Endophthalmitis After Pediatric Strabismus Surgery

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Objective: To report 6 cases of endophthalmitis after pediatric strabismus surgery.

Methods: Retrospective review of initial signs, clinical findings, treatment, culture results, and visual and anatomical outcomes in 6 eyes of 6 children treated at 2 tertiary care institutions between 1983 and 1998.

Results: Four boys and 2 girls aged 8 months to 6 years (median age, 2 years) developed lethargy and asymmetric eye redness, with or without eyelid swelling or fever, within 4 days of surgery. At diagnosis (median, postoperative day 6) clinical findings included periorbital swelling, redness and leukocoria due to vitritis, and, in some cases, hypopyon. Treatment included pars plana vitrectomy and intravitreal and systemic antibiotics in all cases. Vitreous cultures grew *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Staphylococcus aureus*. Within 6 months of strabismus surgery, visual acuity was no light perception in all eyes and 3 eyes had been enucleated. The 3 remaining eyes were prephthisical.

Conclusions: Endophthalmitis after pediatric strabismus surgery is rare. Children may not recognize or verbalize symptoms. Causative organisms are virulent. Visual and anatomical outcomes are poor. Lethargy, asymmetric eye redness, eyelid swelling, or fever in the postoperative period, even if initial postoperative examination results are normal, should prompt urgent ocular examination. The diagnosis of endophthalmitis may be made when biomicroscopic or indirect ophthalmoscopic examination confirms the presence of vitreous opacification with or without hypopyon.


PEDiATRIC endophthalmitis is uncommon and, in most cases, is the result of trauma.¹ There are few reports of endophthalmitis following strabismus surgery.²⁻¹⁰ The estimated incidence ranges from 1:3500² to 1:185000.⁸ The clinical findings and final visual and anatomical outcome of 6 eyes referred to 2 tertiary care institutions during a 15-year period for management of endophthalmitis that developed after pediatric strabismus surgery are presented. Previously published case reports, surveys, and series are reviewed.

REPORT OF CASES

CASE 1

A 3-year-old girl had bilateral inferior rectus recessions and bilateral superior rectus resections for a chronic head-up position due to nystagmus. Her medical history included trisomy 21, chronic otitis media, and hypothyroidism. Examination results on the first postoperative day were normal. On the third postoperative day, mild redness and eyelid swelling were present in the left eye. At the third visit on postoperative day 7 vitreous haze led to the diagnosis of endophthalmitis.

CASE 2

A 7-month-old girl had bilateral medial rectus recession for esotropia, first in the left and then in the right eye. Asymmetric eyelid swelling was noted at home on the first postoperative day. She was examined on the third postoperative day because her mother noted fever. She was lethargic and flaccid and had a white retinal reflex in the left eye. She was referred by the ophthalmologist to her pediatrician, who admitted her to the hospital and treated her with systemic antibiotics for sepsis. Cultures of cerebrospinal fluid, urine, and blood were negative for organisms. On the sixth postoperative day, a hyopyon developed in the left eye and the diagnosis of endophthalmitis was made.

For editorial comment see page 982
PATIENTS AND METHODS

Discharge summaries of all patients aged 18 years or younger treated for endophthalmitis at the Wills Eye Hospital, Philadelphia, Pa (between 1983 and 1998), and the New England Eye Center, Boston, Mass (1990 to 1998), were reviewed. Of the 59 cases identified in the Wills Eye Hospital records, 54 were related to trauma, endogenous infection, or intraocular surgery. The 5 children who had a history of strabismus surgery were included in this study. One child who was treated at the New England Eye Center was also included. Only 1 of the 6 strabismus procedures was performed at one of our institutions (Wills Eye Hospital). During that same period (1983-1998), approximately 8300 surgical procedures for pediatric strabismus were performed at the Wills Eye Hospital.

