Outbreak of *Ochrobactrum anthropi* endophthalmitis following cataract surgery

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ABSTRACT

Purpose: To report an investigation of an outbreak of *Ochrobactrum anthropi* endophthalmitis following cataract surgery and propose a new sterilization protocol to minimize the risk of further cases in the operating environment.

Setting: Hospital das Clínicas, Federal University of Espírito Santo School of Medicine, Vitória, Espírito Santo, Brazil.

Design: Noncomparative consecutive case series.

Methods: The medical records of patients with culture proven *O. anthropi* endophthalmitis or with suggestive clinical findings during the outbreak, but without microbiological confirmation, were reviewed. We also surveyed existing protocols for disinfection and sterilization of surgical materials and discussed their proper application in the hospital routine.

Results: Seven cases of *O. anthropi* pseudophakic endophthalmitis were confirmed between July 24 and November 10, 2010. The average interval between surgery and diagnosis was 5 days. Initial therapy with intravitreal injection of vancomycin and amikacin proved ineffective in 5 of 7 cases (71%). Complications included macular hole, fibrosis in the macula, retinal vein branch occlusion, retinal ischemia and diffuse hemorrhage, retinal necrosis and phthisis bulbi. Final visual acuity was counting fingers or worse in five patients.

Conclusions: Pars plana vitrectomy with partial capsulectomy appeared to be curative in 2 of 3 surgical cases that could be followed. The most likely cause of this outbreak was contamination of the tubing kit of the phacoemulsification machine. Following introduction of a new sterilization protocol involving the use of an enzymatic detergent and more vigorous cleaning of the tubing with

distilled water, no further cases were reported in over a thousand subsequent procedures.

KEYWORDS *Ochrobactrum anthropi*; cataract extraction; endophthalmitis; antibacterial agents; biofilms; sterilization.

PURPOSE

Endophthalmitis is a potentially severe intraocular inflammation which may occur as a complication of intraocular surgery or as a result of nonsurgical trauma or systemic infection. Irreversible photoreceptor cell damage is a frequent occurrence, even with prompt and proper therapeutic intervention.[1]

Postoperative endophthalmitis occurs most frequently following cataract surgery, with a reported incidence ranging from 0.02 to 0.3%.[1-8]

Depending on the time of onset, endophthalmitis may be classified as acute or chronic. The former occurs early (hours or days after surgery) and is caused by virulent organisms. It is often associated with hypopyon and severe inflammation with a commonly aggressive clinical course.[8-10] The latter is an unusual complication of cataract surgery but well documented in several small series. It is caused by less virulent organisms and the clinical condition is a recurrent, often low-grade uveitis which partially responds to topical or systemic steroids.[8-10] The indolent course of chronic endophthalmitis is sometimes difficult to distinguish from a persistent postoperative inflammation. It may develop months or even years after the initial surgical event and commonly presents itself with mild pain, granulomatous uveitis with or without hypopyon, vitreous activity, capsular thickening or plaque and visual loss.[8-10]

In this study, we report the clinical aspects of an endophthalmitis outbreak following cataract surgery secondary to *Ochrobactrum anthropi* at Hospital das Clínicas in Vitória (a state capital of Southeastern Brazil). Our cases differ from the few previously reported cases in many aspects. Surgical management, antibiotic sensitivity and visual outcome are discussed. The

literature was reviewed in order to develop a sterilization protocol capable of minimizing the risk of further outbreaks in the operating environment.

MATERIALS AND METHODS

This is an observational case series study. All patients presented with endophthalmitis following cataract surgery with intraocular lens implantation (IOL) between July 24 and November 10 at Hospital das Clínicas (Vitória, Brazil). The medical records of seven patients with culture-proven *O. anthropi* endophthalmitis or suspected cases without microbiological confirmation observed during the outbreak were reviewed and the clinical presentation of these patients was compared to the few reports found in the literature. We also surveyed existing protocols for disinfection and sterilization of surgical materials and discuss their proper application in the hospital routine.

RESULTS

All patients underwent phacoemulsification with IOL implantation into the capsular bag. There were no complications during any of these surgeries. A sterile drape with an adhesive foil was used to remove the eyelashes from the operative field. Povidone-iodine was administered topically prior to surgery.

