

Coloboma of the Iris, Retina, Optic Nerve, and Lens

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DEVESH K. VARMA, MD, FRCS; AND IQBAL IKE K. AHMED, MD, FRCS

CASE PRESENTATION

A 42-year-old man presents with a progressive decline in visual function and a dense cataract in both eyes. He has had poor vision in both eyes, especially the left, due to retinal and optic nerve colobomata. He has iris and lens colobomata as shown in Figure 1. No phacodonesis is present. The lens is nearly brown with dense nuclear sclerosis.

The patient has decided to proceed with cataract surgery first in his left eye to determine if his decline in visual function is due to the cataract. A dilated examination of the posterior segment reveals retinal and optic nerve colobomata involving most of the inferior posterior pole, which appears unchanged.



(Courtesy of Thomas A. Oetting, MS, MD.)

Figure 1. The patient in this case had a dense cataract with coloboma of the iris, optic nerve, and retina.

KEVIN M. MILLER, MD

Cataract surgery for the patient's left eye is a reasonable course of action if a decline in visual acuity or function can be documented. Before proceeding, however, it would be important to try to determine why his other eye developed a dense nuclear cataract. The case presentation does not tell of any ocular comorbidities for this eye. Is there a family history of autosomal dominant nuclear cataract? Was the patient born prematurely? Did he spend any time in a hyperbaric oxygen chamber? Did he receive a heavy dose of sunlight early in life? Are there nutritional issues?

The case presentation states that the patient has a lens coloboma. The lens is secondarily involved where there is faulty closure of the optic fissure. There is no actual loss of lens tissue as the term *coloboma* implies. The equator of the lens is flattened because the zonules that would normally stretch it are absent. The missing zonules may complicate cataract removal and lessen the stability of the IOL and any artificial iris devices that are implanted.

I would perform standard phacoemulsification and be



(Courtesy of Kevin M. Miller, MD.)

Figure 2. Dr. Miller has found the Artificial Iris to be a nice solution for pseudophakic eyes with partial or complete aniridia that have strong zonules and a normal ciliary sulcus.

careful to minimize the generation of heat and trauma to the corneal endothelium. I would place a dispersive viscoelastic over the area of absent zonules to prevent the anterior migration of vitreous and replace the agent as often as necessary. I would also gently stretch the pupil

(Courtesy of Kevin M. Miller, MD)



Figure 3. According to Dr. Miller, the Morcher model 50F Aniridia Rings are another good solution for partial or complete aniridia in the presence of an intact capsule. He has found the devices work best if there is peripheral iris tissue to block light from entering the eye between the capsular equator and the peripheral cornea.

superiorly to create a more central pupillary opening.

Approximately 2 clock hours of iris tissue are missing. I would not try to close the iris defect with sutures, because doing so would be cosmetically undesirable and optically inadequate. My first choice for treating the defect would be to implant an Artificial Iris (Dr Schmidt Intraocularlinsen GmbH, SanktAugustin, Germany; distributed by HumanOptics, Erlangen, Germany; not available in the United States) in the ciliary sulcus after the IOL's implantation into the capsular bag. I have achieved very nice cosmetic results with this device (Figure 2). My second choice would be to implant two Morcher Aniridia Rings (model 50F; Morcher GmbH, Stuttgart, Germany; not available in the United States) in the capsular bag in front of the IOL. The problem with the latter approach is that it creates a curvilinear slit aperture between the equator of the lens capsule and the periphery of the cornea through which unfocused light may enter the eye (Figure 3). With either technique, it will be necessary for an ophthalmologist practicing in the United States to obtain a compassionate use exemption from the FDA and approval from a local institutional review board before the artificial iris devices can be obtained or implanted.

MICHAEL E. SNYDER, MD

The technical challenges of this case begin with the choice of anesthetic. Almost invariably, such colobomata of the iris, optic nerve, and retina are associated with steep and deep inferior scleral staphylomata, making orbital injection hazardous. General anesthesia is the best choice.

A few iris retractors will likely be needed to allow ade-

quate access to the superior pole of the lens in this very small anterior segment with microcornea. The phacoemulsification should use vital dye staining of the anterior capsule and frequent reinstallation of a dispersive ophthalmic viscosurgical device due to the very dense lens. A 1- to 2-clock-hour zonular defect is likely, although a standard capsular tension ring (CTR) would probably be fine in most similar cases. Preoperative intravenous mannitol can reduce the risk of vitreous gel's prolapsing around the (likely) inferior zonular defect.