Information collected from inpatient and outpatient records of the pediatric ophthalmologists and vitreoretinal surgeons included strabismus surgical procedure, medical history, nature and onset of ocular and systemic signs and symptoms following strabismus surgery, clinical findings at first visit with endophthalmitis, medical and surgical treatment, microbiologic culture results, length of follow-up, and final visual and anatomic results. Access to the complete medical record was limited in 4 of 6 cases because of ongoing litigation. The diagnosis of endophthalmitis was made when biomicroscopic or indirect ophthalmoscopic examination findings confirmed the presence of vitreous opacification with or without hypopyon.

CASE 3

An 18-month-old boy had bilateral medial rectus resections for esotropia. His medical history was positive for asthma. On the first postoperative day he was lethargic and had asymmetric eye redness. He was admitted by the pediatrician to a local hospital and treated for dehydration and presumed sepsis with intravenous fluids and intramuscular antibiotics. Computed tomography showed swelling of soft tissue overlying the left globe and maxillary sinusitis. There was no orbital abscess. The child was discharged on the fourth postoperative day. On the sixth postoperative day, left eye redness was diagnosed and treated as a corneal abrasion by the patient’s ophthalmologist. On the eighth postoperative day, hypopyon was recognized and the diagnosis of endophthalmitis was made.

CASE 4

A 7-month-old boy had bilateral medial rectus recessions for esotropia. His medical history included Dandy-Walker syndrome. He became lethargic on the third postoperative day. Asymmetric redness was noticed on the fourth postoperative day. The first postoperative examination was performed at the parents’ request on the fifth postoperative day. Vitreous haze was recognized and a diagnosis of endophthalmitis was made.

CASE 5

A 6-year-old boy had bilateral medial rectus resections for esotropia first in the right and then in the left eye. Four days prior to surgery his pediatrician had documented an acute upper respiratory infection. No cultures or antibiotic treatment were ordered. On the third postoperative day, he developed lethargy and asymmetric eye redness. He also complained of pain. On postoperative day 8, the first postoperative examination was performed at the parents’ request. Vitreous haze, eyelid swelling, and redness were noted in the left eye and the diagnosis of endophthalmitis was made.

CASE 6

A 4-year-old boy had bilateral medial rectus resections for esotropia. Examination on the second postoperative day revealed mild asymmetric eyelid swelling and chemosis. He also complained of pain and had a fever. When hypopyon developed on the fourth postoperative day, the diagnosis of endophthalmitis was made.

RESULTS

Clinical and laboratory data are summarized in Table 1 and Table 2. No child had a history of opportunistic infection, treatment with systemic steroids, or illness that would cause secondary immunosuppression.

Strabismus procedures were all bilateral. Written operative reports were made available in 2 cases. In one (case 2) infection developed on the eye that was repaired first, while in the other (case 5) endophthalmitis developed in the second eye. There was no specific mention of the use of topical povidone-iodine preparation in either case, and surgical approach was fornix incision in both cases. Incisions were closed with single 6-0 plain gut sutures. Subconjunctival antibiotics were not injected at the end of the procedure in these eyes. No operative complications were documented on the operative summaries.

For all 6 cases, the absence of operative complications, including perforation of the globe, was confirmed verbally with the strabismus surgeon. Postoperative management included combination antibiotic and steroid drops in all cases.

Ocular and systemic signs and symptoms developed in all cases between 1 and 4 days (median, 3 days) after surgery. Only 2 children, aged 4 and 6 years, were able to verbalize eye pain. All patients were lethargic, and some had fever, anorexia, and headache. Ocular signs noted by parents included eye redness and eyelid swelling. Ocular signs and lethargy developed concurrently in 4 cases. In patient 2, eyelid swelling and asymmetric eye redness preceded lethargy, while in patient 4, lethargy preceded eye redness. Examination by the ophthalmologist identified asymmetric eye redness, eyelid swelling, and vitreous inflammation in all patients, while 3 patients had a hypopyon and 2 were photophobic. Three patients were febrile on admission. The interval to diag-
Diagnosis of endophthalmitis was 5 to 8 days (median, 7 days) following surgery, and 3 to 8 days (median, 5 days) following the onset of symptoms.