Prior to the endophthalmitis outbreak, the tubing kit of the phacoemulsification machine was used in 3 cataract surgeries per day. Only the

phaco probe was exchanged between surgeries. Disinfection of the tubing kit was performed according to the manufacturer's recommendations (Allergan®) and the material was autoclaved at the hospital´s central sterilization facility.

A total of 140 patients were submitted to surgery in the same operating room between the first and last detected case of endophthalmitis, following the routine procedures described above. However, only 7 patients develop signs or symptoms suggestive of endophthalmitis.

All patients were initially treated with empiric administration of 0.4 mg amikacin + 1 mg vancomycin + 0.4 mg dexamethasone (IV AVD; 0.1mL each). Vitreous samples were collected and plated on blood agar, chocolate agar, Sabouraud dextrose agar, thioglycollate broth and anaerobic medium. Gram was also performed. Antibiograms were performed in all cases for clinical guidance. Bacterial resistance was evaluated, but since *O. anthropi* has not been standardized by the Clinical Laboratory Standard Institute (CLSI) – the method used in our department of microbiology – the respective levels of sensitivity could not be determined.

Table 1 is a summary of patient data.

Case 1

A 73-year-old woman was submitted to surgery in the left eye (OS) on July 24. On the day after surgery, an anterior chamber inflammation was observed with flare (1+) and cells (2-3+), in addition to a fibrinous pupillary membrane. Steroid therapy was started. On the following day, the ocular inflammation worsened. A clinical diagnosis of endophthalmitis was established and the patient was treated with IV AVD. *O. anthropi* was isolated in culture. The

patient experienced visual improvement but white granular debris was noticed in the lower portion of the IOL.

On September 16, signs and symptoms of endophthalmitis were seen again and a new course of intravitreal antibiotics was initiated. One week later, a branch vein obstruction near the macula was observed.

Clinical follow-up showed complete reduction of intraocular inflammation, but on October 13 endophthalmitis recurred. On the following day, a pars plana vitrectomy (PPV) with partial capsulectomy (PC) plus meropenem injection and silicone oil was done. An area of necrosis in the periphery of the lower retina was observed and endolaser photocoagulation was performed to surround the lesion. This time there was no recurrence.

Case 2

A 59-year-old woman was submitted to surgery in the right eye (OD) on July 30. The patient complained of blurred vision on the tenth day after the surgery but only sought medical care 3 weeks later. She reported no pain during all this period. The examination showed a moderate vitritis with no anterior chamber activity. Due to only partial response to 3 weeks of steroid therapy, IV AVD was administered on September 22. *O. anthropi* was isolated in culture. No recurrence has been observed so far.

Case 3

A 79-year-old man was submitted to surgery in the OS on August 20. He began to complain of mild ocular pain and reduced visual acuity on the seventh day post-surgery (POD). The examination revealed corneal edema (3+),

anterior chamber inflammation with flare (1+) and cells (2+), mild hypopyon and prominent vitritis. Clinical improvement was observed after treatment with IV AVD. *O. anthropi* was isolated in culture.

On October 18, the patient experienced another visual deterioration. On ophthalmoscopy, diffuse retinal hemorrhage was seen on the posterior pole, with moderate vitreous haze. No sign of endophthalmitis was observed this time.

Case 4

A 77-year-old woman was submitted to surgery in the OS on August 25. On POD 6, despite the absence of ocular pain, fibrin in the anterior chamber, cells (2-3+), flare (1+) and mild hypopyon associated with the fibrinous pupillary membrane were observed (Figure 1). The patient was treated with IV AVD. *O. anthropi* was isolated in culture.

On September 29, the patient experienced a recurrence with anterior chamber inflammation (cells 3-4+), diffuse keratic precipitates, posterior synechiae and vitreous haze. A new course of amikacin and dexamethasone was initiated. Despite treatment, the patient developed dense and diffuse fibrin and hypopyon occupying one third of the anterior chamber. Antibiogram testing of the second sample indicated resistance to amikacin.