A highly flexible single-piece acrylic PCIOL will be the easiest to place within the small capsular bag.

The iris defect can and should be closed inferiorly to reduce the risks of edge-related glare and monocular diplopia from the light coming around the IOL's margin in the aphakic space. Closure can often be achieved with a few imbricating sutures through the two inferior pillars, tied with Siesper's knots. The pupil will then need to be enlarged and recentered, achievable either with 23-gauge intraocular curved scissors or, more easily, by sculpting using a 25-gauge vitrector handpiece on I/A-cut settings.

Intraocular carbachol will blunt the potential increase in IOP seen in such cases, because the ophthalmic viscosurgical device will usually migrate into the posterior segment around the (likely) inferior zonular breach.

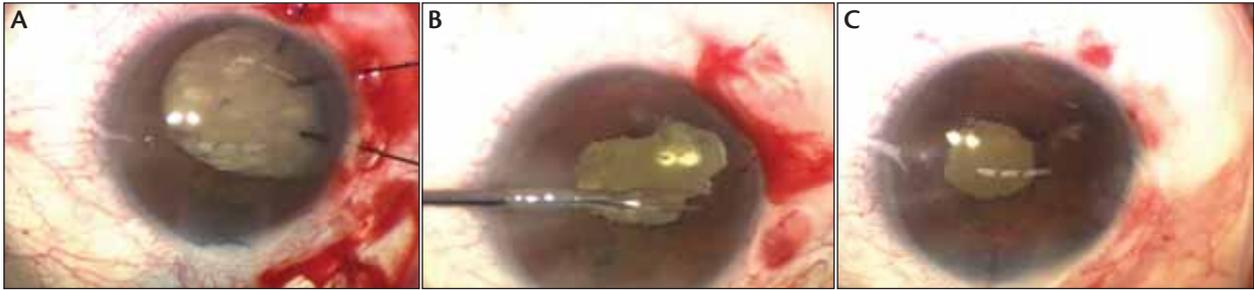
DIAMOND Y. TAM, MD

The plan for this patient should involve cataract extraction, IOL implantation, repair of the iris defect, and recenteration of the pupil to a more physiologic position.

Preoperatively, assessing the zonular apparatus will be important, because patients like this one often have zonular absence or weakness in the region of the coloboma. Further, because these individuals frequently have small anterior segments, I would perform a white-to-white measurement and use gonioscopy to assess the anterior chamber angle. Imaging such as anterior segment optical coherence tomography could also prove useful.

Intraoperatively, I would be prepared to use capsular dye as well as iris retractors. Also, if a relative anterior microphthalmos, a shallow chamber, or a short axial length is present, a pars plana vitreous tap may be required to deepen the anterior chamber for enhanced safety during phacoemulsification as well as protection of the corneal endothelium (Figure 4A). Although a majority of the zonules may be normal in tension and anatomy, I have a low threshold for placing a CTR in the setting of possible zonular compromise.

Although in traumatic iris defects the margins can be simply apposed and sutured, this approach results in an inferiorly decentered pupil in cases of coloboma. Relaxing incisions must therefore be made in the peripheral iris on



(Courtesy of Iqbal Ike K. Ahmed, MD, FRCSC)

Figure 4. In this eye with a dense cataract, an inferior iris coloboma, zonular weakness, and a white-to-white diameter of 9 mm, the surgeon has used trypan blue to stain the anterior capsule. Iris retractors support the edge of the capsulorhexis in an area of known zonular weakness. At bottom right, the site of a pars plana vitreous tap is visible. A CTR was injected into the capsular bag after cortical viscodissection (not visible in image) (A). After successful cataract extraction and IOL implantation, two relaxing incisions are visible on both sides of the colobomatous defect, here created with a horizontal microscissors (MicroSurgical Technology) (B). After apposition of the defect's margins with a 10-0 polypropylene suture, the round shape and central position of the pupil have been restored (C).

both sides in the inferior midperiphery to allow the iris to relax superiorly so that, when the margins of the defect are apposed, the pupil will be centered properly (Figure 4B). This technique provides a superior cosmetic outcome and places the pupil in greater alignment with the corneal center (Figure 4C).