One child (case 1) was seen on the first postoperative day. In 2 cases (cases 4 and 5), the diagnosis of endophthalmitis was made at an initial and unscheduled postoperative visit initiated by parental concern on postoperative days 5 and 8. Three children (cases 1, 3, and 6) had mild signs of infection including eyelid swelling and/or eye redness on visits prior to the one when endophthalmitis was found. No change in antibiotic therapy was made when these signs were noted. Following diagnosis of endophthalmitis by the strabismus surgeons, all patients were referred immediately to a vitreoretinal surgeon for management.

Treatment included emergent pars plana vitrectomy with vitreous biopsy and intravitreal antibiotic injection of 2 antibiotics for empiric treatment of both Gram-negative and Gram-positive organisms in all cases on the day of referral. Conjunctival cultures were performed in 2 cases. Aqueous humour was sampled in 2 cases. All received intravitreal and systemic antibiotics (Table 2). Intravitreal dexamethasone was used in 2 cases.

Culture of vitreous identified Staphylococcus pneumoniae, Haemophilus influenzae, and Staphylococcus aureus (Table 2). No organism was isolated from patient 6, who was treated previously with intramuscular antibiotics. In all cases, isolated organisms were sensitive to intravitreal antibiotics administered. Two conjunctival swabs showed no growth. Aqueous cultures were negative in one case and positive for Propionibacterium acnes, which was believed to be a contaminant, in the one other case. Subsequent surgical procedures performed in 5 of 6 eyes included pars plana vitrectomy for repair of retinal detachment or persistent vitreous debris, lensectomy, and cycloecryotherapy with retrobulbar alcohol injection.

Follow-up ranged from 4 to 48 months (median, 9 months). Final visual acuity was no light perception in all 6 eyes within 1 to 6 months (median, 2 months). Three eyes were enucleated within 6 months of strabismus surgery after phthisis developed. The remaining 3 eyes were prephthisical at most recent follow-up.

Histopathologic specimens of 2 enucleated eyes were obtained and reviewed. Diffuse disorganization and phthisis were evident on the available specimens. No site of scleral perforation could be identified.

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Table 1. Clinical Data

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Affected Eye</th>
<th>Organism</th>
<th>Vitreous Culture</th>
<th>Adj. Surgeon</th>
<th>Antimicrobial Therapy</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Left</td>
<td>Haemophilus influenzae</td>
<td>PPV, PPL</td>
<td>Maxitrol†</td>
<td>Cefazolin, gentamicin</td>
<td>Enucleated</td>
</tr>
<tr>
<td>2</td>
<td>Left</td>
<td>Streptococcus pneumoniae</td>
<td>PPV</td>
<td>NR</td>
<td>Vancomycin, amikacin</td>
<td>Enucleated</td>
</tr>
<tr>
<td>3</td>
<td>Left</td>
<td>No growth</td>
<td>PPV, PPL, CCT</td>
<td>Cetapred‡</td>
<td>Vancomycin, amikacin</td>
<td>Phthisis</td>
</tr>
<tr>
<td>4</td>
<td>Right</td>
<td>Staphylococcus aureus</td>
<td>PPV, PPL</td>
<td>NR</td>
<td>Ceftazidime, vancomycin, dexamethasone</td>
<td>Enucleated</td>
</tr>
<tr>
<td>5</td>
<td>Left</td>
<td>H influenzae</td>
<td>PPV, CE</td>
<td>Cetapred</td>
<td>Vancomycin, amikacin, dexamethasone</td>
<td>Phthisis</td>
</tr>
<tr>
<td>6</td>
<td>Left</td>
<td>S pneumoniae</td>
<td>None</td>
<td>Maxitrol</td>
<td>Vancomycin, gentamicin</td>
<td>Phthisis</td>
</tr>
</tbody>
</table>

* Plus sign indicates present; ellipses, absent or unknown.
† Sign developed along with the corresponding dagger.