On October 20, PPV with PC plus injection of meropenem and silicone oil was performed. A large area of necrosis was observed in the lower retina and endolaser photocoagulation was used to surround the lesion. The inflammatory process persisted, with recurrence of hypopyon. On November 22, the patient was submitted to PPV with total capsulectomy, lensectomy and silicone oil

removal and a new application of meropenem. The affected eye progressed to amaurosis and phthisis bulbi.

Case 5

A 76-year-old woman was submitted to surgery in the OD on September 1. On the fourth day after surgery the patient complained of mild ocular pain associated with decreased vision. Biomicroscopy showed anterior chamber inflammation with cells (2+), flare (2-3+), linear hypopyon and fibrin at the pupillary edge. Given the uncertainty about etiology of the inflammation, steroid therapy was initiated. On the following day the hypopyon disappeared and visual acuity improved.

Five weeks after the surgery it was not yet possible to visualize the ocular fundus due to vitreous haze. On October 6, the patient started treatment with IV AVD, but no material was collected due to dry aspiration.

After a chronic intraocular inflammation with 3 episodes of exacerbation that partially responded to topical steroids, the patient was submitted to PPV on February 8, including intravitreal application of amikacin and ceftazidime. During the surgery, pallor of the optic nerve was noticed. *O. anthropi* was isolated in culture.

The patient experienced good visual clinical improvement but died secondary to a proximal femoral fracture.

Case 6

A 60-year-old woman was submitted to surgery in the OS on September 27. On POD 3, the patient complained of ocular pain and decreased visual

acuity. The examination revealed corneal edema (3+), anterior chamber inflammation with flare (1+) and cells (1+), fibrinous pupillary membrane and prominent vitritis. IV AVD was administered. No organism grew in the culture. Following the resolution of the inflammatory process on the 11th day, cotton-wool spots, retinal hemorrhages and a macular hole were observed (Figure 2). The patient was subsequently lost to follow-up.

Case 7

A 71-year-old man was submitted to surgery in the OS on November 10. Six days later, severe eye pain and marked ocular inflammation with hypopyon occupying one third of the anterior chamber and fibrinous pupillary membrane was observed. The patient was treated with IV AVD. *O. anthropi* was isolated in culture. Considerable anterior chamber activity with no pain was still observed after three weeks. On ultrasound, small vacuoles were seen in the vitreous cavity. A new intravitreal injection of amikacin + dexamethasone was administered.

On December 18 the patient returned with severe ocular inflammation and pain again and was submitted to PPV with intravitreal meropenem and dexamethasone injection. During the surgical procedure, severe vitreous hemorrhage, many areas of retinal hemorrhage and macular fibrosis were observed. The patient was treated with panretinal endolaser photocoagulation and bevacizumab. A month later, endophthalmitis recurred and the patient was submitted to PPV with lensectomy and application of meropenem. The clinical follow-up revealed proliferative vitreoretinopathy followed later by vitreous

hemorrhage. On June 3, the OS was eviscerated due to the persistence of the inflammatory process.

Since *O. anthropi* had not previously been isolated in our hospital, the protocols of infection control were instituted only when the Department of Ophthalmology became aware of a second case (case 4, September 2). The ophthalmic operating room was closed for 3 weeks while individual cases and the literature were reviewed.

We replaced several materials and supplies suspected of being the source of contamination, including IOL, mydriatic eyedrops, povidone-iodine solution and viscoelastic and balanced salt solution. Samples of these materials were submitted to laboratory analysis. In addition, all sterilization procedures and routines of the operating room were reviewed.

Safety precautions were taken and cataract surgeries restarted. However, six weeks later a new case of *O. anthropi* endophthalmitis (case 7) was identified. Another patient (case 6), submitted to surgery only four days after the operating room was reopened, was not diagnosed until the following year. The only point in common with the other surgeries was the tubing kit of the phacoemulsification machine. Flushings were then collected from four sets (all in use at the time) and submitted to culture along with the tubing. Fluid was collected both when flowing through the irrigation system and when returning from the aspiration system and drainage bag, pumping it both ways through the phaco probe.

While completing the purchase of new sets, we performed extracapsular cataract extraction with lens implantation without further cases of

endophthalmitis. The situation was maintained after the resumption of phacoemulsification surgery.