DEVESH K. VARMA, MD, FRCSC, AND IQBAL IKE K. AHMED, MD, FRCSC

The more recent progression of visual loss is likely caused by a cataract. There may, however, be reduced vision at baseline from an underlying compromise of the optic nerve and retina as well as dyscoria from the extensive coloboma. Lenticular astigmatism from subluxation of the crystalline lens can also be a factor when colobomata involve the zonules, although the absence of phacodonesis suggests this may be less of an issue here. Testing with a potential acuity meter (Marco, Jacksonville, FL) can be helpful for patients contemplating the risks and benefits of pursuing surgery in such cases. Most likely, this patient's precataract visual acuity could be restored by cataract surgery. Combining the procedure with pupilloplasty could simultaneously address any photophobia and cosmetic concerns.

Preparation for cataract surgery in this case requires extra care. Like many colobomatous eyes, this one may be microphthalmic with a disproportionately small anterior segment (relative anterior microphthalmos). This anatomy has implications for the IOL power calculation, because the anticipated anterior effective lens position can produce a myopic result. Thus, we often aim for slight hyperopia in these eyes. Microphthalmic eyes are also at risk for intraoperative positive pressure/malignant glaucoma, so we would be prepared to execute a prior pars plana vitreous tap to create adequate working space for cataract sur-

“Zonular loss in colobomata tends to be localized and can typically be managed with a CTR.”

—*Devesh K. Varma, MD, FRCSC, and
Iqbal Ike K. Ahmed, MD, FRCSC*

gery. Furthermore, because phacoemulsification in a shallow anterior chamber can place additional stress on endothelial cells, a preoperative specular microscopy study would be helpful for planning. Determining the axial length can be challenging in the presence of irregularities in the posterior pole, and we recommend optical biometry using the IOLMaster (Carl Zeiss Meditec, Inc., Dublin, CA) or Lenstar LS 900 (Haag-Streit USA Inc., Mason OH). Zonular loss in colobomata tends to be localized and can typically be managed with a CTR, usually without the need for a sutured device.

Preparation for the pupilloplasty would involve noting the patient's degree of photophobia, particularly prior to the cataract's progression, which can blunt these symptoms. We would also assess the iris' color, contour, and thickness in both eyes. Finally, we would take the patient's cosmetic goals into consideration. Testing should include slit-lamp photographs, and specular microscopy would once again be helpful, given the additional intraocular manipulation.

We would modify our surgical technique to handle a shallow anterior chamber as previously discussed. If at any time during the surgery the working space in the anterior chamber became problematic, or if there were excessive convexity of the posterior capsule, we would strongly consider a pars plana limited anterior vitrectomy to deepen the anterior chamber. In microphthalmic eyes, we have found that this positive pressure is often the single biggest