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Table 2. Laboratory, Surgical, and Outcome Data

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Organism</th>
<th>Vitreous Culture</th>
<th>Additional Surgery</th>
<th>Topical Antibiotic</th>
<th>Intravitreal Antibiotic</th>
<th>Systemic Antibiotic</th>
<th>Time to NLP, mo</th>
<th>Anatomical Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Haemophilus influenzae</td>
<td>PPV, PPL</td>
<td>Maxitrol†</td>
<td>Cefazolin, gentamicin</td>
<td>Ampicillin, chloramphenicol</td>
<td>Penicillin</td>
<td>4</td>
<td>Enucleated</td>
</tr>
<tr>
<td>2</td>
<td>Streptococcus pneumoniae</td>
<td>PPV</td>
<td>NR</td>
<td>Vancomycin, amikacin</td>
<td>Vancomycin, gentamicin, ceftazidime</td>
<td>Vancomycin</td>
<td>2</td>
<td>Enucleated</td>
</tr>
<tr>
<td>3</td>
<td>No growth</td>
<td>PPV, PPL, CCT</td>
<td>Cetapred‡</td>
<td>Vancomycin, amikacin</td>
<td>Ampicillin, ceftriaxone§</td>
<td>None</td>
<td>1</td>
<td>Phthisis</td>
</tr>
<tr>
<td>4</td>
<td>Staphylococcus aureus</td>
<td>PPV, PPL</td>
<td>NR</td>
<td>Ceftazidime, vancomycin, dexamethasone</td>
<td>Vancomycin</td>
<td>Vancomycin</td>
<td>6</td>
<td>Enucleated</td>
</tr>
<tr>
<td>5</td>
<td>H influenzae</td>
<td>PPV, CE</td>
<td>Cetapred</td>
<td>Vancomycin, amikacin, dexamethasone</td>
<td>Cefazolin</td>
<td>Cefazidime</td>
<td>6</td>
<td>Phthisis</td>
</tr>
<tr>
<td>6</td>
<td>S pneumoniae</td>
<td>None</td>
<td>Maxitrol</td>
<td>Vancomycin, gentamicin</td>
<td>Vancomycin, tobramycin</td>
<td>Ceftriaxone</td>
<td>1</td>
<td>Phthisis</td>
</tr>
</tbody>
</table>

§Antibiotics were given intramuscularly. All other systemic antibiotics were administered intravenously.

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From this series it appears that endophthalmitis following pediatric strabismus surgery is extremely rare. Affected eyes are likely to become blind and phthisical, as has been reported by others. Visual acuity better than 20/200 has been reported in only 2 cases.

Endophthalmitis in young children poses a unique clinical problem. Unlike older children or adults who may complain of pain or monocular visual loss, young children may be unable either to recognize or to verbalize symptoms. Endophthalmitis-induced lethargy may further affect a child's ability to communicate. Young children may develop signs of systemic sepsis in conjunction with endophthalmitis. As in adults, infection may become manifest after a normal initial postoperative visit.

In this series, 4 important signs—lethargy, asymmetric eye redness, eyelid swelling, and fever—developed in children at a median of 3 days after strabismus surgery. In contrast to normal postoperative changes, redness and eyelid swelling associated with infection worsened rather than improved as the postoperative period progressed. Previous reports describe redness and eyelid swelling associated with endophthalmitis as well as orbital cellulitis. Because children may not be able to report symptoms and infection may develop between scheduled postoperative visits, it is important that parents and physicians are familiar with these signs that may indicate ocular or systemic infection. Because endophthalmitis is typically not noted until the second to fourth postoperative day, additional follow-up such as a telephone call or examination for these signs on the third postoperative day has been recommended.

When parents or physicians notice lethargy, asymmetric eye redness, eyelid swelling, or fever during the postoperative period, the diagnosis of endophthalmitis should be suspected. Urgent biomicroscopic and/or indirect ophthalmoscopic examination for hypopyon and a decreased red reflex will aid in the timely recognition of infection and expedite both ocular and systemic treatment.

The severity and rapidity of progression of endophthalmitis has been associated with the virulence of the infecting organism. In this series, organisms isolated included S pneumoniae, H influenzae, and S aureus. With the exception of one report of Staphylococcus epidermidis, virulent organisms were cultured in all previously reported cases. Visual prognosis and anatomical outcome has been very poor in both clinical and experimental infections caused by Streptococcus species and Gram-negative species, including H influenzae. It is therefore not surprising that visual and anatomical outcome were poor in this and previous series of endophthalmitis after pediatric strabismus surgery.

