POST-CATARACT SURGERY ENDOPHTHALMITIS: AN UPDATE

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INTRODUCTION

Nowadays, endophthalmitis is still a rare but dreadful complication of intraocular surgery, especially cataract and glaucoma surgery. It seems to be useful to review the last data about epidemiology, diagnostic, management and, most of all, prevention.

When thinking about endophthalmitis, many questions arise. What are the risk factors today? What are the most suitable antibiotics to treat endophthalmitis? What is the best way to administer them? Do we have to get vitreous and aqueous humour samples? Do corticosteroids have any place in the treatment of endophthalmitis? How to prevent it? And so on.

The purpose of this update is mainly to review what are our current knowledge about the most frequent type of endophthalmitis, that is the one that can occur after cataract extraction.

DEFINITION AND CLASSIFICATION

Endophthalmitis is the inflammatory answer to a bacterial, fungal, or parasitic invasion of the eye. More simply can we say, in the postsurgical cases, that endophthalmitis is a more-than-expected ocular inflammation (1).

The endophthalmitis may be endogenous, with an intact globe, and arising from a septicemia. But sometimes no systemic infection can be found.

Much more frequently is the endophthalmitis exogenous (95% of the cases), arising through a traumatic or surgical ocular wound.

ENDOGENOUS ENDOPHTHALMITIS: A BRIEF COMMENT

This type of endophthalmitis is rare. The causative germ is more frequently a fungus, most often candida albicans, but also other subtypes of candida and aspergillus (2). The endogenous endophthalmitis may also be bacterial, and the germs most commonly encountered are staphylococcus aureus, and streptococcus, mainly streptococcus pneumoniae (3). Less frequently bacillus can be the causative microorganism.

The risk factors are well known: septicemia, multifocal systemic infection, use of intravenous drugs, immunodepression, parenteral nutrition (4).

Hemocultures often allow the causative organism to be known before the diagnosis of endophthalmitis. However, taking a vitreous sample may be necessary, especially when the endophthalmitis is the first clinical manifestation of a more widespread infection. The treatment first includes systemic antibiotics and the treatment of the risk factors. A functional vitrectomy, in order to restore the best vision as possible, may be indicated later, when the infection is well controlled.

POST-TRAUMATIC EXOGENOUS ENDOPHTHALMITIS

This complication is particularly critical. It follows a penetrating or perforating ocular injury, with or without a retained intraocular foreign body. The incidence of endophthalmitis after

penetrating trauma ranges from as low as 2% to as high as 17% (5,6). The risk of infection is significantly higher when there is an intraocular foreign boby, even if it is a metallic one (7,8). The causative microorganisms may be the same as in any endophthalmitis, but with a strong predilection for the bacillus accounting for approximately one fourth of the infections (5,7,9,10,11). The prognosis is usually poor for two reasons. The first one is the main causative germ, bacillus, that is quickly and uniformly devastating for ocular structures. The second one is a frequently delayed diagnosis, because of the difficulty to make the difference between a normal post-traumatic inflammatory reaction and a true intraocular infection.

POST-SURGICAL EXOGENOUS ENDOPHTHALMITIS

INCIDENCE

The overall incidence of post-surgical endophthalmitis is around 0.3 % (12). However, this figure vary with the type of intraocular surgery. The incidence after phakoemulsification (during the period from 2000 to 2003) is around 0.25% (13).
After trabeculectomy, this figure raise to 1% (14) and even 5% (15) if antimitotic drugs are used.
The incidence is lower after penetrating keratoplasty, the main risk factor being the graft contamination (16).
Surprisingly, episcleral indentation for retinal detachment treatment, even without any perforation, carries a small risk of endophthalmitis: 0.02% (17).
Finally, the incidence of endophthalmitis after vitrectomy is rather low, 0.05 to 0.15%. This favorable figure may be explained by the positive intraocular pressure that is maintained during this kind of intraocular surgery (18).

POST-CATARACT EXTRACTION ENDOPHTHALMITIS

INCIDENCE

On the basis of 3.140 650 cataract extractions, Taban et al have found a variable incidence of post-surgical endophthalmitis, depending on the period of time taken into consideration (13). During the period between 1970 and 1980, the incidence was 0.327%; during the period 1980-1990, it was 0.158%, between 1990 and 2000, the figure was the lowest, that is 0.087%, raising to 0.265% during the last period studied, 2000 to 2003. This worrying increase during the last period may be at least partially explained by a change in the incision location for cataract extraction over the time, the risk of postoperative endophthalmitis being higher with a corneal incision. Indeed, the same authors mention that, during the period 1992 to 2003, the incidence of endophthalmitis was 0.189% if the surgical approach was corneal, 0.074% if it was scleral, and 0.062% if it was limbal.

RISK FACTORS

Several risk factors are well known and common to endophthalmitis of any cause. As mentioned above, immunosuppression is a risk factor, the most frequent situation being diabetes (12, 19).
Other risk factors are specific to cataract extraction.
As seen before, incision in clear cornea increases the risk of post-surgical endophthalmitis (13). A non-watertight incision, most often a corneal one, is an associated risk factor.
Complications during surgery, mainly vitreous prolapse and vitreous loss, as well as increased duration of surgery, the two factors being most often linked, are also risk factors (19, 20).
Finally, another risk factor of post-surgical endophthalmitis has recently been highlighted. It seems that intraocular lenses made in silicone carry a three-fold increase of risk of postoperative endophthalmitis (21).

