biopsy is taken and intravitreal antibiotics (Vancomycin 1mg/0.1 ml, Ceftazidime 2.5 mg/0.1 ml) are given in cases of suspected endophthalmitis. Predisposing conditions like lid abnormalities, dry eyes should be addressed and if required tarsorrhaphy can be performed after keratoplasty

Post operative management: The most important points to look for on the fi rst postoperative day are signs of any residual infection, evidence of any wound leak, thickness of the graft, status of the corneal epithelium, depth of the anterior chamber, intraocular pressure, degree of infl ammation, presence of synechiae and pupillary block.

Complications of therapeutic Keratoplasty2,3: Retro bulbar haemorrhage, globe perforation may occur during anaesthesia. Scleral perforation may occur while suturing the fl eringa ring. Incomplete or eccentric trephination can occur. Damage to the iris can occur specially while trephining the perforated cornea. Supra choroidal haemorrhage and expulsive haemorrhage are the most devastating complications which can occur if there is

increased vitreous pressure after removing the recipient cornea.

Early postoperative complications: Wound leak, endophthalmitis, infectious keratitis (residual or new infection), suture related complications (suture infi ltrate, loose suture etc), fi lamentary keratitis, iritis, anterior synechiae formation and glaucoma are the common complications noted in early postoperative period. Late postoperative complications include cataract, glaucoma, graft failure secondary to rejection, infection, endothelial decompensation, and graft ectasia and phthisis bulbi.

Postoperative management of therapeutic Keratoplasty: The postoperative management of a therapeutic Keratoplasty is as challenging as the surgery itself. Basic principles[1] in guiding the management are: Eradicate all remnants of infection and prevent reinfection: Therapeutic Keratoplasty often provides surgical excision of all the infection but in cases where there is a reasonable doubt, the antimicrobials should be continued till the epithelium heals. Duration of treatment depends on severity of infectious organism. In general, fungal and acanthamoeba infections require very long postoperative treatment. Promote reepithelialization of cornea and wound healing: Prolonged over treatment of cornea with fortifi ed medications, antimicrobials should be avoided when treating for any epitheliopathy. In such situations non preserved drugs are useful. Control infl ammation with corticosteroids: Concomitant use of steroids along with antibiotics is justifi ed in cases of bacterial keratitis. In herpetic keratitis, steroids can be given without risk as long as patient is managed with topical or oral antiviral therapy. There is a controversy as to timing of steroids in acanthamoeba and fungal corneal ulcers. We, at our institute, wait for 2 weeks before starting steroids in fungal keratitis. When there is even a faint doubt regarding the presence of any residual infection steroids should be with held Management of intraocular pressure: Raised intraocular pressure is an important complication postoperatively because of associated infl ammation (iritis, trabeculitis, anterior synechiae) and should be managed aggressively with intravenous mannitol and / or oral acetazolamide.

Corneal debulking procedures: In this initially lamellar dissection is done at the level of posterior stroma using lamellar dissectors such as cresent knife. It is useful in cases of perforated corneal ulcers where iris is adhered to cornea. After the initial lamellar separation anterior chamber is entered and the remaining part of the cornea is removed. This technique described by Vajpayee *et al* is useful to protect the iris.

Lamellar keratoplasty for corneal ulcers: This technique is advised when the ulcers are not too deep and has been shown to be useful in some acanthamoeba and fungal ulcers. However care must be taken in case selection.

Post operative regimen

Bacterial keratitis

- Antibiotic with most sensitivity given hourly and topically
- Combination therapy or a broad spectrum antibiotic is used when antibiotic sensitivity is unknown
- Topical corticosteroids-every 1–2 hours initially if sensitivity of antibacterial is known
- Cycloplegics
- Antiglaucoma medication, if intraocular pressure is elevated

Fungal keratitis

- Topical antifungals-every hour initially
- Systemic antifungals-oral Ketoconazole 200 mg two times daily initially
- Topical nonsteroidal anti-infl ammatory drugs initially
- Corticosteroids-started after 2 weeks once possibility of reinfection and residual infection is ruled out
- Cycloplegics

Acanthamoeba keratitis

- Topical amoebicidal drugs-every 1–2 hours
- Topical corticosteroids given judiciously
- Cycloplegics

No organism in corneal scraping Based on microbiologic and histopathology report of Corneal button, an appropriate antimicrobial may be used

Visual prognosis after therapeutic Keratoplasty: The final visual prognosis for therapeutic keratoplasty depends on the infecting organism and its susceptibility to treatment. Bacterial keratitis generally has a better visual prognosis than fungal and acanthamoeba keratitis5. The severity of infl ammation at the time of surgery also holds an impact on graft survival. Size of the graft also has an impact on graft survival; grafts more than 9.5 mm in diameter have a significantly decreased chance of graft survival. Therapeutic keratoplasty is generally an emergency and a high-risk procedure that challenges the surgical and medical skills of the corneal surgeon. It requires meticulous attention to detail and careful postoperative monitoring. Therapeutic keratoplasty play a definitive role in the treatment of microbial keratitis refractory to medical therapy. Advances in microsurgical technique and antimicrobial therapy, with the availability of new and more effective antibiotics, and better control of inflammation have resulted in an improved prognosis for therapeutic keratoplasty, in turn, leading to improved visual outcomes.

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