While S pneumoniae and H influenzae are less common causes of acute postoperative endophthalmitis in adults, they may be more likely pathogens in children. External bacterial flora from patients' own tissues have been implicated as the source of infection in acute postoperative endophthalmitis. Up to 98% of healthy children may have respiratory tract colonization by H influenzae, and 45% are transitory carriers of S pneumoniae. Although the invasive disease rate decreased to less than 15% after H influenzae type b (Hib) vaccination was instituted, reemergence of invasive Hib disease has recently become evident in some well-vaccinated populations. Streptococcus species were present in 14.9% of conjunctival cultures of uninfected children and only 2.2% of uninfected adults. This suggests that children who develop endophthalmitis may be more likely than adults to be infected by one of these virulent organisms. It has been stated that H influenzae is no longer a significant pathogen in periorbital and orbital disease, owing to widespread use of the Hib vaccination. However, because cultures for H influenzae were positive in 2 of 6 cases of endophthalmitis in this series, we believe it is advisable that the clinician prescribe antibiotics effective against H influenzae until cultures indicate it is not present.

Globe perforation, as defined by retinal and/or choroidal injury visible with indirect ophthalmoscopy during strabismus surgery, has been reported to occur in 0.13% to 1.8% of strabismus procedures, and was higher prior to the widespread use of spatulated needles. Subsequent endophthalmitis following perforation is uncommon. However, the development of endophthalmitis neither requires nor implies that perforation of the globe has occurred. Perforation was not recognized in any case in the present series. Previous authors have also specifically stated that perforation did not occur during strabismus procedures after which endophthalmitis developed. Endophthalmitis has been reported after nonpenetrating extraocular surgery including pterygium removal, laser in situ keratomileusis (LASIK), and radial keratotomy. A localized infection such as an infiltrate, ulcer, or abscess of the cornea or sclera was present in all cases. None of the cases in this series were explored for possible abscess at the time of the vitrectomy surgery. Yet, it is conceivable that these eyes developed a small abscess in the thinnest sclera posterior to the muscle insertion that progressed to intraocular infection. An alternative explanation for the pathogenesis of endophthalmitis in the absence of perforation is endogenous seeding. Two children in this series were diagnosed with sepsis before the diagnosis of endophthalmitis. Systemic cultures were negative for organisms. Whether systemic infection was primary and caused endogenous endophthalmitis or was secondary to exogenous postoperative endophthalmitis is uncertain.

The interval between strabismus surgery and diagnosis is a factor of unknown significance with respect to visual outcome. In our series all eyes became blind, but interval to diagnosis (3-8 days; median, 7 days) was shorter than that reported in previous cases (3-30 days; median, 9 days; mean, 12 days) in which visual outcome ranged from 20/40 to no light perception. Whether earlier diagnosis would have improved visual outcome in eyes with aggressive organisms is uncertain. It is possible that the virulence of the infecting organism is the most significant factor determining visual and anatomical outcome. Nevertheless, the strabismus surgeon should maintain a high clinical suspicion for endophthalmitis to prevent delay in diagnosis.
We were not able to determine whether variation in surgical technique, such as preoperative povidone-iodine prophylaxis, limbal vs cul-de-sac location of conjunctival incision, and suture closure of incisions, may have had an effect on the incidence of endophthalmitis in this or previous reported cases of endophthalmitis after strabismus surgery. Preoperative preparation with povidone-iodine solution was not specifically mentioned in 2 operative reports available for review. In these cases, incisions were closed with suture, but it is uncertain whether sutures were used to close wounds in all cases. Conjunctival incisions may not require sutures in adults. However, in children, who may rub or touch their eyes following surgery, a tightly closed wound may provide a barrier against exogenous infection.