All samples of materials sent to the microbiology laboratory had negative cultures. The Committee of Hospital Infection Control concluded that no specific cause could be identified, but contamination of the tubing kit is the most plausible explanation.

DISCUSSION

O. anthropi is a ubiquitous gram-negative, non-fastidious, highly motile, non-lactose fermenting bacillus with strictly oxidative metabolism and very active urease[11-23] found mainly in water sources (including normal saline, antiseptic solutions and dialysis liquids).[10-13] It is therefore likely to occupy the same microbial niche as Pseudomonas species.[14] The average time required to grow of the cultures was 5 days in our cases (range: 4–6 days), which is consistent with previous reports.[12]

O. anthropi infrequently causes human infection, usually associated with immunocompromised hosts and indwelling catheters.[13-21] This may be due to its ability to adhere to various synthetic materials such as IOL and silicone tubing (demonstrated by *in vitro* experiments).[22] In 1980, the first case of human infection with *O. anthropi* was described in a patient with a pancreatic abscess.[11] Since then, the pathogen has been described in six reported cases of endophthalmitis following intraocular surgery[12,13,18,19,23] or by endogenous spread,[20] with a total of 14 patients affected.

The interval between cataract surgery and onset of signs and symptoms of endophthalmitis in this report ranged from 1–10 days (average: 5 days). This period was shorter than in previous studies (average: 6 weeks; range: 9-70 days).[12,18,19,23]

The clinical presenting signs were similar to *O. anthropi* pseudophakic endophthalmitis reported in the literature. The main presenting features were decreased vision (7/7), anterior chamber reaction (6/7), vitritis (7/7), hypopyon (5/7) and fibrinous pupillary membrane (4/7). However, the severity of disease found in this study contradicted the low virulence observed in previous reports.[12,18,19,23] Final visual acuity was counting fingers or worse in 85% of patients (6/7) after the final clinical follow-up in this report, contrasting with the much better visual outcome observed in the literature (20/60 or better in 11 of 14 patients). Moreover, ocular complications occurred which had never been described in *O. anthropi* endophthalmitis, such as macular hole, venous occlusion, cotton-wool spots, retinal hemorrhage, necrosis and neovascularization. These findings may account for the poor visual acuity of our patients and suggest an underlying vasculitis or perivasculitis.

Several studies have shown that microorganisms can be isolated from the anterior chamber at the end of cataract surgery in 5 to 43% of patients.[24-28] This fact does not necessarily imply infection, suggesting that natural defense mechanisms are capable of eliminating small inocula of bacteria of low pathogenicity thereby preventing the development of endophthalmitis.[7] This appears to be the case of *O. anthropi*, which, despite the severity of our cases, presented an attack rate of approximately 5% during the period of the outbreak,

considering individuals at submitted to phacoemulsification in any intraocular surgery.

All patients had vision of hand motions or better at the initial presentation. Following the guidelines of the Endophthalmitis Vitrectomy Study Group,[29-33] patients initially received empiric treatment with intravitreal antibiotics plus dexamethasone, and vitreous samples were collected for microbiological investigation. The use of aminoglycosides in our hospital is due to its bactericidal dose-dependent action (even at high concentrations of germs) and synergism with vancomycin – characteristics not observed with ceftazidime.[34]

The use of intravitreal corticosteroids in the management of endophthalmitis remains controversial.[35] However, several clinical and experimental reports suggest that intravitreal corticosteroid therapy used in conjunction with antibiotics may reduce the intraocular inflammatory process and secondary complications associated with microbial endophthalmitis.[34-36]

In this report, initial therapy with intravitreal injection of antibiotics proved ineffective in 5 of 7cases (71%). PPV combined with PC, or even total capsulectomy and IOL removal, as described in the literature, does seem to be curative.[12,19,23] Innate resistance to antibiotics[11-23] and sequestration in the capsular bag[12,19,23] justify the need for these additional procedures. A factor probably responsible for this situation is the formation of a biofilm,[37,38] a functional consortium of micro-organisms organized within an extensive exopolymer matrix[39] which confers relative protection from humoral and cellular immunity and from antibiotics.[3] In addition, Griffiths *et al*[40] found that adherence of *Staphylococcus epidermidis* to IOLs *in vitro* appears to confer greater

resistance to antibiotics, while Cusumano *et al*[41] demonstrated that bacterial growth *in vitro* is significantly enhanced on silicone IOLs.