SOURCE OF INFECTION

The conjunctival flora is by far the main source of infection, followed by these of the eyelids and the lacrymal sac (22, 23).

Studies have shown that the contamination rate of the aqueous humour at the end of surgery varies between 5 and as high as 43% (24, 25). The normal conjunctival flora is a mixture of staphylococcus epidermidis (75-90%), staphylococcus aureus (25-40%) and corynebacterium species (20-75%).

SIGNS AND SYMPTOMS

The key symptoms are pain and decreased visual acuity. But it is important to keep in mind that some patients may be asymptomatic (26, 27).
The key signs are hypopion and tyndall in the aqueous humour. Less reliable signs are redness and edema of the eyelids, conjunctival injection and corneal infiltrates.

MANAGEMENT

FIRST PRIORITY: MICROBIOLOGIC DIAGNOSIS

As soon as the diagnosis of endophthalmitis is suspected, the first maneuver to be done is to obtain a vitreous sample in order to find the causal microorganism. A sample of aqueous humour may be useful also, but the priority is to get some vitreous by tap, biopsy or vitrectomy (see below).
The probability to find a microorganism by direct examination or by culture is indeed higher in the vitreous (40 to 69% of the cases) than in the aqueous humour (22 to 30%) (28). The microorganisms found are gram + bacteria in 85 to 94% of the cases (29, 30): staphylococcus epidermidis is the most common (45-50%), followed by streptococcus species (24-38%) and staphylococcus aureus (7-11%). However, the causal germs are changing. In the endophthalmitis vitrectomy study (EVS) (30) methicillin-resistant staphylococcus aureus (MRSA) were found in 1.9% of culture-positive endophthalmitis. In a more recent study, MRSA were found in 18% of the cases, among which 2/3 ended up with a final visual acuity of hand motions or less (31). This change is of concern as we have to deal with an increasing number of intra-ocular infections that are more difficult to eradicate.

SECOND PRIORITY: INTRA-VITREAL ANTIBIOTICS

In order to cover as well as possible all the germs that can be responsible for the endophthalmitis, two combinations of two antibiotics are to be recommended (14). The first one is vancomycin 1 mg + ceftazidine 2.25 mg, and the second one is vancomycin 1 mg + amikacin 0.4 mg. Vancomycin is useful to cover the gram+ organisms and particularly staphylococcus epidermidis, that is still the most common germ responsible for post-cataract extraction endophthalmitis (32). Either ceftazidine or amikacin may be efficient against gram- organisms. However both have a drawback: when used together with vancomycin, ceftazidine may precipitate and become less biodisponible. Amikacin has the advantage to have a synergistic activity with vancomycin against gram+ organisms, but may cause macular infarction in less than 0.5% of the cases (33, 34).
When a fungal endophthalmitis is suspected or proved, amphotericin 5µg is the treatment of choice. If the organism is resistant, voriconazole 100 µg might be useful (oral communication, Euretina meeting, mai 2008) (35).

SYSTEMIC ANTIBIOTICS?

In the EVS study, patients were randomized in two groups, with and without systemic antibiotherapy (30). The treatment used was intravenous ceftazidine and amikacin for 5 to 10 days. There was no difference in final visual acuity or media clarity with or without the use of systemic antibiotics. However, this antibiotic combination shows a poor penetration in the vitreous cavity. Of note is that this penetration is even negligible for intravenous vancomycin. The systemic treatment that was choosen in the EVS study may be described as obsolete in 2009. Certainly can we not base our judgement on the EVS results to decide whether systemic antibiotics are necessary or not in the treatment of acute post-cataract extraction endophthalmitis.
So far, there has been no definitive study to prove that the endophthalmitis patient is better managed with than without systemic antibiotherapy along with intra-vitreal antibiotics (36). In the daily practice, we are inclined to

prescribe systemic antibiotics, and the best choice today would be a quinolone. This family of antibiotics is characterized by a good bio-availability, a long half-life, and a good penetration in the vitreous cavity. The quinolones are quickly bactericidal (37) . Which one to choose? Ciprofloxacine has been the first one to be used, but several cases of bacterial resistance have emerged (38, 39). Experts in the field recommend the use of a third-generation quinolone such as moxifloxacine (AVELOX ®) and gatifloxacine (not commercially available in Belgium) (oral communication, Euretina meeting, mai 2008).

IMMEDIATE VITRECTOMY OR NOT?

In the EVS study, there was no difference in visual outcome whether or not an immediate vitrectomy was performed if the initial visual acuity was hand motions or better (30). However, in those patients with initial light perception only vision, immediate vitrectomy produced a threefold increase in the frequency of achieving 20/40 or better visual acuity and a 50% decrease in the frequency of severe visual loss over immediate vitreous tap or biopsy.