Endophthalmitis prophylaxis has not been the subject of large prospective series of pediatric strabismus surgery. This may in part be due to its rarity and the large numbers of subjects who would be needed for such an investigation. As a consequence, however, the standard of care for infection prophylaxis following strabismus surgery has not been defined. Surveys of practice patterns have pooled the experience of large numbers of cases. But because surveys are subject to reporting bias and are not prospective or randomized, their conclusions represent popular opinions rather than results of controlled experimental trials. It is known that chemical preparation of the eye with preoperative povidone-iodine reduces conjunctival bacterial flora as well as the incidence of culture-positive endophthalmitis following cataract surgery. However, a survey of strabismus surgeons concluded there was no difference in outcome with or without preoperative antibiotic administration or iodine preparation. According to another survey, the use of postoperative topical antibiotics is not routine for all strabismus surgeons. One prospective study of 69 patients found no difference in the incidence of postoperative infection or clinical appearance after strabismus surgery in children treated with or without postoperative topical antibiotics.

It is uncertain whether a variation of route of antibiotic delivery may reduce incidence of postoperative infection. All eyes that developed endophthalmitis in this series were treated with topical antibiotics postoperatively. None received subconjunctival antibiotic injection at the end of surgery. Subconjunctival antibiotic injections are not routinely used in strabismus surgery. However, considering that the source of infection could be located in the orbit, it would be reasonable to consider investigating their usefulness as a prophylactic agent. Prophylaxis with a single oral dose (750 mg) of ciprofloxacin produces an intravitreal concentration of the medication that exceeds the 90% minimum inhibitory concentration for *H influenzae* and the 70% minimum inhibitory concentration for *S aureus* in adults but does not produce intravitreal concentrations effective against *Streptococcus* species. Ciprofloxacin is not yet approved for use in children. No child in this series received prophylactic systemic antibiotics. It is uncertain whether the potential benefit of reducing the very rare incidence of endophthalmitis with a single preoperative dose of oral ciprofloxacin or other broad-spectrum antimicrobials that can reach intravitreal concentrations effective against *Streptococcus* species, *H influenzae*, and *S aureus* would justify the cost, systemic risk, and possible induction of bacterial resistance associated with their use.

In summary, diagnosis of endophthalmitis after strabismus surgery depends on a high index of suspicion. Young children may be unable either to recognize or to verbalize symptoms, and lethargy may confound an affected child’s ability to communicate. Educating parents about signs of endophthalmitis, specifically lethargy, asymmetric eye redness, eyelid swelling, and fever is important. These signs may develop after normal initial postoperative examination results and may herald ocular and systemic infection. Their appearance during the postoperative period should prompt urgent ocular examination that should include evaluation for decreased red reflex. Follow-up examination or a telephone call on the third postoperative day may facilitate timely recognition of infection and expedite ocular and systemic treatment. The use of preoperative chemical prophylaxis with povidone-iodine and postoperative topical antibiotics may be prudent. The usefulness of these and additional prophylactic measures including intraoperative subconjunctival antibiotic injection or a single preoperative dose of oral ciprofloxacin may be clarified in future large, prospective, randomized trials. Even if children have previously received Hib vaccination, it is advisable for the clinician to prescribe antibiotics effective against *H influenzae* until cultures indicate it is not present. Informed consent for strabismus surgery should include the rare but real risks of blindness and loss of one or, in the case of bilateral surgery, both eyes.

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REFERENCES

From the Archives of the ARCHIVES

A look at the past . . .

The history of the intracapsular cataract extraction goes back many years. At the American Congress in 1929, Marquez spoke of a book published in 1789 in which the intracapsular extraction with forceps was described. About 1850, McNamara, of Calcutta, practiced a method of intracapsular extraction by combined external pressure applied just back of the incision with the curet and at the opposite limbus with the tip of the finger; and Wright, of Columbus, Ohio, described a similar method at about the same time.

The two Pagenstechers stated their belief that the remaining capsule and remnants of the lens in the usual cataract extraction were the principal causes of iritis and practiced a method of removing the lens in its capsule by introducing a spoon back of the lens and extracting the lens, with the loss of a few drops of vitreous. De Wecker operated in 66 cases and then abandoned the procedure.

Terson, in 1872 and 1887, reported that he extracted the cataract by applying external pressure after grasping the capsule of the lens with a special forceps. Molroney, of India, in 1894, practiced a method similar to McNamara’s.