Perhaps in an attempt to reduce costs and increase the efficiency of the phacoemulsification machine, it is common practice to use a single tubing kit to perform multiple cataract surgeries on the same day, exchanging only the phaco probe (or simply the phaco tip) between surgeries. However, silicone material has been shown to allow adhesion of bacteria and other biomaterials[22,41,42] and in some studies standard cleaning regimes were shown not to be completely effective at removing debris from previous surgeries.[4,43] Various contaminants were identified, including lens capsule and cells, man-made fibers, squamous cells, bacteria, fungal elements, diatoms, red blood cells and proteinaceous material.[4] The presence of organic debris on instruments interferes with the sterilization process as it insulates the organisms from the killing agent. This fact favors the formation of bacterial biofilm and puts patients at risk for cross-infection.[44,45] This was probably the source of our outbreak of endophthalmitis.

Due to the lack of an established cleaning and sterilization protocol in the literature,[4,5,43,46,47]a new protocol was designed at our hospital: the tubing is flushed with distilled water through the purge cycle of the phacoemulsification machine (repeated three times) immediately after each surgery, according to the manufacturer's recommendations. Upon arrival at the central sterilization facility, the tubing is placed in an ultrasonic bath with a solution of enzymatic detergent (Maxzyme®) at 50 ºC for 10 minutes to remove the debris before sterilization. The tubing is subsequently washed with water, cleaned with compressed air and placed in the autoclave. All tubing kits are submitted to

sterility assurance level testing and are sent to the microbiology laboratory to search for microbial contamination after being used twenty times.

Intraocular surgery using the phacoemulsification machine was recommenced following the implementation of the above sterilization protocol. At the time of writing, 1008 cataract surgeries have been performed without a single case of postoperative endophthalmitis and no further contamination of the tubing kits.

It is also worthy of mention that following the implementation of the new protocol, no cases of Toxic Anterior Segment Syndrome[48,49] have been observed at our hospital despite the use of materials and procedures known to be implicated with this syndrome, such as enzymatic detergents and ultrasonic cleaning.

CONCLUSION

This report describes a series of cases of *O. anthropi* endophthalmitis with unusually severe outcomes, including several complications never reported in the literature. Inefficient sterilization can be a source of endophthalmitis outbreaks. However, it seems cross-infection can be prevented by vigorous cleaning of the tubing with distilled water and ultrasonic cleaning using an enzymatic detergent to remove the debris before sterilization to prevent the formation of bacterial biofilm. Cataract surgery represents a substantial cost to health care systems around the world. The new sterilization protocol proposed in this paper offers improved safety when reusing tubing in phacoemulsification.

WHAT WAS KNOWN

* Only 14 cases of *Ochrobactrum anthropi* endophthalmitis were reported in the literature at the time of writing. Usually, this bacteria cause subacute or chronic disease that evaluated with a good visual outcome.

* Silicone material has been shown to allow adhesion of bacteria and other biomaterials and in some studies standard cleaning regimes were shown not to be completely effective at removing debris from previous surgeries.

WHAT THIS PAPER ADDS

* Our observations differ from previously reported cases of O. anthropi pseudophakic endophthalmitis due to the shorter time of onset of signs and symptoms, the severity of the disease and complications not previously reported.

* Cataract surgery represents a substantial cost to health care systems around the world. Persistence in the practice of reusing tubing is controversial and requires risk-benefit analysis at every hospital or clinic that performs cataract surgery. The new sterilization protocol proposed in this paper offers improved safety when reusing tubing in phacoemulsification.

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FIGURE LEGEND

FIGURE 1: Visualization of pupillary membrane and small hypopyon on slit lamp examination of case 4.

FIGURE 2: Cotton-wool spots, retinal hemorrhages and a macular hole are observed on fundus examination of case 6.