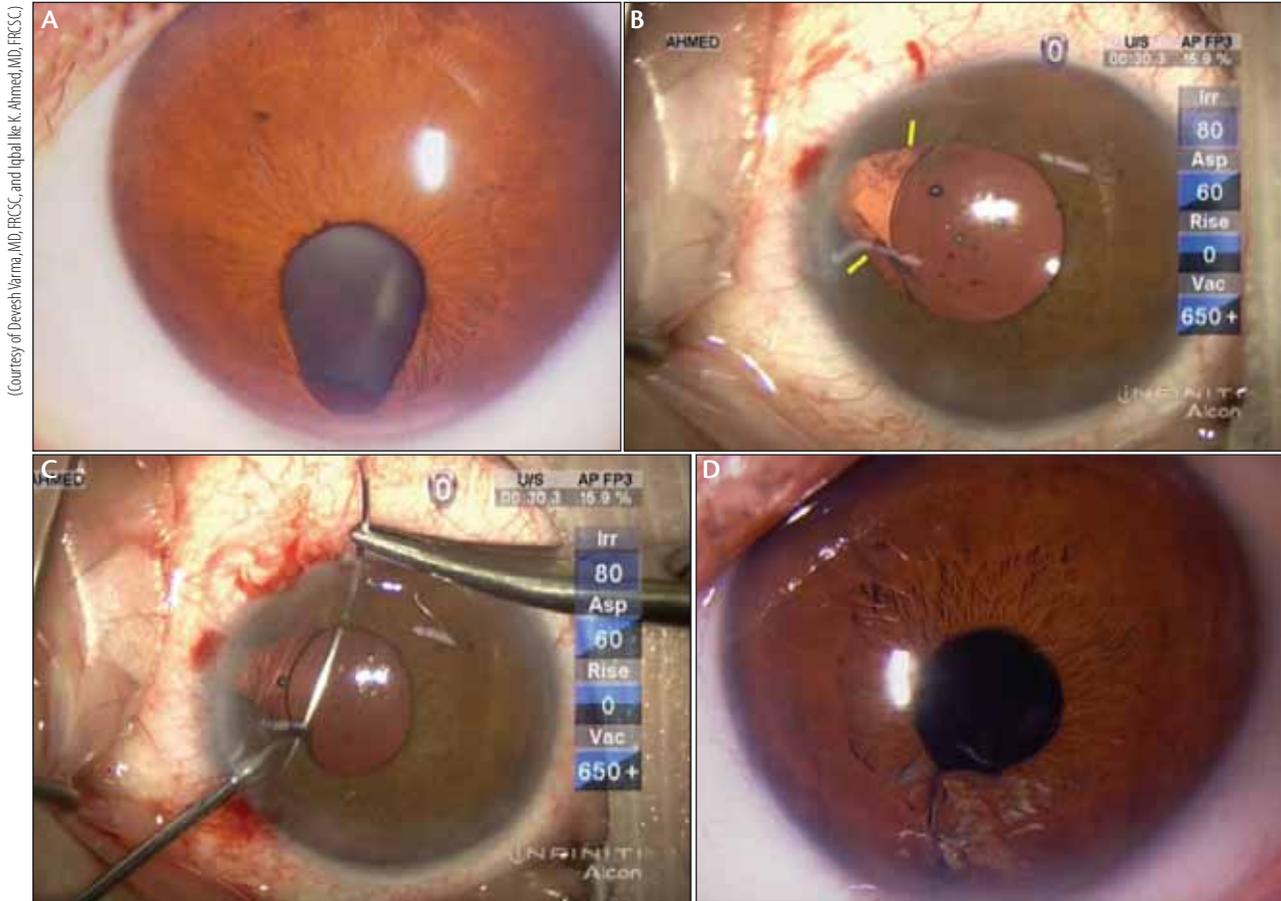


Figure 5. An eye with a cataract and coloboma preoperatively (A). After cataract surgery, the surgeon creates an iris-relaxing incision in preparation for the pupilloplasty (B). A 10–0 Prolene suture is passed through the iris sphincter and tied to generate a 3-mm pupil. (C) The eye’s appearance after cataract surgery and pupilloplasty with relaxing incisions and two interrupted iris sutures (D).

challenge. We would inject a dispersive viscoelastic peripheral to the lens in the area of the coloboma to prevent vitreous prolapse. In anticipation of some (usually mild) zonular laxity, we would then cautiously create the capsulorhexis. Keeping in mind that the lens and capsular bag might be smaller than average, it would be important to maintain an anterior capsular rim of at least 2 mm to provide adequate coverage of a CTR and IOL.

At this point, viscodissection followed by early insertion of the CTR could help prevent vitreous prolapse by expanding the capsular equator over the zonular defect, avoid fluid misdirection syndrome, stabilize the capsular bag for nuclear removal, and keep the capsule in a more posterior position to counteract its tendency toward anterior displacement in a microphthalmic eye. If the zonular defect were large enough, one or two iris/capsular retractors could be placed on the capsulorhexis’ rim in the area of dialysis for intraoperative support. We would remove the nucleus and cortex while minimizing zonular

stress. When changing instruments, we would use a viscoelastic or balanced salt solution to maintain the anterior chamber in an effort to prevent intraoperative malignant glaucoma or vitreous migration through the zonular coloboma. At no time should the anterior chamber be allowed to shallow for the aforementioned reasons.

After inserting the IOL, we would leave viscoelastic in the eye and create paracentesis incisions at the 4- and 8-o’clock positions in preparation for the pupilloplasty. Using a technique described elsewhere,^{1,2} we would make relaxing incisions followed by two or three interrupted iris sutures using 10–0 Prolene (Ethicon, Inc., Somerville, NJ) to close the coloboma and create a 3-mm round pupil (Figure 5). We prefer to use microinstrumentation such as micrograspers and microtying forceps (MicroSurgical Technology, Redmond, WA) to manipulate and suture the iris in a controlled, closed-system environment. Relaxing microsphincterotomies are important to prevent an excessively inferiorly positioned aperture after pupilloplasty. The viscoelastic

Vigamox®

(moxifloxacin hydrochloride ophthalmic solution) 0.5% as base

DESCRIPTION: VIGAMOX® (moxifloxacin HCl ophthalmic solution) 0.5% is a sterile ophthalmic solution. It is an 8-methoxy fluoroquinolone anti-infective for topical ophthalmic use.

CLINICAL PHARMACOLOGY:

Microbiology: The following *in vitro* data are also available, but their clinical significance in ophthalmic infections is unknown. The safety and effectiveness of VIGAMOX® solution in treating ophthalmological infections due to these microorganisms have not been established in adequate and well-controlled trials.