We may recommend immediate vitrectomy when the initial visual acuity is reduced to light perception only, and delayed vitrectomy if there is no clinical improvement 48 hours after intravitreal antibiotic injection.

Once the infection is well controlled, a functional vitrectomy may also be necessary in order to improve the final visual acuity, should the vitreous remains opaque.

CORTICOSTEROIDS: YES OR NO?

The use of corticosteroids in the treatment of endophthalmitis is still a matter of debate. There is not a single prospective randomized study which could have proved the efficacy of corticosteroids in this situation, at least on the visual outcome (40).

The rationale for the use of corticosteroids is that the ocular inflammation that occurs during endophthalmitis may become the main cause of irreversible complications (41). For this reason, several authors advocate early and massive use of corticoids (42, 43, 44).

Corticotherapy may probably be started as soon as 48 hours after the beginning of the antibiotherapy, if a fungal infection is not suspected. Dexamethasone may be injected in the vitreous cavity. The recommended dose is 400 μg (40). However the half-life is quite short, 4 hours.

In our opinion, systemic treatment with corticoids is not advised because of the many general contra-indications and side effects.

Most often corticoids drops and sub-conjunctival injections are used, but their action is mainly directed toward the anterior segment.

FROM THE MICRO-ORGANISM TO THE CLINICAL FEATURES

According to the EVS Study, endophthalmitis share several characteristics when the causal micro-orgasmism is virulent, that means all the germs except for coagulase (-) staphylococci (30). A virulent micro-organism should be suspected when the endophthalmitis occurs less than 48 hours after cataract surgery, when the presenting visual acuity is reduced to LP only, when the pupillary red reflex is lost and when there is a corneal infiltrate or a non-waterthight surgical wound. On the other hand, a coagulase (-) staphylococcus will typically cause a less acute endophthalmitis with a better prognosis (1, 45), occuring not earlier than the fourth day after cataract surgery, or even a subacute or chronic intra-ocular infection. Staphylococcus aureus releases many toxins and may cause an acute, necrotizing endophthalmitis with a guarded prognosis.

Streptocccus species typically cause an hyperacute endophthalmitis with a very poor prognosis. This is especially true for Strepococcus pneumoniae (1, 46).

Propionibacterium acnes and several corynebacteria may cause chronic endophthalmitis that may sometimes improve temporarily with corticotherapy only. The diagnosis may be challenging, but the prognosis is quite good (47, 48).

PROPHYLAXIS

PRE-OPERATIVE EXAMINATION

It is important to detect and treat pre-operatively the patients at risk, such as those with

immunodepression (most commonly diabetes) (12, 19), or chronic infection in the vicinity of the eye (most commonly dacryocystitis (49).

ASEPSIS

General guidelines for hand washing and operative field draping must be followed. But the single most important step is to decontaminate the operative field: lids, ocular surface and conjunctival cul-de-sacs with 10% aqueous polyvidone iodine before surgery. This is the only specific prophylaxis that has been proved to decrease the incidence of post-cataract extraction endophthalmitis (50).

ANTIBIOPROPHYLAXIS

Antibioprophylaxis is a matter of controversy (51). The last published recommendations have been done by the European Society of Cataract and Refractive Surgeons (ESCRS) (52). The only indication for systemic pre-operative antibiotherapy is severe atopia. In this situation, staphylococcus aureus may colonize the lid margins, and antibiotics may be given per os (52). The intravenous route is not advised. Topical antibioprophylaxis, mainly with fluoroquinolones, is commonly used before cataract surgery, without any definite proof of efficacy (53, 54). In spite of the positive results of several studies, antibiotics should not be used in the irrigation fluid during phakoemulsification (55, 56). However, a single prospective randomized study dealing with 16000 cases of phacoemulsification has shown that cefuroxime (1mg in 0.1 ml), a third-generation cephalosporin, given intra-camerally at the completion of surgery would decrease five-fold the risk of post-operative endophthalmitis (21).

CHRONIC ENDOPHTHALMITIS

Chronic endophthalmitis accounts for as many as 20% of post-cataract surgery endophthalmitis. This particular form of intra-ocular infection typically appears several weeks to several months after surgery. It can mimic a chronic uveitis, and the beginning is insidious. A pathognomonic sign is the development of white plaques on the posterior capsule and the intra-ocular implant. This kind of infection is usually corticoid-respondent and may become cor-

ticoid-dependent. The most common causal germs are Staphylococcus epidermidis, propionibacterium acnes, and some corynebacteria (47, 48). These micro-organisms share the particularity to secrete a biofilm that allows them to adhere to prosthesis such as intra-ocular implants, and to survive in a quiescnt state (57). These characteristics explain why this type of endophthalmitis may be triggered by YAG posterior capsulotomy.

CONCLUSION

Diagnosis, management and prevention of post-cataract extraction endophthalmitis in an evolving matter. In each endophthalmitis case, the true challenge is to take right and quick decisions in order to restore the best vision as possible. Nowadays, most cases are still caused by staphylococcus epidermidis, and a useful visual function can mostly be salvaged provided the treatment is promptly started.

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