The following organisms are considered susceptible when evaluated using systemic breakpoints. However, a correlation between the *in vitro* systemic breakpoint and ophthalmological efficacy has not been established. The list of organisms is provided as guidance only in assessing the potential treatment of conjunctival infections. Moxifloxacin exhibits *in vitro* minimal inhibitory concentrations (MICs) of 2 µg/ml or less (systemic susceptible breakpoint) against most (≥ 90%) strains of the following ocular pathogens.

Aerobic Gram-positive microorganisms:

Listeria monocytogenes
Streptococcus mitis
Staphylococcus saprophyticus
Streptococcus pyogenes
Streptococcus agalactiae
Streptococcus Group C, G and F

Aerobic Gram-negative microorganisms:

Acinetobacter baumannii *Klebsiella pneumoniae*
Acinetobacter calcoaceticus *Moraxella catarrhalis*
Citrobacter freundii *Morganella morganii*
Citrobacter koseri *Neisseria gonorrhoeae*
Enterobacter aerogenes *Proteus mirabilis*
Enterobacter cloacae *Proteus vulgaris*
Escherichia coli *Pseudomonas stutzeri*
Klebsiella oxytoca

Anaerobic microorganisms:

Clostridium perfringens *Prevotella species*
Fusobacterium species *Propionibacterium acnes*

Other microorganisms:

Chlamydia pneumoniae *Mycobacterium marinum*
Legionella pneumophila *Mycoplasma pneumoniae*
Mycobacterium avium

Clinical Studies:

In two randomized, double-masked, multicenter, controlled clinical trials in which patients were dosed 3 times a day for 4 days, VIGAMOX® solution produced clinical cures on day 5-6 in 66% to 69% of patients treated for bacterial conjunctivitis. Microbiological success rates for the eradication of the baseline pathogens ranged from 84% to 94%. Please note that microbiologic eradication does not always correlate with clinical outcome in anti-infective trials.

INDICATIONS AND USAGE: VIGAMOX® solution is indicated for the treatment of bacterial conjunctivitis caused by susceptible strains of the following organisms:

Aerobic Gram-positive microorganisms:

*Corynebacterium species** *Staphylococcus hominis*
*Micrococcus luteus** *Staphylococcus warneri**
Staphylococcus aureus *Streptococcus pneumoniae*
Staphylococcus epidermidis *Streptococcus viridans* group
Staphylococcus haemolyticus

Aerobic Gram-negative microorganisms:

*Acinetobacter Iwoffi** *Haemophilus parainfluenzae**
Haemophilus influenzae

Other microorganisms:

Chlamydia trachomatis

*Efficacy for this organism was studied in fewer than 10 infections.

CONTRAINDICATIONS: VIGAMOX® solution is contraindicated in patients with a history of hypersensitivity to moxifloxacin, to other quinolones, or to any of the components in this medication.

WARNINGS:

NOT FOR INJECTION.

VIGAMOX® solution should not be injected subconjunctivally, nor should it be introduced directly into the anterior chamber of the eye.

In patients receiving systemically administered quinolones, including moxifloxacin, serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported, some following the first dose. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, angioedema (including laryngeal, pharyngeal or facial edema), airway obstruction, dyspnea, urticaria, and itching. If an allergic reaction to moxifloxacin occurs, discontinue use of the drug. Serious acute hypersensitivity reactions may require immediate emergency treatment. Oxygen and airway management should be administered as clinically indicated.

PRECAUTIONS:

General: As with other anti-infectives, prolonged use may result in overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, discontinue use and institute alternative therapy. Whenever clinical judgment dictates, the patient should be examined with the aid of magnification, such as slit-lamp biomicroscopy, and, where appropriate, fluorescein staining. Patients should be advised not to wear contact lenses if they have signs and symptoms of bacterial conjunctivitis.

Information for Patients: Avoid contaminating the applicator tip with material from the eye, fingers or other source.

Systemically administered quinolones including moxifloxacin have been associated with hypersensitivity reactions, even following a single dose. Discontinue use immediately and contact your physician at the first sign of a rash or allergic reaction.

Drug Interactions: Drug-drug interaction studies have not been conducted with VIGAMOX® solution. *In vitro* studies indicate that moxifloxacin does not inhibit CYP3A4, CYP2D6, CYP2C9, CYP2C19, or CYP1A2 indicating that moxifloxacin is unlikely to alter the pharmacokinetics of drugs metabolized by these cytochrome P450 isozymes.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long term studies in animals to determine the carcinogenic potential of moxifloxacin have not been performed. However, in an accelerated study with initiators and promoters, moxifloxacin was not carcinogenic in rats following up to 38 weeks of oral dosing at 500 mg/kg/day (approximately 21,700 times the highest recommended total daily human ophthalmic dose for a 50 kg person, on a mg/kg basis).

Moxifloxacin was not mutagenic in four bacterial strains used in the Ames *Salmonella* reversion assay. As with other quinolones, the positive response observed with moxifloxacin in strain TA 102 using the same assay may be due to the inhibition of DNA gyrase. Moxifloxacin was not mutagenic in the CHO/HGPRT mammalian cell gene mutation assay. An equivocal result was obtained in the same assay when v79 cells were used. Moxifloxacin was clastogenic in the v79 chromosome aberration assay, but it did not induce unscheduled DNA synthesis in cultured rat hepatocytes. There was no evidence of genotoxicity *in vivo* in a micronucleus test or a dominant lethal test in mice.

Moxifloxacin had no effect on fertility in male and female rats at oral doses as high as 500 mg/kg/day, approximately 21,700 times the highest recommended total daily human ophthalmic dose. At 500 mg/kg orally there were slight effects on sperm morphology (head-tail separation) in male rats and on the estrous cycle in female rats.

Pregnancy: Teratogenic Effects.

Pregnancy Category C: Moxifloxacin was not teratogenic when administered to pregnant rats during organogenesis at oral doses as high as 500 mg/kg/day (approximately 21,700 times the highest recommended total daily human ophthalmic dose); however, decreased fetal body weights and slightly delayed fetal skeletal development were observed. There was no evidence of teratogenicity when pregnant Cynomolgus monkeys were given oral doses as high as 100 mg/kg/day (approximately 4,300 times the highest recommended total daily human ophthalmic dose). An increased incidence of smaller fetuses was observed at 100 mg/kg/day.

Since there are no adequate and well-controlled studies in pregnant women, VIGAMOX® solution should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: Moxifloxacin has not been measured in human milk, although it can be presumed to be excreted in human milk. Caution should be exercised when VIGAMOX® solution is administered to a nursing mother.

Pediatric Use: The safety and effectiveness of VIGAMOX® solution in infants below 1 year of age have not been established.

There is no evidence that the ophthalmic administration of VIGAMOX® solution has any effect on weight bearing joints, even though oral administration of some quinolones has been shown to cause arthropathy in immature animals.

Geriatric Use: No overall differences in safety and effectiveness have been observed between elderly and younger patients.

ADVERSE REACTIONS:

The most frequently reported ocular adverse events were conjunctivitis, decreased visual acuity, dry eye, keratitis, ocular discomfort, ocular hyperemia, ocular pain, ocular pruritus, subconjunctival hemorrhage, and tearing. These events occurred in approximately 1-6% of patients.

Nonocular adverse events reported at a rate of 1-4% were fever, increased cough, infection, otitis media, pharyngitis, rash, and rhinitis.

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References:

- Kowalski RP, Yates KA, Romanowski EG, et al. An ophthalmologist's guide to understanding antibiotic susceptibility and minimum inhibitory concentration data. *Ophthalmology*. 2005;112:1987-1991.
- VIGAMOX® solution prescribing information.
- Walters Kluwer Health, Source® Pharmaceutical Audit Suite, January 2008-December 2008.
- Wagner RS, Abelson MB, Shapiro A, Torkildsen G. Evaluation of moxifloxacin, ciprofloxacin, gatifloxacin, ofloxacin, and levofloxacin concentrations in human conjunctival tissue. *Arch Ophthalmol*. 2005;123:1282-1283.

CATARACT SURGERY COMPLEX CASE MANAGEMENT

could be removed using an atraumatic dry aspiration technique, again while preventing the anterior chamber from becoming shallow by exchanging it for balanced salt solution in multiple aliquots.

Postoperatively, we would recommend an extended course of topical nonsteroidal anti-inflammatory drugs to prevent cystoid macular edema. ■

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- Gagne S, Ahmed IA. Anterior segment surgery:iris repair. *Contemporary Ophthalmology*. 2009;8(22):1-8.
- Cionni RJ, Karatza EC, Osher RH, Shah M. Surgical technique for congenital iris coloboma repair. *J Cataract Refract Surg*. 2006;32(11):1913-1916.

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